el BISTURÍ

MARZO 2013

LA REVISTA OFICIAL DEL COLEGIO DE MÉDICOS CIRUJANOS DE PUERTO RICO

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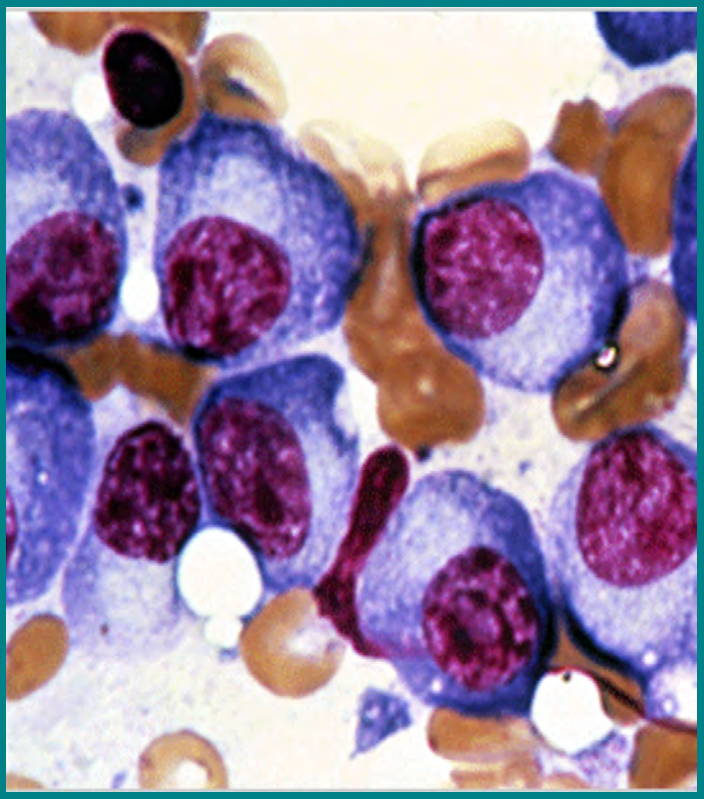

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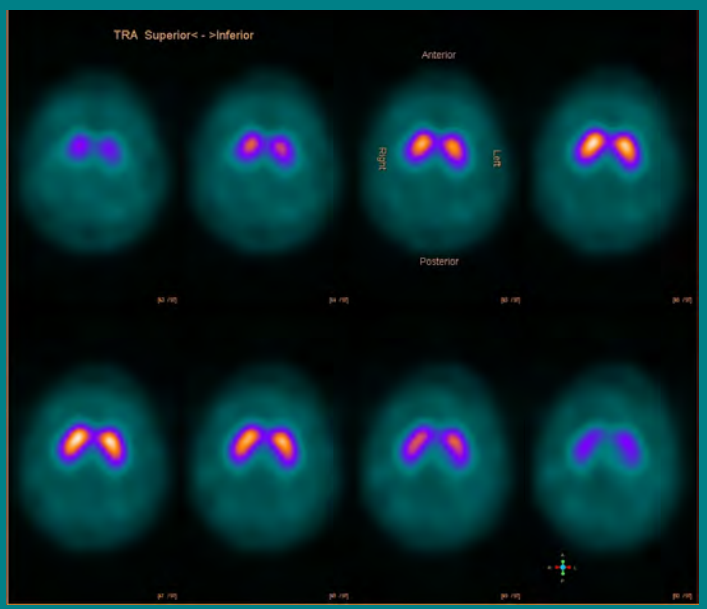

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NOTAS *del Presidente*

Eduardo Ibarra Ortega, MD

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Estimados colegas:

El Colegio de Médicos-Cirujanos de Puerto Rico en forma constante e ininterrumpida ha llevado una campaña para lograr equidad hacia los pagos que se les realizan a nuestros profesionales, esa campaña tiene necesariamente unas limitaciones ya que estamos sujetos a la leyes anti monopolísticas federales y aún de las propias puertorriqueñas.

Muchos de nuestros colegiados constantemente nos preguntan: ¿Qué ha hecho el Colegio por mí en cuanto a los pagos que recibimos por las empresas intermediarias? Nosotros estamos limitados en este sentido a denunciar públicamente que las cantidades que se le pagan a nuestros profesionales son sin duda alguna injustas y son en gran parte la causa de que muchos de los médicos hayan decidido abandonar la isla. Nosotros estamos cónsonos con que se ha llegado a situaciones de verdadero abuso y menosprecio por la clase médica, pero queremos recordarles que más allá de hacer públicas estas denuncias el Colegio no tiene la potestad legal de intervenir directamente en relaciones contractuales o de agrupar a la clase médica para de esa forma darle fin a dichos abusos.

Como hemos dicho en múltiples ocasiones, corresponde al poder político del Estado ponerle coto a las cantidades que las organizaciones intermediarias pueden obtener en el sistema actual de salud de Puerto Rico. Desde luego, todo lo anterior sería subsanado si existiese un Sistema Universal de Salud en Puerto Rico el cual cubriera en forma equilibrada y razonable los pagos a todos los profesionales de la salud, incluidos nuestros médicos.

Seguiremos luchando infatigablemente en defensa de la clase médica y queremos invitarles a todos a que nos manifiesten de qué forma podemos colaborar para lograr justicia y equidad.

Respetuosamente,

Eduardo Ibarra Ortega, MD
Presidente
Colegio de Médicos Cirujanos de Puerto Rico

NOTAS *del Editor*

El Bisturí

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Colegiada / Colegiado:

Te presentamos la quinta edición de El Bisturí, la revista oficial del Colegio de Médicos Cirujanos de Puerto Rico. La forma impresa de una revista, versus la forma digital, es preferida por la mayor parte del público, no solo porque su lectura es más cómoda a la vista sino también es mejor para transportarla, archivarla e incluso coleccionarla. Además, hay un grupo que aún no tienen o no acceden al internet. De lo anterior se desprende la importancia que tiene para toda la matrícula del Colegio esta publicación.

En este número encontrarán artículos médicos sobre Mieloma Múltiple, Manejo de Fallo Cardiaco, Medicina Nuclear en el Diagnóstico de Parkinson, "Gender Differences in the Use of Thrombolytic Therapy for Acute Stroke in a Hispanic Population y "Peripartum Cardiomyopathy: Current Trends, Interdisciplinary Insights, and Future Directions"entre otros. Son artículos bien documentados y todos has sido revisados por sus pares. También, encontrarán un conjunto de resúmenes de casos presentados oralmente y en pósters o afiches durante reunión del "American College of Physicians"(ACP), Capítulo de Puerto Rico, celebrada en octubre de 2012 en San Juan.

Vaya nuestro agradecimiento a todos los autores de artículos, así como también a los directores locales del ACP por sus colaboraciones para con esta edición. Muchas gracias y disfruten la revista.

Carlos A. Falcón, MD
Presidente, Junta Editora

Gender Differences in the Use of Thrombolytic Therapy for Acute Ischemic Stroke in a Hispanic Population: The Puerto Rico Stroke Registry

Juan C. Zevallos, MD[1], Edilberto R. Alvarez[1], Isaac Truelson[1], Sara Attia[1], Juan M. Acuña MD, MSc[1], Juan M. Lozano MD, MSc[1], Grettel Castro, MPH[1], Pura Rodríguez de la Vega, MPH[1], Juan A. González, MD[2], Abiezer Rodríguez, MD[2], Fernando Santiago, MD[2], Ulises Nobo[3], Luis R. Pericchi, PhD[4], Jorge Yarzebski, MD, MPH[5], Rafael Rodríguez - Mercado, MD[2]

RESUMEN

Antecedentes: El uso del r-tPA (recombinant tissue plasminogen activator) para el tratamiento del ataque cerebral isquémico es desproporcionadamente menor en mujeres que en hombres. Datos actualizados son aún más escasos acerca de si existe o no diferencia en el tratamiento de ataques cerebrales isquémicos en poblaciones hispanas.

Objetivo: Examinar si existen diferencias de género en el uso de r-tPA en pacientes puertorriqueños con un ataque cerebral isquémico inicial.

Diseño, Pacientes y Localidad: A través de un diseño prospectivo no-concurrente examinamos a 1,950 pacientes hispanos que fueron hospitalizados en 21 centros médicos localizados en Puerto Rico durante tres años de estudio: 2007, 2009 y 2011.

Medida de Resultado Principal: Tasas de utilización de r-tPA en pacientes con ataque cerebral isquémico.

Resultados: Un total de 1017 mujeres y 933 hombres fueron hospitalizados con un ataque cerebral isquémico. En comparación con los hombres, la proporción de mujeres que recibieron r-tPA fue significativamente más baja (6,9% vs. 3,9%; p=0.004, respectivamente). Las mujeres tuvieron menos probabilidades de recibir r-tPA durante un ataque cerebral isquémico agudo (OR= 0.43, 95% CI= 0.26–0.72; p= 0.001).

Conclusión: Nuestros hallazgos indican que las tasas de uso de r-tPA para ataque cerebral isquémico agudo en Puerto Rico son bajas, de manera particular en mujeres. Las investigaciones futuras deberían enfocarse en disminuir la magnitud de las disparidades de género en el manejo de pacientes hospitalizados con ataque cerebral isquémico, y en determinar las causas para el bajo uso de r-tPA en Puerto Rico.

SUMMARY

Background: The use of recombinant tissue plasminogen activator (r-tPA) for the treatment of acute ischemic stroke is disproportionally lower in women in comparison with men. Currently, there is limited contemporary data in Hispanic populations on whether or not a gender difference in the treatment of acute ischemic stroke exists.

Objective: To examine gender differences in the use of r-tPA in patients with an incident (de novo) acute ischemic stroke.

Design, Patients and Setting: We conducted a non-concurrent prospective study, and our study population comprised 1,950 Hispanic patients admitted with incident acute ischemic stroke in 21 hospitals located in Puerto Rico during three one-year periods between 2007, 2009, and 2011.

Main Outcome Measure: Rates of utilization of r-tPA in patients with acute ischemic stroke.

Results: A total of 1,017 women and 933 men were hospitalized with acute ischemic stroke. Compared to men, the proportion of women receiving r-tPA was significantly lower (6.9% vs. 3.9%; p=0.004, respectively). Women were less likely to receive r-tPA during an acute ischemic stroke (OR= 0.43, 95% CI= 0.26–0.72; p= 0.001).

Conclusion: Our findings indicate low rates of r-tPA use for acute ischemic stroke in Puerto Rico, particularly among women. Future research should focus on reducing gender disparities in the management of patients hospitalized with acute ischemic stroke, and to determine the reasons for the low rate of r-tPA use in Puerto Rico.

Keywords: gender, thrombolytic therapy, r-tPA, ischemic stroke

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INTRODUCTION

In the United States, stroke is the fourth leading cause of death and a main cause of disability [1, 2]. Of all deaths due to stroke in the United States, women make up 60% of the total [2]. Interestingly, women are also more likely to suffer disability following strokes than men [2]. The published scientific literature suggests that this difference may be because women tend to be four to five years older than men when they have a first stroke [2].

Ischemic strokes are the most common type of stroke and comprise 87% of all strokes in the United States[2]. Thrombolytic therapy given as recombinant tissue plasminogen activator (r-tPA) has been established as a treatment modality for acute ischemic stroke, and according to current guidelines from the American Stroke Association and American Heart Association, patients with an acute ischemic stroke who are eligible for intravenous r-tPA should be treated within 3 hours from the onset of stroke symptoms [3]. Overall, only 3% to 4% of patients with acute ischemic strokes in the United States receive r-tPA[4]. This low percentage is somewhat accounted for by the fact that only 11.5% of stroke patients arriving to emergency rooms are eligible for r-tPA[5]. However, Rudd et al. importantly noted that the minority of men and women eligible for r-tPA actually receive thrombolysis[6]. Nevertheless, the question that remains after prior investigations is whether a difference exists in the frequency of thrombolysis administration between genders.

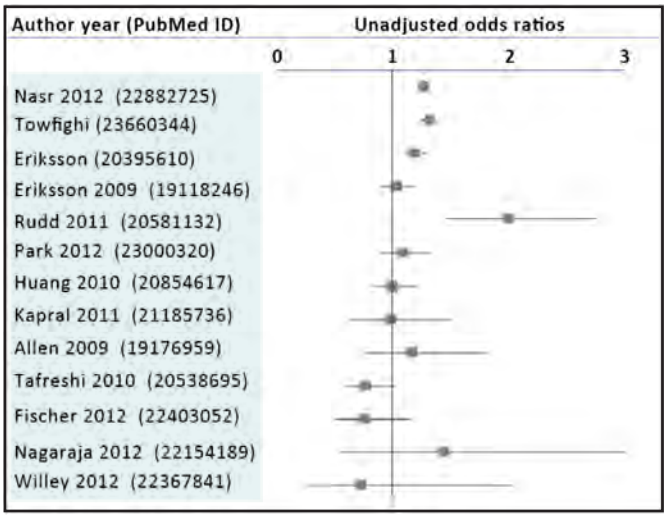
In a 2009 meta-analysis, Reeves et al. found that women were less likely to receive r-tPA compared to men, with an unadjusted odds ratio (OR)= 0.70 (95% CI= 0.55–0.88) [4]. We looked at articles published on this topic since the publication of this meta-analysis and found varied evidence of gender disparities in several populations and geographic regions (Figure 1). However, this topic was not adequately addressed among Hispanics, which currently constitute the largest minority in the United States [7].

The purpose of this study was to determine whether a difference exists between the frequencies of thrombolytic treatment administered to men compared to women hospitalized with incident acute ischemic strokes in Puerto Rico.

METHODS

Study Population and Data Collection: We conducted a secondary analysis of data in order to investigate gender differences in the administration of r-tPA in Hispanic

Figure 1. Summary of studies published since 2009 relating the odds of men to receive r-tPA as compared to women during an acute ischemic stroke. Bar indicates 95% confidence interval



patients hospitalized with ischemic stroke. This study is part of a non-concurrent prospective study, the Puerto Rico Cardiovascular Surveillance Study, which is examining long-term trends in the descriptive epidemiology of stroke in Puerto Rican residents hospitalized with acute ischemic stroke in 2007, 2009, and 2011[8]. Hispanic patients diagnosed with incident acute ischemic stroke at 21 academic and / or non-teaching medical and nonmilitary centers with emergency room capability comprised the study population. Trained nurse and physician abstractors initially reviewed the medical records of patients hospitalized with cerebrovascular disease; International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes 430 to 438 from participating hospitals. For the purpose of this study, an encrypted online database was created with only validated cases of acute ischemic stroke (ICD-9-CM codes 434.00 – 434.91; and 436) with radiologist interpretations of CT/MRI imaging at admission. A random sample of 10% of medical charts was reviewed to perform an audit on possible cases of acute ischemic stroke that were not the primary diagnosis. Since this study focused on patients with de novo acute ischemic stroke, only patients with no history of stroke were included. Patients with a diagnosis of transient ischemic attack (TIA) (ICD-9 CM code 435) were excluded. Patients who were initially admitted to the emergency department and stabilized in one hospital and then transferred to another hospital were only counted once.

Variables: The following variables were selected based on contents of the database, clinical relevance, and the body of existing literature. Demographics: age, gender, and marital status. Anthropometrics: Body Mass Index (BMI).

Comorbidities: current smoking status, history of atrial fibrillation, LDL-Cholesterol (grouped by less than or greater than 100 mg/dL), and history of hypertension and diabetes mellitus. Hospital clinical practices: antiplatelets (aspirin, dipyridamole, clopidogrel, and combined aspirin+dipyridamole) administered at any time during hospitalization, and thrombolysis administered less than 3 hours of symptoms onset.

Mortality: vital status at discharge.

Data Analysis: IBM SPSS Statistics for Windows (Version 20.0, IBM Corp: Armonk, NY) and PSPP (Version 0.7.10-g330012) software were used to perform data analyses. Descriptive analysis was initially carried out to calculate gender-specific means and frequency distributions of patient's demographic and clinical characteristics. The gender groups were compared to each selected variable in order to describe proportions and means between men and women. Pearson's X^2 test was utilized for discrete variables and unpaired t-tests were used for continuous variables comparison. A p-value of less than 0.05 was established as the level for statistical significance. Within each gender group, the process was repeated to each variable of interest comparing the group receiving r-tPA vs. the group not receiving r-tPA. In addition, we conducted collinearity test to rule out multicollinearity between the predictors of the model. Finally, a multivariable logistic regression modeling was performed to control for potential confounders and effect modifiers; the model also checked for interactions that could have influenced the association between gender and r-tPA administration.

Table 1. Characteristics of patients with incident acute ischemic strokes in the Puerto Rico Stroke Registry (2007, 2009, and 2011), according to gender.

Characteristic N (%)	Females 1,017 (52.2%)	Males 933 (47.8%)	P-value (2-tailed)[a]
Demographics			
Age (years), mean ± SD	73.2 ± 13.4	68.6 ± 13.1	<0.001[b]
Age subgroup (years)			<0.001
<55	101 (9.9)	126 (13.5)	
55-64	139 (13.7)	223 (23.9)	
65-74	269 (26.5)	261 (28.0)	
75-84	298 (29.3)	217 (23.3)	
>84	210 (20.7)	106 (11.4)	
Married	425 (44.0)	645 (71.7)	<0.001
Anthropometrics			
BMI, mean ± SD	25.9 ± 6.3	28.3 ± 5.6	<0.001[b]
Comorbidities			
Current smoker status	54 (5.8)	113 (13.4)	<0.001
Atrial Fibrillation	68 (7.9)	62 (7.9)	0.99
LDL-Cholesterol (>100 mg/dL)	255 (65.7)	234 (57.5)	0.018
Hypertension	834 (89.1)	733 (85.0)	0.01
Diabetes mellitus	497 (56.0)	440 (54.8)	0.61
Prescribed Medication			
Aspirin at any time of hospitalization	440 (43.3)	488 (52.3)	<0.001
Antiplatelet[c] at any time of hospitalization	799 (78.6)	748 (80.2)	0.401
Thrombolysis	40 (3.9)	64 (6.9)	0.004
Died before discharge	54 (5.3)	31 (3.3)	0.032

[a] Pearson's χ^2.
[b] Unpaired sample t-tests without assuming equal variances were performed for age and BMI.
[c] Antiplatelets prescribed prior to or during hospitalization which included aspirin, dipyridamole, clopidogrel, and dipyridamole/aspirin.

RESULTS

A total of 1,950 Hispanic patients (52% women) were hospitalized with incident acute ischemic strokes at 21 study medical centers located in Puerto Rico.

CHARACTERISTICS OF PATIENTS ACCORDING TO GENDER

As shown in Table 1, women were older and had higher proportions of LDL-Cholesterol levels > 100 mg/dL, history of hypertension, and deaths during hospitalization than men. In comparison with women, a higher proportion of men were overweight, married and currently smoke.

HOSPITAL TREATMENT PRACTICES

Overall, the proportion of hospitalized women receiving r-tPA during an incident acute ischemic stroke was significantly lower than their counterparts (3.9% vs. 6.9%, respectively; p=0.004). Bivariate, unadjusted analyses revealed that women were less likely than men to receive treatment with r-tPA (OR= 0.56, 95% CI= 0.37–0.83; p<0.05). After adjustment for potential confounders, the odds of women to receive r-tPA during an acute ischemic stroke decreased by 23% as compared to men (OR= 0.43, 95% CI= 0.26–0.72; p=0.001). Indeed, the only characteristic found to be statistically significant among those who received r-tPA vs. those who did not receive r-tPA during an acute ischemic stroke was gender (Table 2).

Table 2. Association of r-tPA administration and selected characteristics of patients with incident acute ischemic stroke.

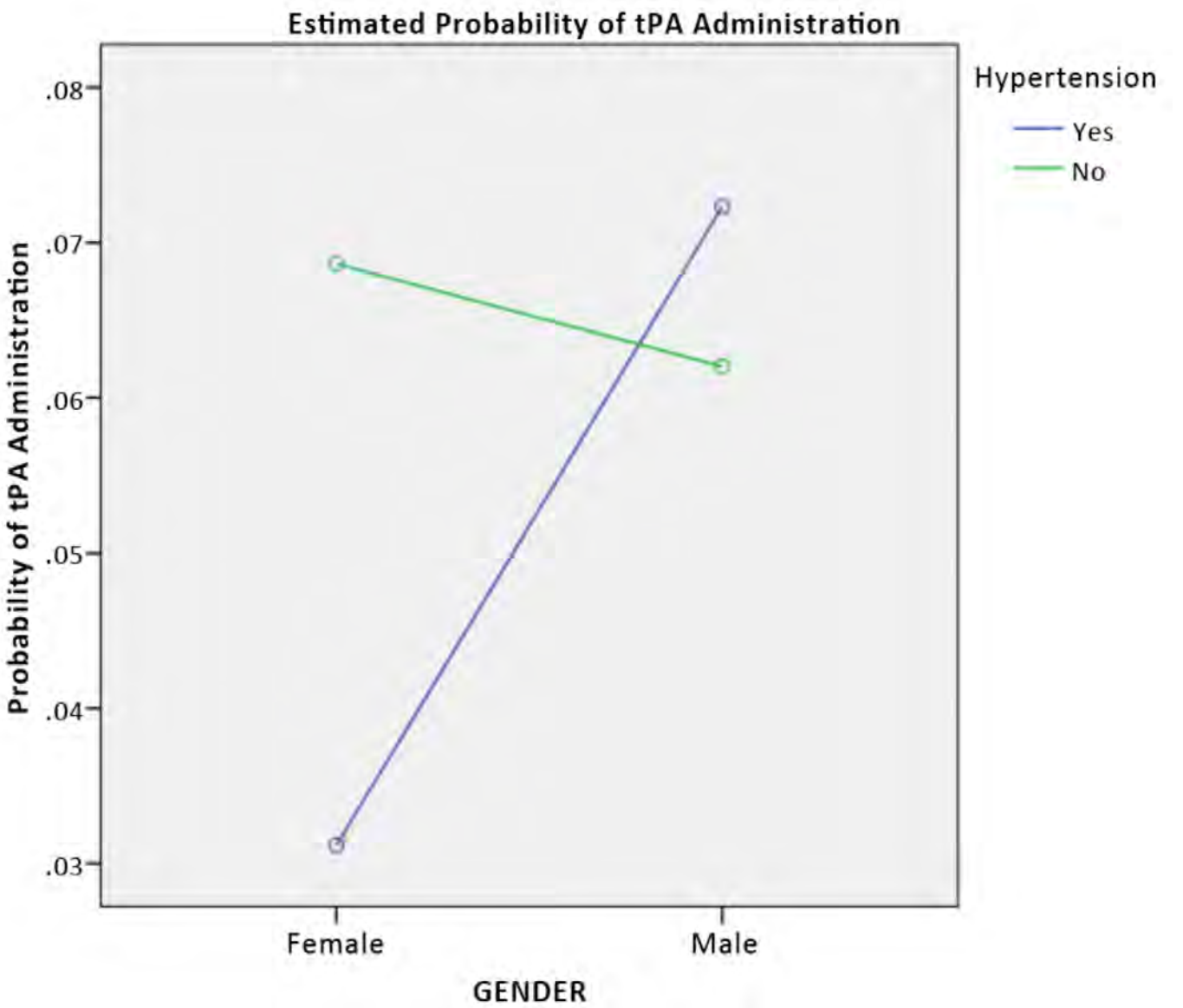
Characteristic N (%)	r-tPA Not-Administered 1,846 (94.7)	r-tPA Administered 104 (5.3)	P-value (2-tailed)[a]
Demographics			
Gender			0.004
Female	977 (52.9)	40 (38.5)	
Male	869 (47.1)	64 (61.5)	
Age (years) mean ± SD	71.0 ± 13.3	72.0 ± 16.1	0.73[a]
Age Group (years)			0.49
<55	214 (11.6)	13 (12.5)	
55-64	347 (18.8)	15 (14.4)	
65-74	498 (27)	32 (30.8)	
75-84	492 (26.7)	23 (22.1)	
>84	295 (16)	21 (20.2)	
Married	1013 (57.4)	57 (57.6)	0.97
Anthropometrics			
BMI, kg/m^2, mean ± SD	27.1 ± 6.1	26.9 ± 5.9	0.78[a]
Comorbidities			
Current smoker	156 (9.3)	11 (11.6)	0.46
Atrial fibrillation	124 (8.0)	6 (7.1)	0.79
LDL (>100 mg/dL)	467 (37.7)	22 (51.1)	0.07
Hyperlipidemia	492 (31.2)	26 (29.6)	0.75
Hypertension	1488 (87.3)	79 (84.0)	0.36
Diabetes mellitus	891 (55.5)	46 (54.4)	0.80
Aspirin administered at any time of hospitalization	871 (47.2)	57 (54.8)	0.130
Antiplatelet[c] at any time of hospitalization	1,465 (79.4)	82 (78.9)	0.900
Died before discharge	80 (4.3)	5 (4.8)	0.818

[a] Pearson's χ^2.
[b] Unpaired sample t-tests without assuming equal variances were performed for age and BMI.
[c] Antiplatelets given prior to or during hospitalization which included aspirin, dipyridamole, clopidogrel, and aspirin+dipyridamole.

CHARACTERISTICS ASSOCIATED WITH RECEIPT OF THROMBOLYTIC THERAPY

Several effect modifiers were identified during the analysis including age sub-group, marital status, current smoking status, diagnosis of hypertension or atrial fibrillation, being prescribed clopidogrel prior to the hospitalization, or being prescribed antiplatelets (aspirin, dipyridamole, clopidogrel, and aspirin+dipyridamole) during hospitalization. Among patients who were treated with r-TPA a significant interaction was found between gender and hypertension. Adjusting for the interaction, the term of gender-hypertension decreased the odds of receiving r-tPA (adjusted OR= 0.23, 95% CI= 0.07-0.77) with a complete shift of significance away from gender alone. Shows an interesting effect modification by hypertension on the relationship between gender and r-tPA use (Figure 2).

Figure 2. Interaction between gender and hypertension with respect to administration of r-tPA



DISCUSSION

Our study included population-based data over a span of five years about the treatment of acute ischemic stroke in Puerto Ricans, a mostly Hispanic population that has not been previously well-studied in this regard. Overall, the proportion of Puerto Rican patients hospitalized with an acute ischemic stroke who received r-tPA was only 5.3%; thus indicating low use of the state of the art treatment for acute ischemic stroke. This low proportion of r-tPA use, provided a challenge in isolating relationships during the analysis as there was limited variability within such a small group of the study population. Nevertheless, similar proportions of r-tPA administration during an acute ischemic stroke have been reported elsewhere in studies, including an even lower proportion (3% to 4%) in the United States[4]. Our findings suggest that, among those who received thrombolytic treatment, women had an approximately 60% decreased likelihood of receiving r-tPA as compared to men.

Subsequent investigations in this population-based study should explore the possible determinants (including the extent of delay time between the onset of symptoms, hospital diagnosis and receipt of thrombolytic treatment for an acute ischemic stroke). In addition, an examination of the reasons for gender disparities in the management of acute ischemic stroke in Puerto Rico is guaranteed. By identifying these disparities in a timely manner, physicians may improve patient's outcomes. In addition, it appears that great efforts need to be taken to increase the overall use of r-tPA in Puerto Rico.

After analyzing the effect of other variables on the relationship between gender and r-tPA administration, a significant interaction was found between gender and hypertension. Hypertension seemingly had a disproportionate effect on whether women received r-tPA or not. As shown in Figure 2, hypertensive females had lower probability of receiving r-tPA than non-hypertensive women; whereas male patients showed the opposite pattern. The association between gender and r-tPA did not held statistical significance after adjusting for hypertension status, even though the proportions of patients treated with r-tPA was unbalanced between genders (Table 3). Furthermore, the tendency of hypertensive patients to have hemorrhagic strokes may have influenced the physician's decision to administer r-tPA to patients with hypertension, particularly women. This fact raises several questions about the true association between gender and r-tPA use during acute ischemic stroke, which should be investigated further with respect to hypertension.

Table 3. Unadjusted and adjusted odds ratios for receiving r-tPA.

Variable	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted with interaction OR (95% CI)
Female	0.56 (0.37-0.83)	0.43 (0.26-0.72)	1.46 (0.48-4.39)
Age category			
<55	(Ref)	(Ref)	(Ref)
55-64	0.71 (0.33-1.53)	1.21 (0.47-3.13)	1.24 (0.48-3.22)
65-74	1.06 (0.54-2.06)	1.86 (0.78-4.45)	1.95 (0.81-4.67)
75-84	0.77 (0.38-1.55)	1.41 (0.57-3.51)	1.47 (0.59-3.67)
>84	1.17 (0.57-2.39)	2.11 (0.81-5.51)	2.24 (0.86-5.87)
Hypertension	0.77 (0.43-1.35)	0.84 (0.45-1.56)	1.43 (0.62-3.31)
Current smoker	1.28 (0.67-2.45)	1.50 (0.75-3.01)	1.50 (0.75-3.01)
Atrial fibrillation	0.89 (0.38-2.08)	0.55 (0.20-1.52)	0.54 (0.20-1.49)
Warfarin before hospitalization	1.15 (0.52-2.54)	1.59 (0.65-3.87)	1.59 (0.65-3.86)
Aspirin before hospitalization	1.22 (0.73-2.05)	1.43 (0.81-2.53)	1.46 (0.82-2.57)
Clopidogrel before hospitalization	0.62 (0.35-1.10)	0.64 (0.34-1.23)	0.63 (0.33-1.20)
Married	0.99 (0.66-1.49)	0.99 (0.60-1.64)	0.98 (0.59-1.62)
Gender*Hypertension	--	--	0.23 (0.07-0.77)

This study included a number of limitations. The administration of r-tPA was dependent upon proper application of its lengthy exclusion criteria by clinicians. Given the design of this study, we were unable to determine the number of patients eligible for r-tPA. Additionally, findings from other studies have suggested that the actual rates of r-tPA use are lower according to ICD-9 documentation [9]. The database we used was constructed from medical records, which may have contained incomplete information. Although the database contained a relatively large number of patients, individuals who had an acute ischemic stroke at home or died prior to reaching the hospital were not included in this study.

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DISCLOSURES

None.

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Multiple Myeloma

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RESUMEN

Mieloma múltiple es una malignidad de células plasmáticas en la cual cambios en el microambiente medular y genéticos han contribuido a la transformación de la célula plasmática normal a una maligna. En los últimos años la biología de mieloma múltiple ha sido parcialmente entendida, de tal manera que nos ha dado la oportunidad de manejar esta enfermedad con diferentes modalidades de tratamiento como lo son altas dosis de quimioterapia seguido de transplante autólogo de medula ósea en pacientes menores de 65-70 años, uso de agentes immunomoduladores como talidomida y lenalidomida e inhibidores de proteasomas como bortezomib. Todas estas modalidades de tratamiento han cambiado el manejo de mieloma múltiple en la última década y han contribuido de manera fundamental a una supervivencia mayor, nunca antes vista, de los pacientes con esta enfermedad.

SUMMARY

Multiple myeloma is a plasma cell malignancy in which multistep genetic and microenviromental changes has contributed to the transformation of the plasma cells into a malignant neoplasm. In the last decade the biology of multiple myeloma has been partially unraveled, giving us the opportunity to approach this disease with different therapeutic applications, such as high dose chemotherapy with autologous bone marrow transplantation, the immunomodulatory agents such as thalidomide and lenalidomide and the protaesome inhibitor, bortezomib, that has change the management of multiple myeloma and contributed to an extended overall survival that has not been seen before.

Keywords: serum electrophoresis, m-spike, anemia

INTRODUCTION

Multiple myeloma is a neoplastic plasma cell disorder. Plasma cells are the end-stage development of the B-cell maturation. The stem cells go through different stages of maturation to the pre-B cell, to the B lymphocyte and finally to the plasma cell. The primary function of the plasma cells is the production of antibodies. We have a broad range of different polyclonal immunoglobulin that provides us protection against different antigens. In multiple myeloma you lose that broad polyclonal antibody peak; instead, there is a clonal proliferation of malignant plasma cells in the bone marrow microenvironment, (Fig.1) with a monoclonal protein (M-spike) in the blood and or urine (Fig.2) and organ dysfunction. Myeloma cells, although a malignant cell, continue to produce lots of antibodies, immunoglobulin, heavy chains, and

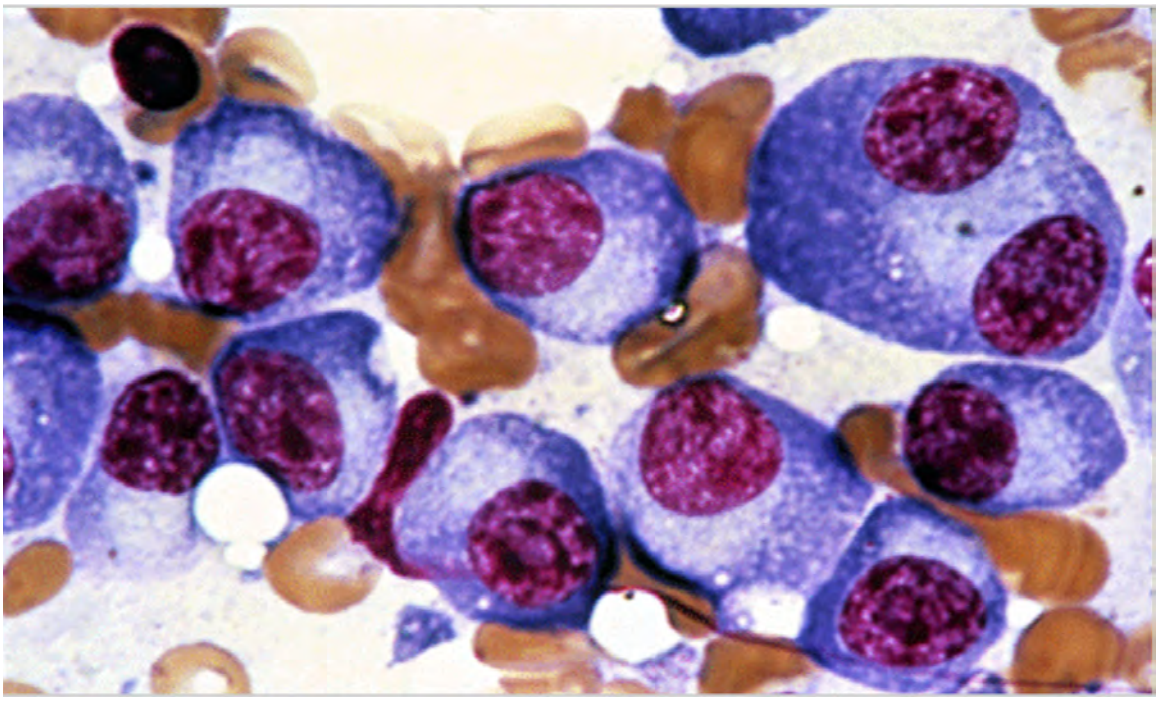
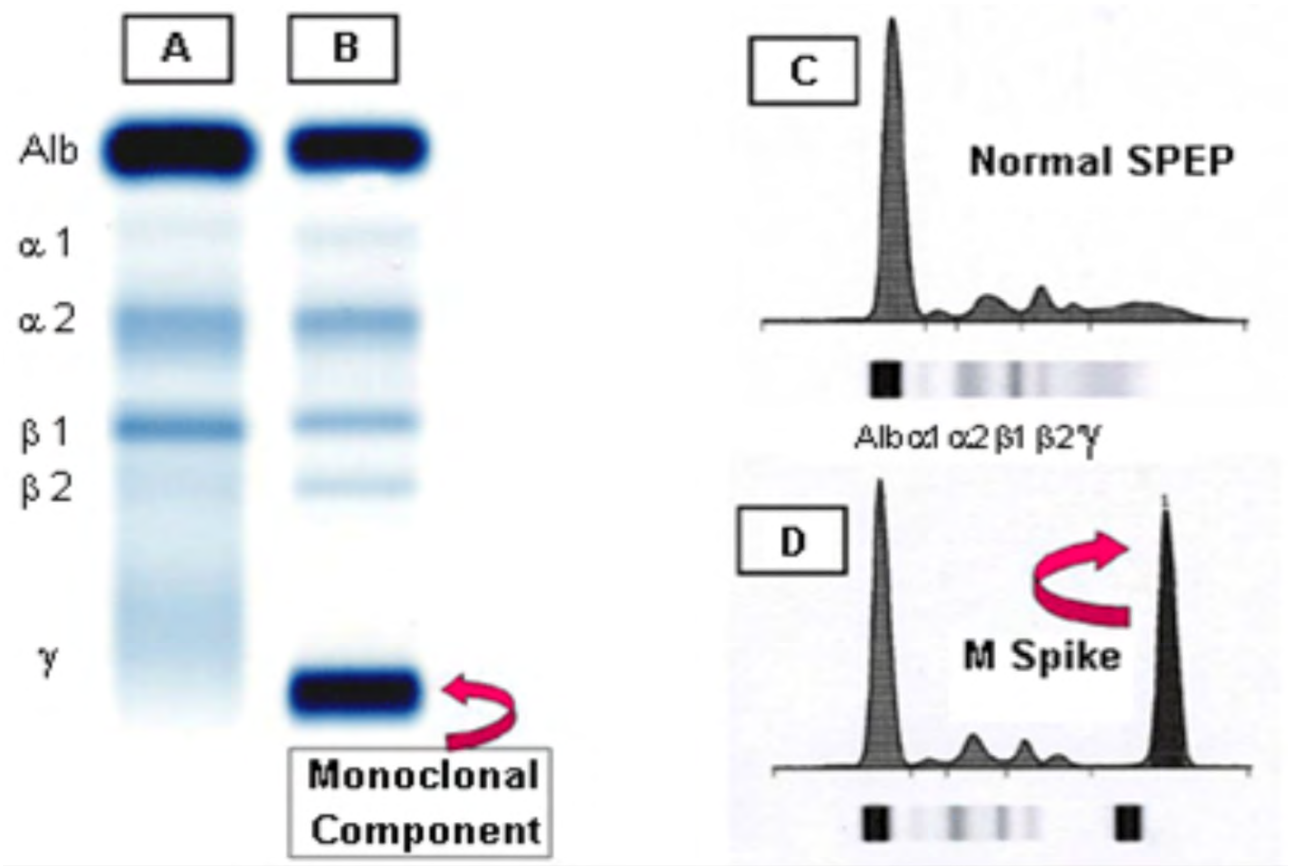


Fig. 1. Clonal proliferation of malignant plasma cells in bone marrow aspirate in multiple myeloma.

Fig. 2. Normal serum electrophoresis compared to serum electrophoresis in multiple myeloma.



light chains that are secreted into the blood. We use those secreted proteins to follow the disease as a surrogate (M-spike protein).

Not all patients who have increased plasma cells in their bone marrow have myeloma. There are 3 different types of plasma cell disorders. The first of the plasma cell disorders is called MGUS: monoclonal gammopathy of unknown or undetermined significance. In MGUS, patients have a monoclonal protein spike of less than 3gm/dL; fewer than 10% plasma cells in the bone marrow, and no CRAB criteria. The CRAB criteria (organ involvement), represents C for calcium, R for renal, A for anemia and B for bone. CRAB criteria will help us define who needs treatment and who doesn't, independent of how big or small the protein spike level is or how many plasma cells are present in the bone marrow. In general, patients with MGUS will progress to multiple myeloma at an average rate of 1% per year.

The second group consists of patients with asymptomatic myeloma, or smoldering myeloma. Smoldering myeloma was the original term that Dr. Robert Kyle gave to this disorder over 20 years ago; asymptomatic myeloma is the recent name given by the International Myeloma Working Group. Patients with asymptomatic multiple myeloma may have higher M protein levels, greater than 3g/dL, or they may have more than 10% plasma cells in the bone marrow. However, they continue to have no evidence of CRAB criteria (no evidence of organ involvement). Smoldering multiple myeloma will progress at a rate of 10% per year to myeloma with a relatively high peak within the first 5 years of diagnosis, and then it reaches a plateau (1). Usually these patients are observed; they are not empirically treated.

The third group is patients with multiple myeloma. In multiple myeloma, patients have increased monoclonal plasma cells in the marrow or a proven plasmacytoma; they may have M protein in the blood and/or urine; but they all have 1 or more of the CRAB criteria. If the patient has a non-secretory myeloma—a myeloma that does not make either heavy chains or light chains-, but have CRAB criteria and clonal plasma cells, you have myeloma that requires treatment. (Table 1).

EPIDEMIOLOGY

The American Cancer Society (ACS) estimates there will be 22,350 new cases of multiple myeloma diagnosed in 2013; it is slightly more common in men than in women; estimates note 12,440 cases expected in

Table 1. Diagnostic criteria for multiple myeloma and related disorders

Multiple myeloma (all 3 criteria must be met)
Presence of a serum or urinary monoclonal protein Presence of clonal plasma cells in the bone marrow or a plasmacytoma Presence of end organ damage felt related to the plasma cell dyscrasia, such as: - Increased calcium concentration - Lytic bone lesions - Anemia, or - Renal failure
Smoldering (asymptomatic) multiple myeloma (SMM, both criteria must be met)
Serum monoclonal protein ≥3 g/dL and or ≥10 percent to <60 percent bone marrow clonal plasma cells No end organ damage related to plasma cell dyscrasia (see list above)
Monoclonal gammopathy of undetermined significance (MGUS, all 3 criteria must be met)
Serum monoclonal protein <3 g/dL Bone marrow plasma cells <10 percent No end organ damage related to plasma cell dyscrasia or a related B cell lymphoproliferative disorder (see list above)

Adapted from: Br J Haematol 2003; 121:749 and Rajkumar SV, et al. Leukemia 2001; 15:1274 and Rajkumar SV, et al. N Engl J Med. 2011; 365:474.

men compared to 9,910 in women. Multiple myeloma represents about 1% of all new cancer with an annual incidence in US of approximately 4 to 5 per 100,000; and 2% of all cancer deaths and 13% of all hematologic cancers. The median age of presentation is 70 years, but 37% of patients are younger than 65 years. It is over-represented among African Americans compared to Caucasians (2:1 ratio). The highest incidence of MGUS, smoldering, and symptomatic myeloma is seen on the African subcontinent, and the lowest incidence in China and the Far East. A small fraction of cases are familiar. Multiple myeloma survival is improving through the use of high-dose chemotherapy and autologous bone marrow transplant, as well as through the use of novel agents such as proteasome inhibitors and immunomodulatory drugs. The 10-year survival in patients 60 years or younger is approximately 30 %[2].

PRESENTATION

Patients with multiple myeloma can present a number of symptoms. Anemia (normocytic, normochromic), is a prominent finding in 73 % of the patients. This can be related to the plasma cells infiltration in the bone marrow as well as renal dysfunction [3]. Bone pains can be present in 60% [4]. Often patients will present vertebrae compression fractures, and it is not uncommon to have myeloma patients actually lose 3 to 4 inches of height over the course of their disease because of multiple compression fractures. Bone lesions are caused by an imbalance in the function of osteoblasts and osteoclasts. Other symptoms are constitutional symptoms; these can include weakness, fatigue, and weight loss. Renal impairment occurs in 20 to 40% of newly diagnosed patients[4,5] secondary to direct tubular damage from excess protein, hypercalcemia, dehydration, and use of nephrotoxic substances [6]. Rarely, (2%), hyperviscosity is a finding and it tends to be with an IgA or with an IgM myeloma. Not all patients with IgMs have Waldenström's; a small subset of patients can have IgM myeloma, and those patients are predisposed to hyperviscosity. Neurologic dysfunction can also be seen. Patients can have neuropathy as a consequence of light chain deposition or amyloid; they can present with spinal cord or nerve root compression, representing a potential oncologic emergency requiring immediate treatment with steroids, and surgical or radiologic decompression.

DIAGNOSIS

Detailed medical history and physical examination are imperative. Routine complete blood counts, chemical analysis, serum and urine protein electrophoresis with immunofixation and quantification of the monoclonal protein and a bone marrow aspirate with biopsy for cytogenetic analysis and fluorescence in situ hybridization (FISH) should be done[7,8]. In addition, serum free monoclonal light chain analysis should be ordered. A skeletal survey including long bones to identify bone lesions should be part of the work-up, and if normal, a magnetic resonance imaging (MRI) should be order to further evaluate for very small lytic lesion not identified with conventional X-rays.

STAGING

The International Staging System (ISS) was introduced after a multivariate analysis of parameters predictive of survival in over 10,700 patients. (ISS) defines three risk groups (I, II, III) on the basis of albumin and serum B2 microglobulin levels (table1). If the patient has a B2 microglobulin of less than 3.5 and an albumin equal or greater than 3.5, is classified stage 1 with a median survival of 62 months; if the B2 microblobulin is greater than 5.5, it is a stage III with a median survival of 29 months; and if values are in between, the patient is a stage II with a median survival of 44 months [9].

Table 2. New International Staging System (ISS)

Stage	Criteria	Median Survival (months)
I	Serum β_2 - microglobulin < 3.5 mg/L Serum albumin ≥ 3.5 g/dL	62
II	Not stage I or III*	44
III	Serum β_2 - microglobulin ≥ 5.5 mg/L	29
Two categories for stage II; serum - β2microglobulin < 3.5mg/L and serum albumin < 3.5 g/dL ; or serum - β2microglobulin 3.5 to < 5.5mg/L.		

Cytogenetic abnormalities detected either by karyotyping or FISH analysis play a major role in the prognosis of multiple myeloma. Any chromosomal abnormality is associated with a worse outcome in comparison to a normal karyotype. Specific translocations in the immunoglobulin heavy chain region such as t (4; 14), deletion 17p13, and chromosome 1 abnormalities are associated with poor prognosis[10] as well as hypodiploidy. Standard risk is associated with hyperdiploidy or t (11; 14).

TREATMENT

Symptomatic disease should be treated immediately. Asymptomatic disease (smoldering multiple myeloma) should be clinically observed as there is no benefit in treating these patients with conventional chemotherapy. In the past, the standard of treatment for multiple myeloma was melphalan, (alkylating agent), and prednisone. Multiple combinations of chemotherapies, studied over the years, did not improve the overall survival over melphalan and prednisone. It was not until 1996 that the Intergroupe Francais du Myelome published an improvement in overall survival and progression-free survival associated with the use of high-dose chemotherapy with autologous bone marrow transplantation[11]. With this treatment the incidence of complete responses and very good partial responses is much higher than with conventional-dose chemotherapy. Patients that achieved a complete response (elimination of detectable disease on routine testing) had improved long term outcomes compared to patients who only achieved a partial response. Achieving a major response following induction and high-dose chemotherapy therapy with autologous transplant is now the major goal of induction therapy for almost all patients. Induction therapy with thalidomide, lenalidomide (immunomodulatory drugs that stimulate apoptosis and inhibit angiogenesis, adhesion, and cytokine circuits), or bortezomib (a proteasome inhibitor that stimulates multiple apoptotic pathways as well as help in the down regulation of angiogenesis factors, cytokine signaling and cell adhesion in the bone marrow microenvironment) followed by autologous bone marrow transplant have increased the rates of complete response in patients under the age of 65 without substantial lung, heart, renal or liver conditions and is the current standard of treatment. [12]. In patients older than 65, conventional therapy combined with thalidomide, lenalidomide or bortezomib should be offered [13]. In patients over 75 years, less intensive approaches, with limited toxic effects, should be considered.

The induction therapies followed by consolidation with two to four cycles of combination therapies with bortezomib or lenalidomide based regimens, improve the rate of complete response [14,15]. Maintenance therapy (essential in delaying tumor re-growth) with single agents until the time of disease progression have the potential to improve outcomes.

In patients with relapsed or refractory myeloma, the quality and duration of response to previous treatments are important prognostic factors. The patients, who relapsed after two years of treatment, may be re-treated with the same regimen. But patients that recurred after a short period of time should receive a different treatment. Again, combination therapy with dexamethasome and either bortezomib or lenalidomide is the treatment of choice. New drugs have now been approved for relapsed and/or refractory myeloma. Pomalidomide is one of these new drugs approved by the FDA as of February of this year. It is a third-generation immunomodulatory agent and it has clear-cut activity in the context of relapsed/refractory myeloma. Carfilzomib, a second-generation proteasome inhibitor, has a very different safety profile than bortezomib and, in fact, can be used in patients who have bortezomib resistance or who developed significant neuropathy associated with bortezomib-based therapy.

CONCLUSION

Multiple myeloma is a very complicated disorder of malignant plasma cells. As the population ages, the frequency of multiple myeloma is likely to increased. Patients now can be stratified according to basic demographics, variables such as cytogenetic or FISH markers that can help us identify differences in the biology of the disease, and this biology translates into differences in clinical outcomes. Induction with high-dose chemotherapy and autologous transplant is the treatment of choice to achieve complete response, and in high-risk patients we need to consider maintenance therapy to retain complete responses. New drugs in the relapsed and refractory disease setting can make a difference in outcomes. There are new agents with new targets including monoclonal antibodies in phase one and phase two trials. We hope that with this advances we can cure, in the near future, a significant fraction of patients with multiple myeloma.

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Basic Medical Management of Heart Failure

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RESUMEN

El propósito de este repaso es ofrecer de una manera breve y concisa un entendimiento de los conceptos básicos del manejo medico de fallo cardiaco. Según aumenta la incidencia de fallo cardiaco el costo de su manejo se convierte en una carga significativa a la economía. Todo médico debe de entender tanto las terapias indicadas por las guías de fallo cardiaco como las limitaciones de estas terapias. Los médicos deben también reconocer cuando referir el paciente para manejo más especializado.

SUMMARY

The purpose of this revised article is to give a straightforward and concise understanding of the basic concepts of the medical management of heart failure. As heart failure becomes more common and the cost becomes a larger burden on the economy, all physicians should have a clear grasp of the guidelines for therapy and some of the caveats of such therapy. Physicians should also know when to refer a patient for management by a specialist.

Keywords: heart failure, pharmacology therapy devices

It is estimated that from 2010 to 2030 the prevalence of heart failure (HF) will increase by 25% yet the cost to the United States (US) economy during this same period will increase 215% (1). The impact on the population and the magnitude of cost, demand that all physicians be versed in the optimal management of patients with heart failure. By optimal medical therapy we refer to that management which is guideline driven and cost effective. In this article we will discuss all the medications and therapies that have been proven to reduce mortality and hospitalizations of HF due to systolic dysfunction, as it is commonly termed, or HF with reduced ejection fraction[2,3,4]. Although up to 40% of patients admitted to hospitals with diagnosis of HF have normal or nearly normal ejection fractions, discussion of diastolic dysfunction or HF with preserved ejection fraction (HFPEF) is beyond the scope of this article. The definition of HF we will use in this article will be patients who have the clinical syndrome of HF whose hearts have an ejection fraction of 40% or less and are unable to keep up with the body's metabolic requirements.

BETA BLOCKERS

Beta blockers are the pinnacle of the triumvirate of heart failure medications, also composed of ACE inhibitors, or angiotensin receptor blockers (ARB) if intolerant to ACEI, and an aldosterone blocker.

Only beta blockers with proven studies in HF should be used, so the FDA approved alternatives in the US and PR are carvedilol [5,6] and long acting metoprolol succinate [7,3]. The dosage of these medications should be optimized to maximum possible dose as tolerated by blood pressure and heart rate because, of all medications used in HF, these are the ones that increase LVEF the most and provide the largest reduction in mortality [8].

ACE INHIBITORS

Almost all ACE inhibitors are indicated for treatment of HF. The difference between them is the frequency of dosing of each of these medications[3,2]. Captopril, one of the most commonly used agents in Puerto Rico, needs to be used three times a day; ramipril and enalapril have to be used twice a day; yet, agents such as lisinopril and monopril, can be used once a day. The reason for using one agent over the other depends on the patient, yet with the multiple medications needed for the treatment of HF and the patient's comorbidities, the simplicity of once a day therapy can help increase compliance. The dose of medications should be optimized to the highest tolerated dose by the patient's blood pressure.

A common mistake is with-holding medication in patients with renal dysfunction. In these patients medication should be used in low doses and only with-held if there is an increase in creatinine of 30% above baseline or if the patient has hyperkalemia [9].

ALDOSTERONE BLOCKERS

Spironolactone[10] and eplerenone[11] have both demonstrated reduction in mortality of patients already on good medical therapy with ACE and beta blockers. They should be avoided in patients with creatinine clearance of 30mg/dL or less, and/or potassium levels of more than 5. Eplerenone has less side effects, such as gynecomastia, and can be used in patients with lower NYHA classes.

Blood pressure should not be considered a limitation, as study data has demonstrated a mild increase in blood pressure in patients using eplerenone.

ARB's

If patients are intolerant to ACE inhibitors, an ARB can be an adequate substitute, but only two medications in this class have FDA approval and studies to substantiate equivalence: candesartan which is used once daily and valsartan which has to be use twice a day.

DIGOXIN

When used properly, digoxin can reduce hospitalizations. It should be avoided in patients with severe renal dysfunction of a GFR of 30mg/dL or less. Levels should be monitored and kept at 1or less. Use with amiodarone which increases digoxin serum levels should be avoided [14,15].

A common caveat in the use of all HF medications is blood pressure. Depending on the degree of dysfunction, these patients tend to have low blood pressure, so hypotension should only limit optimization of therapy if the patient expresses symptoms of hypotension and should not depend on the numeric value of the blood pressure reading.

DEVICE THERAPY

Use of automatic implantable cardiac defibrillators (AICD) in combination, if appropriate, with cardiac resynchronization (CRT) can reduce mortality in patients with ejection fractions of 35% or less. All patients with these low ejection fractions need evaluation by a cardiologist to determine if they have criteria for use of these devices as these have recently changed.[4]

CONCLUSION

All physicians should have a basic working knowledge of HF and the medications that need to be used. Beta blockers, ACE inhibitors and aldosterone antagonists are cornerstone therapies. These medications need to be used in adequate doses and frequency, and only the ones proven by studies and recommended by guidelines should be used. Cardiology evaluation and, when appropriate, evaluation by a heart failure specialist should be considered for optimization and addition of adequate therapies, such as electrical therapy with CRT and prevention of death with AICD.

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Medicina Nuclear y Molecular en el Diagnóstico de la Enfermedad de Parkinson

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SUMMARY

Parkinson's disease is caused by a progressive degeneration of dopaminergic neurons in the substantia nigra which projects towards the striatum. This degeneration creates a shortage of the neurotransmitter dopamine, causing the difficulty of movement that characterizes the disease. An early and accurate diagnosis is very important in the prognosis and management of patients to avoid unnecessary therapies and studies. This is where nuclear and molecular medicine makes a major contribution to the clinician, as it helps in the diagnosis and differentiation of these neurodegenerative diseases. The nuclear medicine study, brain SPECT (single photon emission computed tomography) with ^{123}I-ioflupane detects the degree of degeneration or loss of striatal dopamine transporters DaT, allowing the diagnosis of parkinsonian syndromes with high specificity and sensitivity even at very early stages

RESUMEN

La enfermedad de Parkinson resulta de la degeneración progresiva de las neuronas dopaminérgicas de la sustancia negra que se proyectan hacia el estriado. Esta degeneración crea una escasez del neurotransmisor dopamina, provocando la dificultad de movimiento que caracteriza a la enfermedad. Un diagnóstico temprano y acertado es muy importante en el pronóstico y manejo del paciente para evitar estudios y terapias innecesarias. Es aquí donde la medicina nuclear y molecular hace una gran aportación al clínico, pues le ayuda a diagnosticar y diferenciar estas enfermedades neurodegenerativas.
El estudio de medicina nuclear SPECT (tomografía computarizada de emisión de fotones) de cerebro con ^{123}I-ioflupane detecta el grado de degeneración o pérdida de los trasportadores de dopamina DaT en el estriado, permitiendo hacer el diagnóstico de síndromes parkinsonianos con una alta especificidad y sensibilidad aún en sus etapas bien tempranas.

Keywords: neurotransmitter, dementia, tremors

IMPACTO DE LA ENFERMEDAD

La enfermedad de Parkinson es el segundo desorden neurodegenerativo después de la enfermedad de Alzheimer. Se cree que en los Estados Unidos, al menos 500,000 personas sufren de la enfermedad de Parkinson, y se reportan unos 50,000 casos nuevos anualmente.[1] Se espera que estas cifras aumenten en la medida en que la edad promedio de la población aumenta. La enfermedad parece ser ligeramente más común en hombres que en mujeres. La edad promedio de aparición es alrededor de 60 años, siendo las tasas muy bajas en personas menores de 40 años. La prevalencia y la incidencia aumentan con el avance en la edad.[2]

A menudo, el primer síntoma de la enfermedad de Parkinson es temblor de una extremidad, especialmente cuando el cuerpo está en reposo. El temblor comienza usualmente en un lado del cuerpo, frecuentemente en una mano. Otros síntomas comunes incluyen movimiento lento (bradiquinesia), incapacidad para moverse (acinesia), extremidades rígidas, una marcha arrastrando los pies y una postura encorvada. Las personas con enfermedad de Parkinson a menudo presentan una reducción de expresiones faciales y un hablar con voz suave. Ocasionalmente, la enfermedad también causa depresión, cambios de personalidad, demencia, trastornos del sueño, alteraciones del habla y/o dificultades sexuales. La severidad de los síntomas tiende a empeorar con el tiempo.[2]

DIAGNÓSTICO

Los síndromes parkinsonianos son un grupo de enfermedades que comparten signos similares de parkinsonismo como bradiquinesia, rigidez, temblor en reposo e inestabilidad postural.[3] Los Síndromes Parkinsonianos incluyen la enfermedad de Parkinson, la atrofia multisistémica, y la parálisis supranuclear progresiva.[1] La enfermedad de Parkinson es el más común de estos síndromes. Aunque la enfermedad de Parkinson es la causa más común de parkinsonismo, hay otras etiologías, además de los Síndromes Parkinsonianos, que pueden tener los mismos síntomas, incluidos el

temblor esencial, parkinsonismo inducido por fármacos, parkinsonismo vascular y parkinsonismo psicogénico.[3] El temblor esencial usualmente ocurre durante el movimiento, sin embargo, algunos pacientes pueden demostrar temblor en reposo, rigidez u otras características parkinsonianas, imitando otras etiologías.[3]

Para el especialista, el diagnóstico clínico de la enfermedad de Parkinson en pacientes con una presentación clásica es frecuentemente simple. Sin embargo, puede ser un reto diferenciar entre las diferentes causas de parkinsonismo en pacientes con cuadros clínicos incompletos, especialmente en las etapas iniciales o leves de la enfermedad, o con síntomas que se solapan entre múltiples condiciones concurrentes.[1] Por esta razón la medicina nuclear y molecular juega un papel importante, pues ayuda a diagnosticar y diferenciar estas enfermedades neurodegenerativas para que el especialista pueda determinar el pronóstico y manejo del paciente evitándole terapias innecesarias.

PATOFISIOLOGÍA DEL PARKINSON Y ROL DE LA MEDICINA NUCLEAR Y MOLECULAR EN LAS IMÁGENES DEL TRANSPORTADOR DE DOPAMINA (DaT)

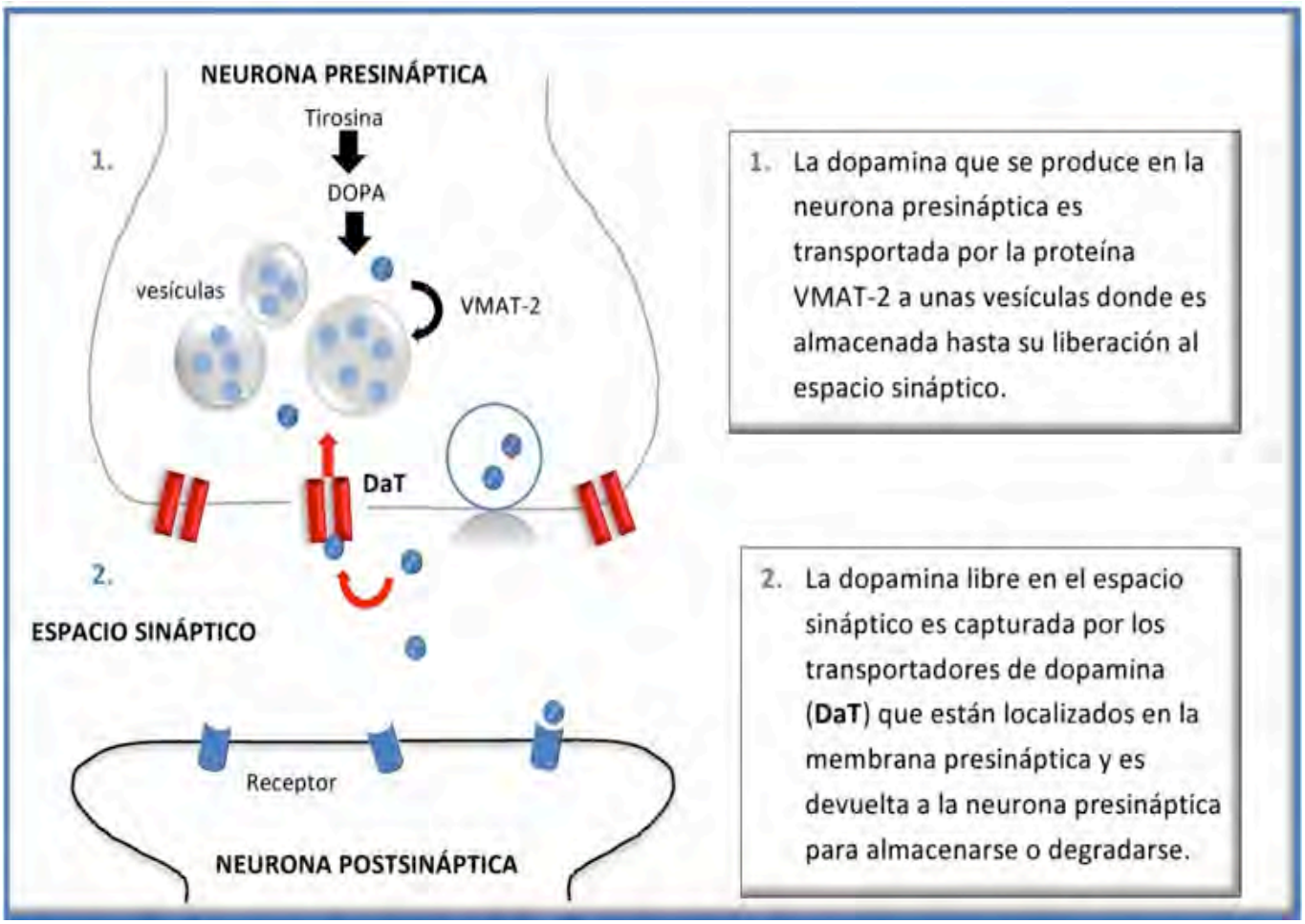

Imagen 1: Diagrama de una sinapsis dopaminérgica

La dopamina es un neurotransmisor que tiene un rol primordial en la regulación y control del movimiento. La ruta nigroestriatal dopaminérgica se evalúa a nivel del estriado donde los terminales presinápticos de las neuronas dopaminérgicas liberan la dopamina que interacciona con los receptores en la neurona postsináptica.[3] La dopamina que se produce en la neurona presináptica es transportada por la proteína VMAT-2 a unas vesículas donde es almacenada hasta su liberación al espacio sináptico.[3,4] La dopamina que queda libre en el espacio sináptico es capturada por los transportadores de dopamina (DaT) que están localizados en la membrana presináptica y es devuelta a la neurona presináptica para almacenarse o degradarse.[3,4] (imagen 1). Los síndromes parkinsonianos, incluida la enfermedad de Parkinson, se caracterizan por una degeneración de estas neuronas. Por esta razón, como

mecanismo de autorregulación, se reduce la densidad de los transportadores DaT para aumentar la dopamina disponible en el espacio sináptico.[3]

Esta sinapsis dopaminérgica provee múltiples marcadores potenciales de imágenes moleculares para demostrar la integridad de la neurona dopaminérgica.[5] (imagen2). Se han desarrollado varios radiofármacos, tanto para la tomografía de emisión de positrones (PET) como para la tomografía computarizada de emisión de fotones (SPECT), que pueden evaluar tanto la neurona presináptica como la postsináptica. En el lado postsináptico hay varios marcadores del receptor de dopamina pero todos son para estudios de investigación. En el lado presináptico tenemos ^{18}floro-DOPA (^{18}F-DOPA) un radiofármaco de PET que provee una medida de la integridad bioquímica de la neurona. ^{18}F-DOPA es convertido en florodopamina y es almacenado temporeramente en las vesículas del terminal nervioso. El ^{11}C-DTBZ es otro radiofármaco de PET utilizado para marcar el transportador de la vesícula (VMAT-2).

Sin embargo, el ^{18}F-DOPA y el ^{11}C-DTBZ no están disponibles comercialmente y solo se utilizan en centros de investigación.[1,3,4,5] Hay varios marcadores para proteína del transportador de dopamina DaT, pero el único que esta disponible comercialmente en los Estados Unidos es el ^{123}I-FP-CIT (^{123}I-ioflupane).

El ^{123}I-ioflupane fue aprobado en Europa en el 2000 bajo el nombre comercial de DaTscan®, para diferenciar pacientes que sufren de síndromes parkinsonianos de otras condiciones como temblores esenciales.[3,5] En el 2006 se aprobó su uso en Europa para diferenciar la enfermedad de Alzheimer de la demencia de cuerpos de Lewy.[5] En enero del 2011 el FDA aprobó su uso en los Estados Unidos y actualmente es el único radiofármaco aprobado para diferenciar síndromes parkinsonianos de

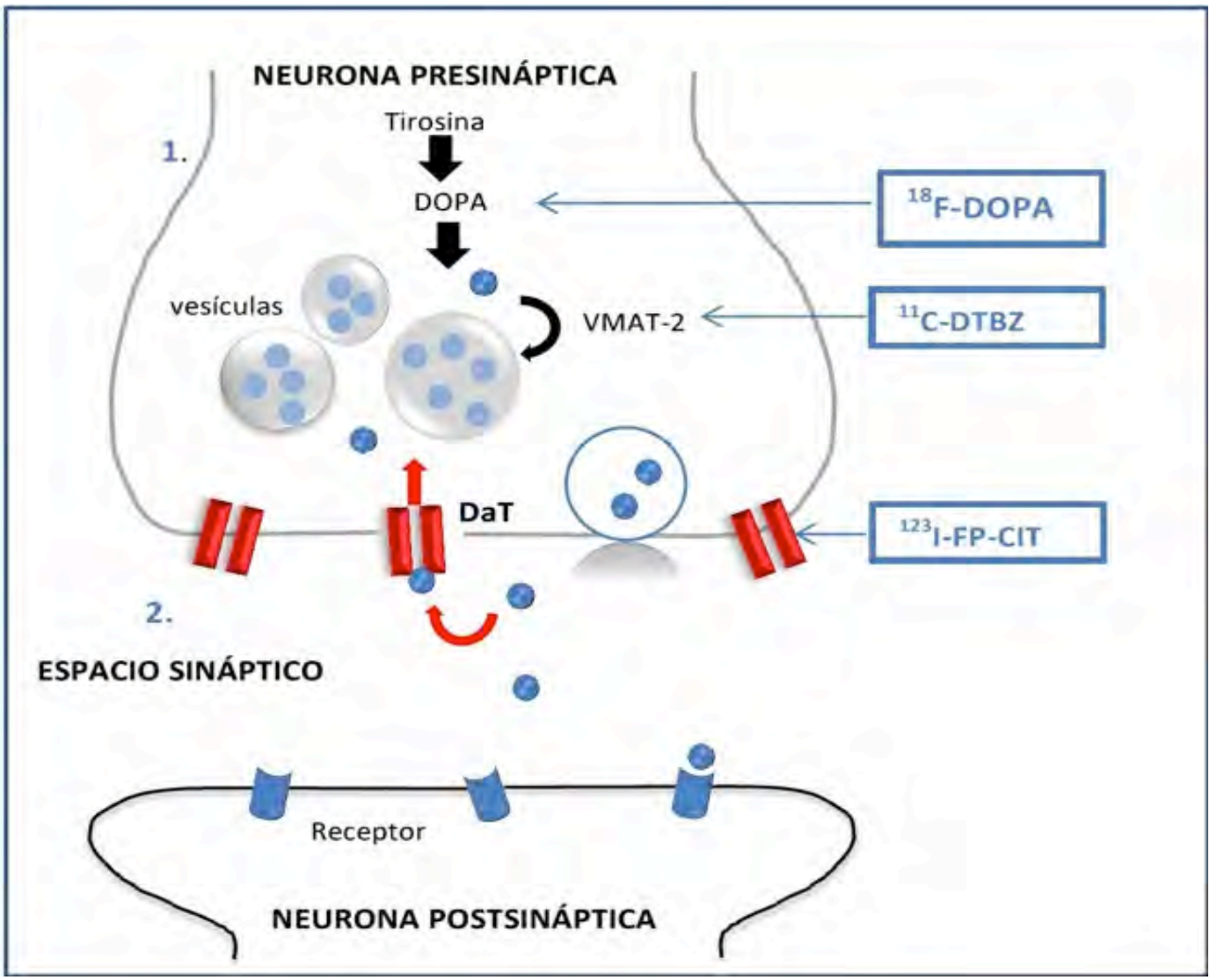

Imagen 2: Lugar de acción de radiofármacos de Medicina Nuclear en la sinapsis dopaminérgica

temblores esenciales. En septiembre del 2012 se realizó el primer estudio de DaTscan® en Puerto Rico.

El ^{123}I-ioflupane es un análogo de cocaína que se pega selectivamente a la proteína del DaT en el estriado. Las concentraciones de DaT están disminuidas en los síndromes parkinsonianos y en la demencia con cuerpos de Lewy.[3] Las imágenes de SPECT con ^{123}I-ioflupane ayudan a visualizar la localización y concentración de los trasportadores de dopamina DaT en la sinapsis. Los estudios de imágenes anatómicas (CT y MRI) son de poca ayuda para determinar la integridad del sistema dopaminérgico.[3]

El detectar el grado de degeneración o perdida de DaT en el estriado permite hacer el diagnóstico de síndromes parkinsonianos presinápticos con una alta especificidad y sensibilidad aún en etapas bien tempranas, pues el paciente no se pone sintomático hasta que ha perdido un número significativo de neuronas estriatales. En el momento que los síntomas motores son evidentes en los pacientes con la enfermedad de Parkinson, hasta el 60% de los marcadores neuronales dopaminérgicos ya se han perdido.[6] Por otro lado, las concentraciones de DaT están normales en pacientes con parkinsonismo sin pérdida de neuronas dopaminérgicas presinápticas como temblores esenciales, parkinsonismo psicogénico y parkinsonismo inducido por drogas.[3] En el parkinsonismo vascular, la captación de ^{123}I-ioflupane es normal o levemente disminuida a menos que el infarto envuelva el estriado. Estudios clínicos han demostrado que utilizar las imágenes de medicina nuclear con ^{123}I-ioflupane en pacientes con síndromes parkinsonianos no típicos pueden cambiar el diagnóstico en un 52% y cambian el manejo en un 72%.[7] De la misma manera, las concentraciones de DaT están reducidas en la demencia con cuerpos de Lewy y normales en la demencia de tipo Alzheimer.[1,3]

IMÁGENES DE ^{123}I-ioflupane	
DIAGNÓSTICO	**Nivel del Transportador DaT**
Sindromes Parkinsonianos: Enfermedad de Parkinson, Atrofia Multisistemica, Parálisis Supranuclear Progresiva	↓
Temblores esenciales	Normal
Parkinsonismo inducido por drogas	Normal
Parkinsonismo psicogénico	Normal
Parkinsonismo vascular	Normal o levemente ↓
Enfermedad de Parkinson con demencia	↓
Demencia con cuerpos de Lewy	↓
Demencia tipo Alzheimer	Normal

Adaptado de [8]Waxman A. How to use dopaminergic imaging to distinguish Parkinson disease from other movement disorders. Medscape: Nov 12, 2012.

SPECT DE CEREBRO CON ^{123}I-IOFLUPANE (DaTscan®)

Indicaciones: [3,9,10]

- Evaluación de pacientes adultos con sospecha de síndromes parkinsonianos (enfermedad de Parkinson, atrofia multisistémica, parálisis supranuclear progresiva) para diferenciarlos de otras condiciones donde no hay pérdida de células dopaminérgicas presinápticas como los temblores esenciales. Es importante aclarar que ^{123}I-ioflupane no puede diferenciar entre los síndromes parkinsonianos pues todos tienen degeneración de las neuronas presinápticas

Otros usos: [3,4]

- Diferenciación entre síndromes parkinsonianos de parkinsonismo farmacológico o psicogénico.
- Diagnóstico temprano de la enfermedad de Parkinson en las primeras etapas de la enfermedad.
- Evaluación de la severidad de la enfermedad.
- Diferenciación entre demencia tipo Alzheimer y demencia de cuerpos de Lewy.

Contraindicaciones: [3,9,10]

- Hipersensibilidad al producto
- Embarazo
- Pacientes que no cooperen con el estudio

Contraindicaciones relativas: [3]

- Hipersensibilidad al producto
- Embarazo
- Pacientes que no cooperen con el estudio

Como ordenar el estudio:

- El estudio se ordena como un "**Brain SPECT with DaTscan®**". El estudio está codificado y cubierto por Medicare (CMS).

Preparación y precauciones: [1,3,4,5,9,10]

- Es muy importante evaluar los medicamentos que el paciente está usando antes de realizar el estudio. Hay múltiples medicamentos que alteran el enlace entre el ^{123}I-ioflupane y el DaT interfiriendo con el estudio. Incluidos drogas y medicamentos como cocaína, anfetaminas, metilfenidate, estimulantes del sistema nervioso central, algunos anestésicos, antidepresivos como los TCA, SSRI, SNRI y bupropion, algunos antipsicóticos, entre otros. Se recomienda, en la medida que sea posible, suspender esos medicamentos por lo menos por un periodo equivalente a 5 vidas medias del ingrediente activo. Los medicamentos para el tratamiento de Parkinson, como los agonistas de dopamina, carbidopa/levodopa y los inhibidores de MAO no interfieren significativamente con el estudio.
- El día del estudio se le administra al paciente una dosis de perclorato de potasio o solución de Lugol para disminuir la exposición del tiroides al yodo radioactivo.

Protocolo de imágenes: [3,9]

- El ^{123}I-ioflupane se administra por vía endovenosa. Las imágenes se hacen en una cámara gamma SPECT de múltiples detectores, usualmente de 3 a 6 horas después de inyectado el paciente. La adquisición de las imágenes usualmente toma de 30 a 45 minutos.

Interpretación: [9]

- Las imágenes son analizadas por un especialista en medicina nuclear y se interpretan visualmente evaluando la apariencia y simetría del estriado (caudado y el putamen)en ambos lados. La apariencia normal de la imagen es en forma creciente o de "coma".[3] En los casos positivos, la pérdida de DaT se identifica por una disminución en la forma y la intensidad de estas estructuras. Frecuentemente el putamen se afecta más que el caudado y con mayor envolvimiento en el putamen contra lateral a los síntomas.[3] La interpretación precisa de estas imágenes depende de la calidad del estudio, la experiencia del especialista en medicina nuclear y la familiaridad con los hallazgos normales y anormales.[8]

ESTUDIOS NORMALES Y ANORMALES

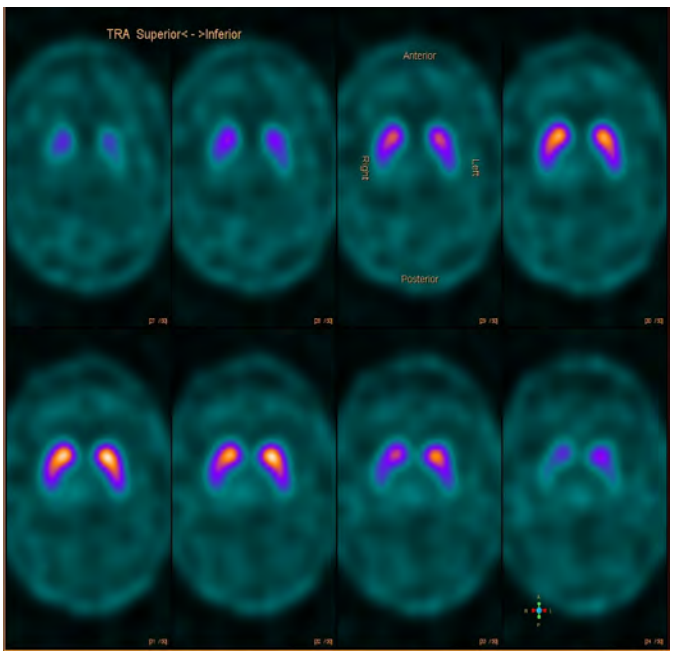

Imagen 3: Estudio Normal

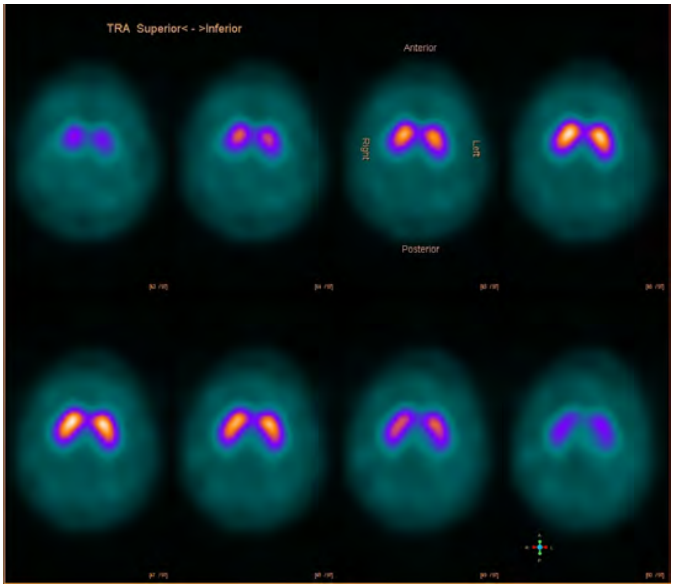

Imagen 4: Estudio Normal

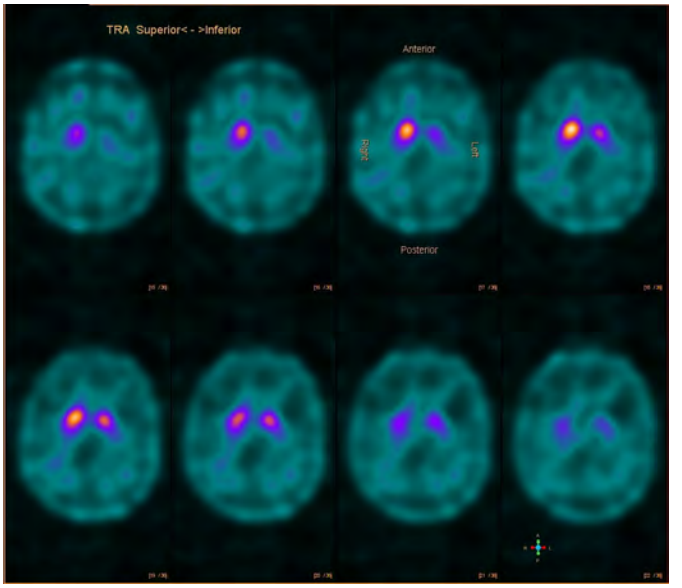

Imagen 5: Estudio Anormal

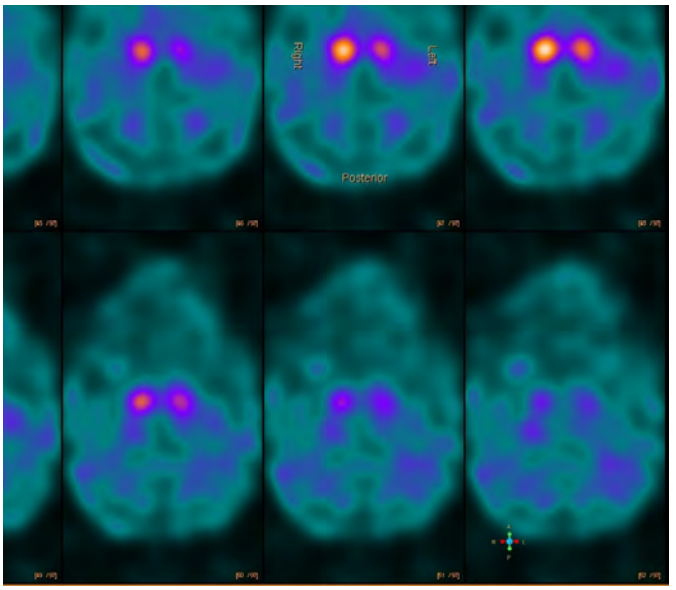

Imagen 6: Estudio Anormal

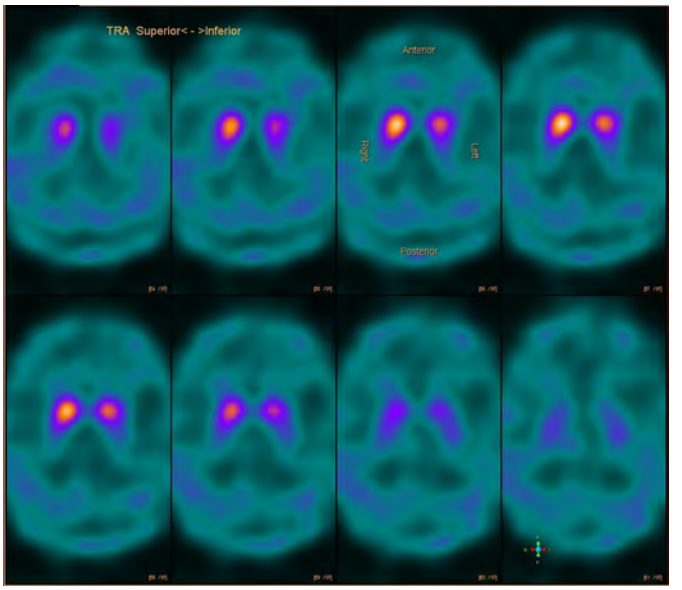

Imagen 7: Estudio Anormal

CONCLUSIÓN

En conclusión, la evaluación de un paciente con síntomas de parkinsonismo puede ser un reto para el especialista, tanto en la fase temprana de la enfermedad, como en presencia de sobreimposición de los signos y síntomas. Aunque en la mayoría de los pacientes con cuadros clínicos clásicos, el diagnóstico de un síndrome parkinsoniano es bastante certero, hay muchos pacientes que tienen cuadros clínicos incompletos o leves, o síntomas que se solapan con otras condiciones. Un diagnóstico temprano y acertado es importante en el pronóstico y manejo del paciente de manera que se puedan evitar estudios y tratamientos innecesarios, disminuyendo costos y la posibilidad de efectos secundarios no deseados a los medicamentos.[1]

El estudio de medicina nuclear SPECT de cerebro con ^{123}I-ioflupane detecta el grado de degeneración o pérdida de los trasportadores de dopamina DaT en elestriado, permitiendo hacer el diagnóstico de síndromes parkinsonianos con una alta especificidad y sensibilidad aún en etapas bien tempranas de la enfermedad. Esta tecnología se puede incorporar a los hallazgos clínicos para mejorar la certeza y confiabilidad del diagnóstico de los síndromes parkinsonianos, permitiendo diferenciarlos de otras condiciones como temblores esenciales, parkinsonismo inducido por medicamentos y parkinsonismo psicogénico. El SPECT de cerebro con ^{123}I-ioflupane no puede diferenciar la enfermedad de Parkinson de los otros síndromes parkinsonianos como la atrofia multisistémica y la parálisis supranuclear progresiva. Este estudio también puede ayudar en la evaluación de pacientes con demencia para diferenciar la demencia de tipo Alzheimer de la demencia con cuerpos de Lewy.

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Instituto de Educación Médica Continua del Colegio de Médicos Cirujanos de Puerto Rico

"Proveedor de Educación Médica Continua de Excelencia al Servicio de Nuestros Colegiados"

La Plataforma Educativa del Colegio de Médicos Cirujanos de Puerto Rico tiene como objetivo principal y enfatiza que es responsabilidad del Colegio el promover el mejoramiento profesional de todos los colegiados mediante la viabilización de la educación médica. Por lo tanto al establecerse la ley para la creación del Colegio se dispone en el inciso L del Artículo 4 de esta ley (Ley 77 del 13 de agosto de 1994), según enmendada, el establecimiento del Instituto de Educación Medica Continua, el cual será responsable de cumplir con este objetivo.

El Instituto de Educación Médica Continua se rige por los requisitos establecidos y áreas esenciales por el "Accreditation Council for Continuing Medical Education" (ACCME), la Junta Americana de Especialidades Medicas [ABMS] y la Junta de Licenciamiento y Disciplina Médica de Puerto Rico. La planificación de las actividades de educación continua siguen los requisitos de las Agencias Reguladoras de la Educación Médica a nivel local y nacional. El IEMC es proveedor certificado por la Junta de Licenciamiento y Disciplina Médica (JLDM) y del "Accreditation Council for Continuing Medical Education" (ACCME), para el periodo 2011-2017.

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En el IEMC estamos seguros que debemos continuar ofreciendo a nuestros colegiados aquellas alternativas de desarrollo profesional y herramientas que sean de utilidad en su práctica médica sin olvidar nunca la calidad y valor científico de estos. Para información adicional pueden comunicarse al Colegio de Médicos Cirujanos de Puerto Rico al 787-751-5979.

Peripartum Cardiomyopathy: Current Trends, Interdisciplinary Insights, and Future Directions

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RESUMEN

La cardiomiopatía periparto es una condición rara de etiología desconocida que afecta a mujeres embarazadas durante el último mes del embarazo o los primeros cinco meses postparto. La misma está asociada con una gran morbilidad y mortalidad secundaria a una función cardiaca reducida y sus complicaciones asociadas. Las modalidades de tratamiento son similares a aquellas dirigidas a pacientes con fallo cardiaco con función sistólica reducida. Sin embargo, aun con terapias médicas apropiadas, algunas pacientes desarrollan una disfunción cardiaca permanente. Se necesitan estudios de investigación adicionales para caracterizar las variables clínicas en pacientes hispanas con cardiomiopatías periparto.

SUMMARY

Peripartum cardiomyopathy is a rare disease of unknown etiology that affects pregnant women during the last month of pregnancy or the first five months postpartum. It is associated with severe morbidity and mortality due to a compromised myocardial function and its associated complications. Treatment modalities are similar to those directed at patients with heart failure with reduced left ventricular ejection fraction. Nevertheless, even with adequate therapy, some patients develop persistent cardiac dysfunction. Further research is needed to characterize the clinical variables of peripartum cardiomyopathy in Hispanic patients.

Keywords: peripartum cardiomyophaty, hispanics

INTRODUCTION

Peripartum cardiomyopathy (PPCM) is a rare and life-threatening form of cardiac failure that is unique to pregnant women of all reproductive ages. It is a separate entity from other known existing cardiomyopathies with a poorly understood etiopathogenesis. PPCM is defined as cardiomyopathy developing in the last month of pregnancy or within 5 months of delivery in an otherwise healthy individual and in the absence of an identifiable etiology for the condition [1,2]. Wide variation exists regarding the true incidence of PPCM, but it is estimated to be between 1 in 1,300 to 1 in 15,000 pregnancies. Much of this difference may be attributed to the geographic dissimilarities, as well as older reports, in which the causes of cardiomyopathy were not adequately investigated[3]. The natural history of PPCM has not been entirely elucidated. However, hypothesized pathways may involve an exacerbation of underlying subclinical cardiac disease related to the hemodynamic changes of normal pregnancy in addition to inflammatory or autoimmune processes. The potential complications associated with PPCM makes the diagnosis of this condition extremely valuable. Doing so remains a challenging task often requiring a multidisciplinary approach. In this review, pregnancy we attempt to present the current state of knowledge regarding this condition and the future directions of research in PPCM.

DEFINITION

Peripartum cardiomyopathy is defined on the basis of the following four criteria [4]:

1. Development of heart failure in the period between the last month of pregnancy and the first five months postpartum.

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2. Absence of another cause that could explain the patient's heart failure.

3. Absence of recognizable heart disease prior to the last month of the pregnancy.

4. Left ventricular systolic dysfunction as demonstrated by a decreased LV ejection fraction or a reduced fractional shortening on an echocardiogram.

For the purposes of PPCM, left ventricular systolic dysfunction is defined by echocardiographic criteria as a left ventricular ejection fraction less than 45% or an M-mode fractional shortening less than 30%, or both; and a left ventricular end-diastolic dimension greater than 2.7 cm/m2 [5]. It is important to note that the term associated cardiomyopathy (PACM) has often been used to describe the cases of heart failure arising earlier in the pregnancy of women without pre-existing cardiac disease. The clinical characteristics of patients with this so called early onset disease were compared to patients meeting the classical definition of PPCM, and they were found to be similar [6]. This has led to the proposition of an expanded definition for PPCM to include those patients with PACMP as part of a continuum of the same disease entity. An expanded definition was adopted by the Heart Failure Association of the European Society of Cardiology in a recent position statement [7].

The reported incidence of PPCM varies widely; however, most reports have estimated that the incidence in the United States is between 3000 and 4000 live births [4,8,9]. Population based studies have shown that even though it is still considered a rare disease, the incidence of PPCM has steadily increased over the past few years [8]. When analyzed according to race, it has been shown that the incidence of PPCM is highest among African-Americans and lowest among Hispanic-Americans [9]. Even though it is still a topic of debate, a higher incidence in women of African descent has been noted in multiple studies and it is usually considered to be one of the strongest risk factors for the disease [10]. Other risk factors for PPCM include: age; chronic hypertension; preeclampsia, eclampsia, or gestational hypertension; obesity; multiple gestations; multiparity; and prolonged use of tocolytics [4,11].

PATHOPHYSIOLOGY

The pathophysiology of peripartum cardiomyopathy is not entirely elucidated. Several mechanisms have been proposed including: infections, autoimmune disorders, genetic predisposition and oxidative stress [12]. For years, the accepted theory regarding the pathogenesis of PPCM revolved around the concept of a ventricular dysfunction secondary to a viral myocarditis. This theory was supported by early studies which indicated a higher prevalence of biopsy proven myocarditis among patients with PPCM [13,14]. Several viruses have been implicated in the pathogenesis of PPCM, including: parvovirus B19, human herpes virus 6, Epstein–Barr virus, and human cytomegalovirus. However, subsequent studies have questioned this hypothesis by demonstrating a similar incidence of viral markers in patients with PPCM when compared to selected control populations [15,16].

Several studies have identified autoimmune mechanisms in the pathogenesis of PPCM. A case series study published by Lamperter et al, demonstrated circulating cardiac autoantibodies in all of their patients with PPCM while also establishing the absence of any evidence of viral infection in the patients with PPCM who underwent endomyocardial biopsy [17]. These antibodies are usually directed against cardiac proteins, such as actin and myosin. This is important given a study by Warriach et al that identified an IgG3 inmunoglobulin against the myosin heavy chain as a discriminatory factor with regards to the NYHA functional class at diagnosis in patients with PPCM [18]. On the other hand, others have suggested that the pathogenesis of PPCM could be due to a pathological immune response against circulating fetal cells that have entered the maternal circulation [19]. Additional studies are still needed to fully evaluate the role of autoimmune mechanisms in the pathogenesis of peripartum cardiomyopathy.

A few reports have hinted at the possibility of a connection between a genetic predisposition and PPCM. Case reports of familial clustering and the finding of genes known to be linked to dilated cardiomyopathies in family members with PPCM have opened a brand new area of research into PPCM and offer the possibility to further characterize this disease [20,21]. This interaction highlights the possibility that peripartum cardiomyopathy is a manifestation of dilated cardiomyopathy in which pregnancy related factors contribute to the development of heart failure in genetically susceptible women.

A more recent approach to the pathophysiology of PPCM revolves around the role of oxidative stress as the causative agent of PPCM, particularly through the cathepsin D-prolactin cascade. This model is based on the role of cathepsin D in the cleavage of prolactin into a 16 kDA isoform. This 16 kDA prolactin isoform has

antiangiogenic and proapoptotic properties which have been demonstrated to be cardiotoxic. A study by Hilfiker-Kleiner et al demonstrated the development of PPCM in a genetic female mouse model with a cardiac signal transduction and activator of transcription 3 (STAT 3) deletion [22]. Activation of STAT 3 results in protection from oxidative stress by inducing the production of antioxidant enzymes, such as manganese superoxide dismutase [23]. The STAT 3 deficient mice had an overexpression of cathepsin D leading to increased production of the 16 kDA prolactin. The STAT 3 deficient mice were noted to have the PPCM phenotype; and treatment with bromocriptine, a prolactin production inhibitor, prevented the development of PPCM [22]. This model could be an explanation for the observed clinical improvement in patients with PPCM who have been treated with bromocriptine [24,27].

CLINICAL PRESENTATION AND DIAGNOSIS

The clinical presentation of patients with peripartum cardiomyopathy may include symptoms and signs such as: cough, dyspnea, fatigue, orthopnea, parosxysmal nocturnal dyspnea, chest pain and peripheral edema. Some of these symptoms can be confused with the usual symptoms of pregnancy, which further delays diagnosis [12]. The majority of patients develop symptoms during the first few months post partum [7]. In terms of functional classification, patients with PPCM often presents with symptoms consistent with a NYHA class III or IV [27]. Patients with PPCM have an increased risk of thromboembolic disease owing to the natural procoagulant state of pregnancy and the increased incidence of left ventricular thrombus formation in severely dysfunctional left ventricle. Electrocardiographic findings may include sinus tachycardia, non-specific ST and T wave abnormalities, LV hypertrophy, left atrial enlargement and conduction abnormalities [12]. It is important to note that a QRS complex duration of more than 120 msec has been identified as a predictor of mortality in patients with PPCM [28]. An Echocardiogram usually shows a left ventricular dilation with a depressed systolic function; however, other abnormalities may also be seen. Echocardiographic parameters at diagnosis, such as left ventricular systolic function and end diastolic dimensions, have been shown to have prognostic significance [29].

THERAPY

Therapy for PPCM is very similar to the usual therapy for reduced LVEF heart failure, with the exception that particular care must be taken to avoid agents that are contraindicated in pregnancy or during breast feeding. In this regard, a multidisciplinary approach is recommended with the inclusion of obstetricians, cardiologists and pediatricians [4]. Agents that should be avoided during pregnancy include ACE inhibitors and ARBs due to their teratogenic potential. The use of other medications such as beta-blockers, digoxin, hydralazine, loop diuretics and nitrates appears to be relatively safe during pregnancy, and are considered to be the cornerstone of therapy for PPCM. Patients with a very low left ventricular ejection fraction (less than 35%) are at risk for the development of ventricular thrombi. As such, it is recommended that these women be started on anticoagulation therapy, with particular attention to the agent used as warfarin is a known teratogenic agent. In these patients, heparin is the preferred agent [12].

When medical therapy fails, patients with severe PPCM can be treated with cardiac transplantation. Outcomes of cardiac transplantation in patients with PPCM, when measured in terms of survival and complication rates, are comparable to the age-matched controlled patients who undergo cardiac transplantation [30]. Several studies have demonstrated the efficacy of mechanical assist devices as a bridging therapy for recovery or for cardiac transplantation [31,33].

Research into the efficacy of additional pharmacological agents is underway. For example, it has been shown that adding bromocriptine to the standard treatment regimen has been shown to improve outcomes, particularly the recovery rate of the left ventricular systolic function [34]. On the other hand, the use of immunosuppressive agents has been suggested due to the correlation between PPCM and biopsy proven myocarditis. However, as in patients with myocarditis, the efficacy of immunosuppressive agents in PPCM remains unclear and their use is associated with significant risks and side effects [35]. The use of immunoglobulins has shown promise in a small study that demonstrated an improvement of LVEF in patients with PPCM treated with intravenous immunoglobulins when compared to conventional therapy [36]. However, given the limitations of this study, further research is required before a strong recommendation can be made. Finally, Sliwa et al demonstrated that the addition of Pentoxifylline to conventional therapy improved mortality, left ventricular ejection fraction and functional class in patients with PPCM [37]. Further research is required to establish the efficacy of Pentoxifylline in PPCM and its safety during pregnancy.

PROGNOSIS

Peripartum cardiomyopathy is associated with significant morbidity and mortality. Even though earlier reports

indicated that the mortality of PPCM fluctuated between 25-50%, more recent studies have estimated the maternal mortality from PPCM to be between 2-6% [8,38]. Racial differences have also been noted when studying morbidity and mortality. African American women with PPCM have been noted to have a more severe disease course, a higher mortality and an overall worse prognosis when compared to white patients [38,39]. The normalization of the left ventricular ejection fraction occurs in the majority of women with PPCM, being 54% in one series [6]. However, this is directly proportional to the LVEF at presentation, with a lower LVEF associated with a decreased rate of myocardial function recovery [40]. Nevertheless, it is widely accepted that this correlation between LVEF at presentation and recovery should not be used to guide therapeutic decisions in individual patients. Recovery usually occurs during the first 6 to 12 months after diagnosis [41]. Subsequent pregnancies are associated with a high risk of recurrence of PPCM [42]. When evaluating neonatal outcomes, one report noted that babies born to women with peripartum cardiomyopathy tend to be small for gestational age, have a low or very low birth weight, have a lower Apgar score, and tend to be premature [2].

NEW FRONTIERS IN PPCM RESEARCH

There is no specific data about the epidemiology or clinical characteristics of women with peripartum cardiomyopathy in Puerto Rico. To address this question, our group has started a study which seeks to determine the clinical and echocardiographic characteristics of a cohort of Puerto Rican patients with peripartum cardiomyopathy from a tertiary care center in Puerto Rico [43].

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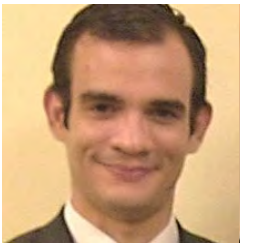

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Fundación Médica del Colegio de Médicos Cirujanos de Puerto Rico

"Al Servicio De Nuestra Comunidad"

La Ley 77 del 13 de agosto de 1994, según enmendada, dispuso la creación y organización de la Fundación Médica del Colegio de Médicos Cirujanos de Puerto Rico.

La Fundación es el organismo interno que planifica la estructuración de los programas de servicio a la comunidad en general, y sirve de apoyo en toda otra gestión relacionada al cumplimiento de las encomiendas y política institucional del Colegio.

Dentro de las facultades y objetivos de la Fundación Médica se encuentran el ayudar al mejoramietno de la salud del pueblo de Puerto Rico, incluyendo nuestros médicos colegiados, ya que ellos son parte esencial de nuestra comunidad.

Por tanto, nos sentimos comprometidos con este postulado para así lograr mejorar la calidad de vida de nuestro país. La Fundación Médica está compuesta por compañeros médicos, electos en asamblea, provenientes de las 12 regiones que representan a nuestro Colegio.

Algunas intervenciones y logros por parte de nuestra Fundación han sido crear enlaces comunitarios, ofrecer ayudas meritorias a la comunidad y sus médicos, fomentar la enseñanza médica y contribuir en estudios de investigación que promuevan el adelanto de la medicina y la salud pública.

Nuestra Fundación Médica continua trabajando arduamente y sin pausa en pro de nuestra comunidad y sus médicos, teniendo como visión el mejorar la calidad de vida de TODOS los habitantes de Puerto Rico. Agradezco la buena voluntad y tenacidad de todos los compañeros miembros de la Junta Directiva, y aquellos que de alguna forma u otra nos han ayudado a cumplir nuestra misión. Para solicitar información adicional de nuestra Fundación, puede comunicarse al Colegio de Médicos Cirujanos de Puerto Rico al (787) 751-5979.

The American College of Physicians (ACP) Vignette's Competition 2012

RESUMEN

"Los Internistas son especialistas que aplican el conocimiento científico y su experiencia clínica en el diagnóstico, tratamiento y cuidado compasivo de los adultos, a través de todo el espectro desde la salud hasta la enfermedad compleja" según lo define el ACP. Los residentes y fellows de Medicina Interna se exponen a los pacientes muy interesantes y complicados durante sus años de adiestramiento. Esperan con ilusión la oportunidad de presentar y discutir esos casos, a la vez que compiten con sus compañeros en una forma saludable y académica. Los exhortamos a continuar trabajando en equipo para fortalecer además nuestras tareas de investigación científica. Estas experiencias son una parte muy importante de su adiestramiento.

Los siguientes abstractos fueron presentados en la más reciente competencia de Monografías celebrada en octubre, 2012. Es con mucho orgullo y satisfacción que compartimos estas perlas de sabiduría para el disfrute de toda nuestra comunidad médica. Felicitamos además, a los residentes y sus mentores por un trabajo extraordinario. Iniciativas como esta responden a la misión de nuestros programas y del Colegio Americano de Internistas, nuestra asociación más prestigiosa. ¡Enhorabuena!

SUMMARY

"Internal medicine physicians are specialists who apply scientific knowledge and clinical expertise to the diagnosis, treatment, and compassionate care of adults across the spectrum from health to complex illness", as defined by the ACP. Internal Medicine residents and fellows are exposed to very interesting and complicated patients during their training years. They look forward to the opportunity to present and discuss those challenging cases as well as to compete with their peers in a healthy, academic way. We also encourage teamwork to strengthen the outcome of scientific research in all sub-specialty programs. These experiences are a very important part of their training.

The following abstracts were presented at the most recent ACP Vignette's Competition in October, 2012. It's with great pride and satisfaction that we share these pearls of wisdom for the enjoyment of all our medical community. We congratulate our residents, from all training programs in PR, as well as their mentors for this extraordinary work. It responds to the mission of our programs and of the American College of physicians, our most prestigious association. Congratulations!

- Ivonne Z. Jiménez-Velázquez, MD, FACP
ACP Governor - Interim

VO= Vignette Oral VP= Vignette Poster

VO#1

MALE PATIENT WITH NECK MASS: ECTOPIC CANCER VS METASTASIC DISEASE

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José Hernán Martínez, MD, FACP [1];
Frieda Silva, MD[2]; Gloria Rodríguez, MD[2];
Madeleine Gutiérrez, MD[3] ;
Eva González, MD[2];
María de Lourdes Miranda, MD[3]

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Case of 33 y/o male patient with an unremarkable past medical history, who after a car accident, a cystic nodular right neck mass was incidentally found by CT

scan. Physical examination revealed a mildly tender right neck mass. He was clinically and biochemically euthyroid. Denied history of neck irradiation. No family history of thyroid disease or thyroid cancer. Excisional biopsy of right neck mass showed metastasic well differentiated papillary carcinoma of thyroid gland at lymph node. Total thyroidectomy with right modified neck dissection was performed. Histopathological report disclosed no evidence of malignant tumor within the thyroid gland as well as sixteen right lymph nodes obtained from surgery. One month after surgery, Thyroglobulinn levels were elevated, 133.61 ng/ml, with negative antithyroglobulin antibodies (Thyroglobulin antibodies: 11.8 uU/ml). Thyroid scan and Whole Body Scan showed evidence of functional thyroid tissue remnants; this appears to be a right thyroid lobe. Also, a faint visualization of a smaller focus in the left thyroid bed region was seen. Thyroid ultrasound showed two right medial neck nodules. Fine needle aspiration biopsy of neck nodules reported positive for metastasic thyroid papillary carcinoma. Radioidine ablation therapy was given. Ectopic thyroid gland is defined as thyroid tissue not located anterolaterally in the second to fourth tracheal cartilages. Ectopic Thyroid tissue is a rare entity with an incidence of 1 in 300.000. An ectopic thyroid gland in the region of the submandibular gland, intra-trachea or laterally is very rare. Malignant transformation of ectopic thyroid tissue is an uncommon event; only 43 cases have been reported. Only 10 of those cases were papillary carcinoma.

VO#2

MILITARY TRAINING: AN UNCOMMON CAUSE OF BRAIN EDEMA

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Jesús Casal Hidalgo, MD, FACP;
Julio Valentín Nieves, MD

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A 29-year-old man developed fever and altered mental status during his fifth day of military training. He complained of headaches and vomiting, denied flu-like symptoms, recent travel, sick contacts, exposure to animals, and previous similar episodes. He then developed erratic behavior with incoherent speech. He was taken to a community hospital for evaluation where Head CT without contrast revealed brain edema and no evidence of blood, infarction, or mass. He was given an unknown amount of sedatives due to aggressive behavior, which led to neurologic deterioration with a reported GCS of 8/15, requiring endotracheal intubation and mechanical ventilation for airway protection. He was started on antibiotics and transferred to San Juan VA hospital with a presumptive diagnosis of meningitis versus encephalitis. He presented to our hospital with a temperature of 38.8 &#730, C; tachycardia; dry, warm skin; slowly reactive pupils; and bilateral plantar extensor response. Laboratories revealed leukocytosis with neutrophilia, hyponatremia, low serum osmolality, rhabdomyolysis, and acute respiratory alkalosis. Head CT confirmed evidence of brain edema and treatment was initiated with anti-pyretics, anti-edema measures, intravenous fluid hydration, antibiotics, and glucocorticoids. Neurology and Infectious Diseases made a clinical diagnosis of meningoencephalitis and agreed with empiric treatment. He was pan-cultured and multiple serologic tests were requested. After 24 hours, hyponatremia resolved, he tolerated extubation, and his neurological status improved significantly. Upon further questioning, he revealed that at noon on his fifth day of military training, his supervising officer punished him by increasing the amount and intensity of exercise (running and push-ups). This was followed by nausea, vomiting, headaches and a collapse with loss of consciousness. The diagnostic impression was reevaluated and exertional heat stroke was included in the differential. Lumbar puncture revealed increased intracranial pressure and no other abnormalities. EEG revealed diffuse cortical dysfunction as seen in toxic-metabolic encephalopathy or medication side effects. Brain MRI showed resolution of edema and no evidence of meningitis after 72 hours. He completed intravenous antibiotic treatment for meningoencephalitis without complications and was discharged home symptom-free. Serologic test results revealed positive West Nile Virus IgG antibody, and negative Herpes Simplex Virus antibodies, VDRL, RPR, and HIV. In the United States, an average of 334 deaths per year were attributed to excessive heat exposure from 1979-2003. When therapy is delayed, the mortality rate may be as high as 80%. This case illustrates the need to raise awareness of this diagnosis in the medical community of Puerto Rico, where the incidence of heat stroke is unknown. Prompt recognition is critical since early diagnosis and treatment reduces mortality rate to 10%.

VO#3

SYPHILIS UNDER A NEW LIGHT: A CASE OF UNCOMMON PRESENTATIONS OF A COMMON DISEASE (OSTEOMYELITIS AND UVEITIS)

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Case of a 50 year old man with history of arterial hypertension, diabetes mellitus type 2, acquired immunodeficiency syndrome and syphilis by sexual contact who was admitted to our institution after acute loss of vision of right eye for the 3 past days. A head CT was performed and revealed a left frontal bone osteolytic, expansile lesion extending into the scalp with a differential diagnosis including neoplastic disease and syphilitic osteomyelitis for which a contrast enhanced MRI was recommended. A lumbar puncture was performed revealing clear cerebrospinal fluid with high protein (=65) and glucose (=95), sample sent for VDRL analysis. Intravenous antimicrobials (Penicillin G), AIDS prophylaxis, fluconazole strated due to findings of oral thrush, Infectious disease and Ophthalmology services consulted, and the patient admitted with a diagnosis of suspected neurosyphilis. Upon physical examination, patient with findings of oral thrush, right eye visual loss, labial vesicular rash, left forehead mass (2.5 cm x 2.5 cm), but otherwise no other abnormalities. Initial laboratories revealed an acute kidney injury with prerenal azotemia. Infectious disease evaluated patient and recommended Acyclovir due to evidence of labial herpes outbreak (discontinued after 3 days) and Pyrimethamine, Sulfadiazine, Leucovorin for toxopolasmosis coverage (discontinued after a day). Patient also evaluated by Ophthalmology service who agreed with management at time after fundoscopic examination revealed corneal ulcers and evidence of chronic uveitis highly suggestive of syphilitic disease. Neurosurgery consulted for left frontal mass biopsy after a reactive VDRL test was disclosed (1:16 titers) and CSF VDRL returned negative. Brain MRI with contrast performed revealed left frontal bone lytic lesion, with evidence of periosteal reaction and contrast enhancement without evidence of cortical breakthrough. At this moment (almost 2 weeks after antimicrobials started with subsequent diminishing of mass dimensions), an infectious process among main differential, specifically osteomyelitis by syphilis.Skull mass biopsy performed by Neurosurgery perfomed (almost a month after IV antimicrobials instituted) revealed bone with medullary fibrosis and reparative changes (low Ki-67; Warthin Starry non-contributory; HHV-8, CD34 negative; Grocott, PAS negative for fungi; and AFS negative for mycobacteria). Syphilis is a chronic infection caused by Treponema pallidum. During the initial phase of infection, the organism disseminates widely, setting the stage for subsequent manifestations. If untreated, syphilis can have a number of significant late manifestations, including cardiovascular, gummatous, and neurologic complications.Management is based on its classification into stages of disease: early syphilis (includes primary, secondary, and early latent syphilis); late or tertiary syphilis (includes cardiovascular and gummatous syphilis); and neurosyphilis (includes central nervous system disease and ocular syphilis). Neurosyphilis can involve the meninges, brain, or spinal cord and may present in a wide range of ways, including meningitis, general paresis, tabes dorsalis, or meningovascular disease. Our patient was found with syphilitic uveitis and suspected osteomyelitis

VO#4

"AND THE FATIGUE GOES ON"

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Introduction A 19 y/old man is brought to our institution with chief complaint of hypoactivity and dyspnea of 2 months evolution.Symptoms got progressively worse until he was no longer able to do daily activities.He was evaluated at another institution were a 2D ECHO was done with findings compatible with valve disease, aneurysm of the aorta and a heart block.Congenital heart disease was diagnosed,patient was informed nothing could be done at this point and he was discharged home.We present the evolution of prolonged exposure to high aortic pressures in the development of a very atypical congenital aneurysm.Case Report:Patient was immediately admitted to Coronary Cardiac Unit (CCU). PM Hx included gastritis,and heart block diagnosed at 2 yo. No NKDA and no medications. Only surgery was an appendectomy. Social Hx:Student -tobacco, -alcohol or illicit drug use. On physical exam the patient was cooperative, appeared fragile, unable to speak in full sentences, oriented. V/S were T:37.1,HR:60regular,RR:30 pm,BP: 130/50 mm/Hg, Sat at 99% with NC at 3l/min.HEENT:NC/AT, EOMI,PERRLA.NECK: Supple without carotid bruits, no JVD, bounding carotid pulse. Cardio:heart sounds

were rapid, irregular, with a displaced PMI.A 4/6 diastolic blowing decrescendo murmur heard best at LSB that worsened with hand grip and expiration. Another 4/6 holosystolic murmur was heard at the apex with radiation to the axilla.Lungs:CTAB ABD:NT/ND.Soft+BS. Laboratory work was unremarkable except for a PROBNP of 8,672and TSH=10.14. All three sets of Troponins were negative.AP chest x-ray showed cardiomegaly with blunting of costophrenic angles.CT-Chest angiography showed pulmonary edema, small right sided pleural effusion and dilated inferior vena cava and hepatic veins.EKG showed complete AV block. Three days after admission patient developed SOB with nausea and emesis.Then developed bibasilar crackles.Lasix 40mg I.V. followed by 20 mg I.V.q 12 hours was given with good response.Discussion:Sinus of Valsalva aneurysm(SOVA)is a rare condition with a U.S. frequency of 0.09%.About 25% of reported cases are clinically asymptomatic.The primary cause is congenital,presenting with infective endocarditis,but palpitations or syncope may present secondary to obstruction of the left or right ventricular outflow tract. Dyspnea is by far the most common presenting symptom. Due to clinical presentation,our management consisted of relieving heart failure symptoms and treating arrhythmia. Learning from this case included unusual presentation of complete heart block (from compression of conduction tissues by unruptured SOVA)and arrhythmia associated to SOVA.Congenital SOVA most commonly rupture between 15-30years either spontaneously or secondary to strenuous physical activity,trauma or endocarditis.Asian series demonstrate a higher incidence of right SOVA which more commonly rupture into the RV,higher incidence of VSD and lower incidence of bicuspid AV compared to Western populations.Prognosis is poor with progressive aneurysmal dilatation or rupture unless early surgical repair is performed.Ten year survival post-surgical repair is 94%.Four days after admission patient was transferred to Cardiovascular Center and underwent aortic valve replacement and SOVA repair.

VO#5

CUSHING'S SYNDROME: A RARE CASE OF ATYPICAL THYMIC CARCINOID

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Thymic carcinoid is a rare condition that accounts for .0000001% of all neuroendocrine tumors, 15% of all ectopic ACTH producing tumors, and 2-4% of all anterior mediastinal neoplasms. It is usually diagnosed as incidentaloma on routine chest x-rays. In other instances it is associated with endocrinopathies like Cushing's Syndrome (CS) or multiple endocrine neoplasia type 1 in association with other paraneoplastic syndromes. Its clinical course, dictated by the subtype, typical or atypical, is usually more aggressive in the latter and the diagnosis and treatment is more challenging when associated to endocrinopathies. Clear guidelines for staging and management of this disease are not available in current literature and approximately less than 500 cases have been documented. We review a case of a 39 year old female with history of hypertension and recently diagnosed CS who presented with a 3 month history of generalized weakness, sleeplessness, hyperpigmentation of skin, facial acne, hirsutism, amenorrhea, decreased libido, truncal obesity, emotional instability, skin fragility, weight gain, and alopecia. Symptom onset was abrupt and progressive and due to their severity the patient sought medical advice at outside institution where CS and mediastinal mass were diagnosed. Patient then sought advice at our institution where severe hypokalemia and impaired glucose tolerance was noted. A complete histochemistry panel, CT imaging, and subsequent cardiothoracic surgery evaluation led to a midsternotomy with incisional biopsy of mediastinal mass, excisional biopsy of pericardial tumor seedings, and atrial repair with bovine pericardium patches. Tumor immunohistochemistry showed immunoreactivity with AE1/AE3, synaptophysin, and chromogranin, demonstrating an atypical thymic carcinoid with ACTH producing granules. The patient recovered uneventfully from surgery and was discharged on potassium supplements, antihypertensives, and close surveillance by oncologist and endocrinologist. On follow-up, the patient has developed vertebral compression fractures from excess endogenous glucocorticoids, but tumor recurrence by serial CT's of chest and abdomen have not been detected. At 7 months post-operatively, ACTH levels

remained at slightly above normal levels and AM cortisol at appropriately suppressed levels with octreotide, everolimus, and ketoconazole. All symptoms have gradually vanished with treatment and patient can now freely perform activities of daily living. This case shows the importance of early recognition of ectopic foci of endocrinopathies in particular neuroendocrine tumors. This patient benefited from prompt surgical intervention which is the treatment of choice despite tumor grade. Patient nevertheless needs complex neoadjuvant chemotherapy to prevent recurrence which at this moment no clear guidelines exist. We illustrate a successful multidisciplinary approach towards atypical thymic carcinoids with ectopic CS with radical incisional biopsy of tumor and local seedings, postoperative octreotide, oral potassium supplementation, neoadjuvant chemotherapy, oral antiandrogenic azoles, and teriparatide as a proposed method of management for the disease. Additionally, we revise available literature about current management algorithms for these neoplasms.

VO#6

A PLEURAL EFFUSION OF STRANGE ORIGIN

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Introduction: Primary intestinal lymphangiectasia (PIL) is a rare disorder characterized by dilated intestinal lacteals resulting in lymph leakage into the small bowel lumen and is responsible for protein-losing enteropathy leading to lymphopenia, hypoalbuminemia and hypogammaglobulinemia. The main symptom is predominantly bilateral lower limb edema that may be moderate to severe with anasarca and includes pleural effusion, pericarditis or chylous ascites. Case Presentation A 23-year-old female who had lower extremities edema, nausea, diarrhea and cough, 1 week prior to examination. Physical examination revealed generalized edema, ascites, thoracic dullness to percussion and decreased tactile fremitus bilaterally. Her family and past histories were noncontributory. Chest x-rays revealed moderate size bilateral pleural effusions. Abdominopelvic CT SCAN showed a 5.8 x 5.1 cm thick right wall adnexal mass that suggests ovarian malignancy. Laboratory examination revealed low total serum protein (5.8g/dl) and albumin (2.8g/dl), increased WBC count (15.2 x10^3), thrombocytopenia (71 X10^3), lymphocytopenia (2.3%) and neutropenia (11.5%). Liver function, pancreatic enzymes, urinalysis, occult blood and fecal leukocytes were normal. Transthoracic echocardiogram revealed a mild pericardial effusion. Tumor markers CEA, CA-19-9 and Alpha-Fetoprotein were negative but CA125 was high. Right ovarian mass pathology showed a hemorrhagic theca-lutein cyst. Exudative pleural fluid was negative for malignant cells. Bone marrow reported no evidence of significant immnunophenotype abnormalities. All cultures from blood, urine, stools, pleural fluid and ascitic fluid were negative for the presence pathogen. Finally after extensive workup and rule out of most of the principal causes of pleural effusion, an upper and lower endoscopy with biopsy of the duodenum, terminal ileum and right colon showed findings for protein-losing enteropathy and malabsortion accompanied by endoscopic snow flake appearance; characteristic of PIL. Discussion PIL is a rare cause of protein-losing enteropathy, which is developed primary or secondary. It should always be considered in cases with generalized edema, ascites, pleuritis, and hypoalbuminemia. Diagnosis is confirmed by the presence of intestinal lymphangiectasia based on endoscopic findings with the corresponding histology of intestinal biopsy specimens. Low-fat diet associated with supplementary medium chain triglycerides (MCT) is the cornerstone of PIL medical management. Conclusion Considering the patient's age, symptoms, and unknown underlying factor; intestinal lymphangiectasia should be the cause of protein-losing enteropathy.

VO#7

GIANT CORONARY ANEURYSMS IN A YOUNG ADULT WITH KAWASAKI DISEASE

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Introduction: Kawasaki Disease (KD) is an acute self-limited vasculitis of unknown origin. It is essential to institute early treatment with intravenous gamma globulin to prevent aneurysm formation. We report a case of KD in a previously healthy young man.
Case Presentation: A 21-year-old car mechanic came to the emergency department with a seven day history of

general malaise, lower extremities pain, fever, pharyngitis, headache, and dry cough. He was treated with cefadroxil for 3 days without improvement. On admission the T 38.1o, P 102, RR 18/min, BP 130/71, Wt 252, Ht 78" and BMI 29 Kg/cm2. There was jaundice, conjunctival injection, fissured lips and the tongue was bright red. He had lower extremity muscle tenderness and bilateral non pitting edema at the dorsum of the feet. The Hgb was 11.4gm, WBC 16x103 (neutrophil 87%), PLT 464x103, sedimentation rate 79mm/h, and C-reactive protein 11.60mg/L. The ALT was 432U/L, AST 130U/L, LDH 215U/L, alkaline phosphatase 180u/L, and total bilirrubin 5.4mg/dL. Monospot and influenza tests were negative. An echocardiogram during the acute illness showed a normal ejection fraction, no wall motion abnormalities and a small posterior pericardial effusion. Work-up for diseases with similar clinical findings as KD were normal or negative.

The fever spikes persisted despite treatment with intravenous ceftriaxone. Blood and urine cultures remained negative. By the 7th hospital day, the patient was afebrile with complete resolution of the symptoms. The patient was discharged without a definite diagnosis.

Eleven days later he was admitted to the hospital with intense, persistent oppressive retrosternal chest pain with radiation to the medial aspect of the left arm. On admission the physical exam was normal. The ECG showed ST segment elevation of 1.5mm on leads II, III and AVF. After 50mg of tenectaplase IV bolus the chest pain resolved. Troponin I increased to 21.5ng/ml. The echocardiogram showed normal left ventricular ejection fraction with slight inferior wall hypokinesis and increased of the pericardial effusion.

Coronary angiography demonstrated giant aneurysms of the proximal left anterior descending, circumflex, and right coronary arteries (RCA). Thrombi were evident in the RCA. Therapeutic anticoagulation with warfarin and aspirin started and the patient was discharged.

Discussion: It is crucial, in young adults, to include KD in the differential diagnosis when presenting with febrile illness of more than 5 days duration associated with conjunctival injection, upper respiratory tract changes, rash and lymphadenopathy. A 2-D echocardiogram should be performed to detect coronary arteries abnormalities. When the diagnosis of acute KD is considered treatment with aspirin and IV immunoglobulin is indicated to prevent aneurysm formation.

VO#8

VITAMIN DEFICIENCIES: A CASE OF HOW IT PASSES UNDER THE RADAR

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We present the case of a 57 year old man with no history of systemic illness who presented to our institution transferred from a periphery hospital after laboratories revealed a severe anemia. Patient had been found hours before lost at the edge of the road, with no idea of whom he was or what he was doing in Vega Baja, PR. Patient had awaken that morning as usual and left for work (resident of Caguas, PR) and does not remember why or how he arrived to where he was found. Patient denies visual changes, nausea, vomiting, photo- or phonophobia, fever, chills or history of prior episodes. Upon evaluation at our institution, patient found disoriented in person, time, and place, in no acute distress. Patient slightly pale but appeared talkative and in good mood. Blood work revealed severe pancytopenia (white blood cell count on 2.7 per mL3 with later nadir of 0.7; hemoglobin of 3.3 grams per deciliter; platelet count of 29,000 per microliter of blood with nadir at 6,000), with red cell indices reflecting hyperchromic-macrocytic anemia (mean corpuscular volume of 112.7 femtoliter and mean corpuscular hemoglobin of 37.8, red cell distribution width of 49.9) and a high reticulocyte count (10.7). Chemistries showed hypovolemic hyponatremia, an acute kidney injury with prerenal azotemia and high total bilirubin levels (=3.08 milligrams per deciliter) with indirect bilirubin predominance (=2.24), high lactate dehydrogenase (>2290 units per liter). Head CT without contrast performed revealing no acute intra- or extracranial pathology. Packed red blood cells and platelet transfusions, vitamin B12/folate/TSH/homocysteine levels were ordered, folic acid and subcutaneous vitamin B12 given, and Hematology-Oncology and Gastroenterology services consulted for further recommendations. Patient's hospital stay was uncomplicated, receiving supportive treatment along with vitamin B12 supplementation (low vitamin B12 [=56] and normal serum folate levels found on blood workup). Patient discharged when blood cells stabilized at adequate values with referral to primary care physician, gastroenterologist with intrinsic factor-antibody evaluation and Hematologist-Oncologist. Vitamin B12 is present in foods of animal origin only, with total body stores sufficient for about 2-3 years. It binds to intrinsic factor and absorbed in terminal ileum, and its deficiencies may

be due to numerous etiologies (malnutrition, pernicious anemia, decreased absorption or increased competition of its use as seen in bacterial or tapeworm infections). In the "classic" advanced case of vitamin B12 deficiency, the patient presents with severe anemia and macrocytic red cells with or without varying neurologic disturbances (Hypersegmentation of neutrophils, if present, should suggest the diagnosis, particularly in patients who also have neurologic symptoms, even in the absence of anemia).

VO#9

AN UNEXPECTED ETIOLOGY OF LIVER DISEASE

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A 53 year old man arrived to the Veteran's Affairs Emergency Room (VAER) with a complaint of diffuse abdominal pain of five days of duration, intermittent, 5/10 of intensity, diffuse, non-radiating, without alleviating or worsening exacerbating factors, no inciting events and abdominal distention. Patient reported active drinking of one glass of hard liquor daily and denied family history of liver disease. At evaluation patient found with stable vital signs. Physical examination remarkable for abdominal distention, bilateral gynecomastia, spider angiomata and palmar erythema. Abdominal CT scan demonstrated cirrhosis with portal hypertension, splenomegaly and small amount of ascites. Abdominal ultrasound was performed for possible paracenthesis, but no significant ascitic pocket identified. Empiric antibiotic therapy with intravenous cefotaxime was started to cover for possible spontaneous bacterial peritonitis (SBP). Laboratories revealed a mildly elevated aspartate aminotransferase (AST) of 82 IU/L with mild alkaline phosphatase elevation. Chemistry also showed hypoalbuminemia with coagulation panel with elevated INR (1.79) and prothrombin time (PT) of 20.9 seconds. Serologic studies for hepatitis as well as liver autoantibodies were negative. The patient was admitted to the internal medicine service with a diagnostic impression of chronic liver disease of undetermined etiology. A record review showed that in November, 2009 a monoclonal spike 2.8 g/dl IgG kappa was identified. At that moment a bone marrow biopsy was consistent with 6% of plasma cells. Transferrin saturation was 8% (not compatible with hemochromatosis), with a normal alpha-feto protein level, ceruloplasmin of 22.7 and alpha 1 antitrypsin of 127. Echocardiogram from April, 2012 had pseudo-normalization and concentric hypertrophy, with preserved ejection fraction. Concern for other etiologies of unexplained cirrhosis arose since alcohol ingestion did not correlate with the degree of liver dysfunction. Abdominal fat pad biopsy done which stained positive for Congo Red. Hematology-Oncology Service performed a bone marrow biopsy which demonstrated 18% of plasma cells. Based on the diagnostic studies, our final diagnosis was Light-chain (AL) Amyloidosis consistently with a paraproteinemia (Multiple Myeloma) as the primary cause. This case illustrates an atypical presentation of chronic liver disease with AL amyloidosis as the underlying etiology. The possibility of hepatic amyloidosis should be carefully considered by clinicians in cases of cirrhosis without an apparent cause, especially when the history is not suggestive of alcoholic liver disease. Therefore we cannot assume a patient has cirrhosis secondary to alcohol without a careful history because we may miss important facts: not only that the patient has amyloidosis, but also there could be delay of other life threatening diagnoses such as multiple myeloma.

VO#10

NOT JUST ANOTHER CASE OF SMALL INTESTINAL OBSTRUCTION

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Introduction: Small bowel obstruction is a common cause of hospitalization. The more common causes for mechanical intestinal obstruction are post-operative adhesions, hernias and tumors. In non-complicated patients, a reasonable time before considering surgery is between 2 to 5 days with close monitoring of the patient. We present an atypical case of a 46 yo woman who presented with small bowel obstruction. Case Presentation: A 46 yo woman is admitted to our institution after two previous visits to other institutions. She was presenting nausea, vomiting, some diarrhea, and abdominal distension associated to a 35-pound weight loss. Onset of symptoms was 6 months prior to our admission. Extensive review of previous admissions, including upper endoscopy, colonoscopies and radiologic studies was accomplished. Physical exam of patient was significant for exquisite pain and tenderness of superficial and deep palpation of the epigastric region of abdomen associated to remarkable abdominal distention and rushes Oral

mucosa was very dry with poor turgor of the skin. Rest of the physical exam was unremarkable. Laboratory findings of a previous visit to ER were completely normal with Hgb of 13.9, Hct of 41.3 and platelet count of 358. Patient also had a normal CBC & diff with absolutely no electrolyte disturbances, amylase 40 U/L and lipase 24 U/L. EKG showed tachycardic but regular rhythm, no axis deviation, no ST changes. Abdominopelvic-CT scan with intravenous contrast suggested partial small bowel obstruction without lymphadenopathy. No masses were identified. During admission patient was placed on nasogastric tube suction, I.V. fluids and antibiotics. Given persistence of symptoms she underwent exploratory laparotomy. A mass involving the ileum and cecum was found. Hemicolectomy with segmental small bowel resection was performed. Immediate post-operative course was uneventful and after three days in the ICU, patient was transferred to general ward. Mass pathology was reported as endometrioma. Patient was discharged home six days after admission. Discussion: Ileo-cecal endometrioma as the cause for small bowel obstruction is a rare occurrence. It presents a real challenge to the clinician itself. Depending on the level of obstruction, it can present with a series of non-specific symptoms such as abdominal pain, distension, fecal vomiting, weight loss and constipation. This patient presented with weight loss, abdominal pain and significant abdominal distention. Although clinical dehydration was a key element for admission, she was never complicated by electrolyte abnormalities, respiratory issues or bowel ischemia. We need to consider the possibility of endometriosis, as the cause of small bowel obstruction in any childbearing age female.

VO#11

IDENTICAL TWINS ARE NOT ALWAYS THE BEST OPTION FOR AN ALLOGENIC BONE MARROW TRANSPLANT IN ACUTE MYELOGENOUS LEUKEMIA

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Stem cell transplantation between identical twins, also termed syngeneic transplantation, is rare accounting for fewer than 3% of transplants. We report the case of a 23 y/o male without history of systemic illness that presented with easy bruising, fatigue, nose bleeding and fever. He was found with pancytopenia and a bone marrow aspiration was performed. A diagnosis of an acute myelogenous leukemia with a monosomy of chromosome 7 was done. Induction chemotherapy with cytarabine as continuous infusion for 7 days and idarubicin for 3 days was given. A bone marrow performed 14 days after induction chemotherapy, showed active disease. As a result, reinduction chemotherapy with clofarabine and high dose cytarabine was given, achieving a complete remission. Of note, the patient donated his bone marrow to his identical twin with acute myelogenous leukemia, eight years prior to developing acute leukemia himself. His identical twin, received an allogeneic bone marrow transplant from our patient after achieving complete remission with chemotherapy. Unfortunately, he relapsed few months after the transplant at the age of sixteen. Interestingly, the cytogenetic aberration developed by the recipient after the transplant was monosomy in chromosome 7. Syngeneic stem cell transplant provides a unique opportunity to evaluate the clinical effects of receiving stem cells from an identical haplotype. Unfortunately, no cytogenetic analysis was performed in the donor prior to the transplant. As a result and given that both twins shared the same chromosomal aberration, the recipient received a diseased bone marrow. This case illustrates a situation in which identical twins had the same chromosome aberration causing their leukemia. Higher relapse rates on syngeneic stem cell transplant may be caused, not only because of the lack of graft versus leukemia effect, but also because of the sharing of the same cytogenetic abnormality between the recipient and the donor.

VO#12

SMALL BOWEL OBSTRUCTION IN A PATIENT WITH GOOD SYNDROME

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A 65-year-old man with type II diabetes mellitus and hypertension presented to the emergency room with nausea, vomiting, abdominal pain, and diarrhea of three days duration. The vomit was described as forcible, green, with food content, and no associated blood. Abdominal pain was continuous, involving the epigastrium, right

and left upper quadrants with a pressure quality, 8/10 in intensity that worsened during the night without any alleviating factors. Loose bowel movements were reported to have been present for more than one month with 1-2 episodes a day but intermittent with normal bowel movements in between episodes. He also referred weight loss of approximately 16 pounds during the last year with no change in appetite, along with unquantified fever and chills with profuse nocturnal sweating for the past 2 months. A macular erythematous rash with associated itching on chest and upper extremities was also reported. Two weeks prior to admission, he had been hospitalized with Enterococcus faecalis bacteremia and findings of an anterior mediastinal mass on Chest CT. He received IV antibiotics for 7 days with ampicillin/sulbactam and was discharged to complete therapy as outpatient with amoxicillin/clavulanate for 14 days. Pertaining to the anterior mediastinal mass, sclerosis mediastinitis was diagnosed through biopsy. During this admission, nausea and intractable projectile vomiting continued. An abdominopelvic CT scan showed dilation of the proximal jejunum as well as thickening of the transverse colon, with partial small bowel obstruction. Esophagogastroduodenoscopy showed erythematous mucosa with granular/friable appereance on proximal jejunum and biopsy of the area revealed numerous rhabditiform larvae and eggs. Final diagnosis was small bowel obstruction due to Strongyloides stercoralis. Additional laboratories revealed absolute eosinophil count of 0.5; HTLV-1 and 2 antibody assays were negative. HIV ELISA was non-reactive. Serum Histoplasma antibody as well as urine Histoplasma antigen were negative. IgG levels: 595.0 mg/dL (744 – 1660 mg/dL), IgM: 49.6 mg/dL and IgA: 248.3. Median sternotomy with biopsy of mediastinal mass was done and pathologic analysis was consistent with thymoma. Complete resection was not possible due to involvement of the innominate vein and left pulmonary hilum. Hyperinfection syndrome presents in 1.5-2.5% of patients with Strongyloidiasis. The presentation is insidious, mainly with respiratory and gastrointestinal manifestations as in the case of this patient. Associated mortality when disseminated infection occurs can rise to 87%. Etiologies include malnutrition, chronic infection and immunosupression. This is a very unique case in which the patient presented with Hyperinfection Syndrome and small bowel obstruction, secondary to Strongyloidiasis. Only 8 cases have been reported from 1970 to 2010 with duodenal obstruction as a rare complication. In this patient, predisposing factors for dissemination are immunosupression associated to hypogammaglobulinemia and concomitant presence of a thymoma- also known as Good Syndrome.

VO#13

MYOCARDIAL ABSCESS: A RARE AND LIFE-THREATENING DISEASE

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Our case presents a myocardial abscess secondary to an infected arterio-venous fistula without the presence of infective endocarditis. This is the case of 46-year-old male patient with end-stage renal disease (ESRD) on hemodialysis (HD) for 21 years, an arterio-venous fistula (AVF) in the right arm for 15 years, coronary artery disease, hypertension and mitral valve endocarditis, 2 years ago. Patient arrived at emergency room due to fever, chills, nausea, general malaise, disorientation, arthralgia, chest congestion and worsening of dry cough, which presented one week before hemodialysis. Physical examination remarkable for oriented only in person and place, acutely ill, tachycardic and with bilateral lower extremity edema. No cardiac murmmurs were auscultated. Arterial blood gases revealed respiratory alkalosis and hypoxemia. C-reactive protein: 22.9 mg/dl (normal:5mg/dl). Electrocardiogram showed ectopic atrial tachycardia. Chest x-ray presented a right pleural effusion ,cardiomegaly and an interstitial infiltrate in the lower lungs. Patient was admitted to the hospital with sepsis and suspected pneumonia. Sputum cultures were negative and blood cultures showed a methicillin resistant staphylococcus aureus. On transesophageal echocardiography (TEE) a posterior mitral valve abscess with mitral valve perforation, mild mitral stenosis and moderate mitral regurgitation was observed. Patient received 42 days of daptomycin. Due to calcifications in the aortic arch no surgical intervention was done. After clinical improvement and blood cultures negative patient was discharged home. To our knowledge this is the second case of a myocardial abscess(MA) in a hemodialysis patient with Staphylococcal bacteremia due to an infected arterio-venos fistula without infective endocarditis. Myocardial abscess is a very rare but life-threatening condition. The incidence of myocardial abscess described in the literature in post-mortem series range from 0.1%-1.5%. A high clinical suspicion is needed to make an early diagnosis. Aggressive medical therapy, multidisciplinary team care and early surgical intervention save lives in an otherwise fatal condition.

VO#14

LUPUS ANTICOAGULANT IN A YOUNG MAN AS A RARE CAUSE OF BLEEDING

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Introduction: Lupus anticoagulant (LAC) increases the risk of a hypercoagulable state. It is usually seen in women and associated with arterial and venous thromboembolic events. Less commonly it may produce bleeding. An example of this in a man is presented below.
Case presentation: A 35-year-old morbidly obese man with the diagnosis of LAC, came to the emergency department with jaundice, and a large abdominal wall hematoma, 5 days after laparoscopic cholecystectomy. At age 16 two molars were removed without complications. He had no history of easy bruising, recent infections, use of any medication causing LAC, or family history of coagulopathies. Three weeks before admission a planned cholecystectomy was delayed because a persistently elevated aPTT of 57 seconds (control 26.9) The bleeding time, clotting factors, von Willebrand factor (vWF), and vWF antigen were within normal limits. A 1:1 mixing study not correcting and a positive LAC with its repeat assay established the diagnosis of LAC. Cholecystectomy was performed without plasma transfusion or intraoperative bleeding complications. Hospital course was uneventful except for a 4 cm hematoma around the umbilical incision. On admission : T 38° C, RR 18/ min, P 109 bpm, BP 123/79 mm Hg, Ht 73", Wt 240 lbs (BMI 33.5). The physical examination showed generalized jaundice, a large hematoma with surrounding ecchymoses around the umbilicus. There was no active bleeding or oozing of blood from the surgical incisions. The Hb was 9.9 gm, Hct 30.2%, Plt 456x10^3, WBC 16.2x10^3, and aPTT 50.2 secs (control 27.6). A repeated mixing study 1:1 of aPTT after 2 hours of incubation showed a correction of >70%. Complement levels, rheumatoid factor, antinuclear and anti-ds DNA antibodies and a hepatitis panel were normal or negative. LAC was confirmed by a mixing study with 4:1 dilution that showed an immediate and aPTT-1hr with 37% correction. The patient was treated with dexamethasone 10 mg IV daily for 3 days. There was no further bleeding. He was discharged after 8 days.

Discussion: Excessive postoperative bleeding has been rarely associated to LAC. As in our patient, a prolonged PTT bleeding may occur without a previous history bleeding diathesis.

VO#15

TB OR NOT TB

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43 year old female with past medical history of arterial hypertension who suffered a ground level fall, landing on her upper back, without loss of consciousness. Patient was taken to CDT where a chest x-ray was obtained. Imaging showed a large right sided pulmonary cavitation, reason why she was transferred to our institution. Upon questioning patient stated aprox 5 day history of generalized weakness, associated with pleuritic chest pain, radiated to the upper back, also intermittent cough mostly in the morning with clear yellowish non bloody sputum, poor appetite and subjective fevers. Of note patient was treated for active TB when she was 16 years old, at that time she was in Dominican Republic and her therapy lasted aprox 6 months, she recalls receiving her treatment at home and was visited by a doctor every month. Most recently in November/2011 she had a positive PPD but a negative chest x-ray, however no therapy was offered at that time. Laboratory workup showed mild leukocytosis and thrombocytosis with no major electrolyte disturbances. A noncontrast chest CT revealed a large cavitating lesion involving the right upper/mid lobes, measuring approximately 8cm by 7.7cm by 11cm, with air fluid level with associated varicose bronchiectasis, no lymphadenopathy was identified. Given the possibility of active TB patient was placed in isolation. Infectious disease and pulmonary services were consulted. PPD test was positive with 20mm induration. Sputum samples were negative for AFB three times. In the mean time Interventional radiology was consulted for fluid aspiration but given the high suspicion for TB the procedure was not performed. Subsequently a Bronchoscopy was executed. As a positive finding the right upper lobe had white-greenish appearance. BAL samples were taken. Patient's

clinical status remained unchanged since admission, but given the possibility of lung abscess, Clindamycin IV was initiated, in the mean time patient's condition was being followed by serial chest x rays and chest CTs. Cultures and cytology from BAL were negative for bacterial infection and malignancy respectively, however on 5/30/12 BAL cultures turned out to be positive for Aspergillus Niger, immediately antifungal therapy with Voriconazole was initiated. Patient was then diagnosed with Chronic Pulmonary Aspergillosis which describes a pattern of disease in immunocompetent patients in whom there is formation and expasion of one or more pulmonary cavities over months. One of the most common underlying disease that predispose patients to chronic pulmonary aspergillosis include pulmonary tuberculosis.

VO#16

RAPIDLY PROGRESSIVE AND ALMOST LETHAL PNEUMONIA

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Ivonne Rodríguez MD, Julio Valentín, MD;
Carlos Robles MD, William Rodríguez MD

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65-year-old man with history of coronary artery disease status post coronary artery bypass surgery, aortic valve replacement, hepatitis C and chronic liver disease, who arrived to the emergency room with a chief complaint of fever, chills cough, pleuritic chest pain and shortness of breath for two days. Upon evaluation, he was found with borderline hypotension, tachycardia and fever. Physical examination was remarkable for acutely ill male patient with bibasilar rhonchi with chest radiography significant for right lower base consolidations. Admission labs showed leukocytosis with left shifting, acute renal failure, metabolic acidosis and howell jolly bodies on peripheral smear. He was admitted to internal medicine ward with a diagnostic impression of community acquired pneumonia and empirical treatment was started with ceftriaxone and azithromycin as well. His clinical picture deteriorated drastically in less than 24 hours. Patient required transfer to the Intensive Care Unit due to refractory hypotension, severe lactic acidosis and tachypnea requiring Non invasive positive pressure ventilation. Follow up radiography at this time showed worsening bibasilar consolidation. Antibiotic therapy was changed to vancomycin and cefepime after blood cultures preliminary reported gram positive cocci. After therapy optimization his clinical scenario greatly improved with complete resolution of acidemia and hypotention. As part of the evaluation for fever and positive blood cultures in a setting of a prosthetic aortic valve a transesophageal echocardiogram was requested and reported with evidence of 0.4 cm mitral valve vegetation. During the hospital course he developed confusion with evidence of meningeal signs in physical examination. A lumbar puncture was attempted but unsuccessful. Nonetheless empirical treatment with ceftriaxone was started with excellent response. On the fifth day of hospitalization final blood cultures where reported with Streptococcus pneumoniae serotype 3. The triad of endocarditis, meningitis and pneumonia caused by invasive pneumococcal disease has been described as Austrian's syndrome. This syndrome is a rare disease described in 54 cases with only 20 cases confirmed by laboratory. We present this case as highly suggestive clinical presentation of Austrian syndrome. As described above, mitral valve vegetations were confirmed by TEE, consolidations were found on chest radiography and even though lumbar puncture was unsuccessful, patient neurologic picture is highly depicted as meningitis. Streptococcus pneumoniae is a leading cause of pneumonia, sepsis, and meningitis among adults. Mortality of invasive disease can range from 5-50% depending on serotype. S. pneumoniae serotype 3 is highly virulent associated with major mortality rate secondary to increased content of capsular polysaccharide. This pathogenicity increases resistance to phagocytosis, in addition to wall components and toxins which interplay in the inflammatory response. Prompt recognition by physicians is crucial to provide early goal directed therapy due to its rapid progression to lethal septic shock.

VO#17

A DUAL LEUKEMIA

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A 68-year-old man with medical history of type II diabetes mellitus, hypertension and prostate cancer status post prostatectomy without radiation in 2009 arrived to the emergency department complaining of fatigue and dyspnea on exertion for one month. He also referred an intentional weight loss of 25 pounds in the previous 3 months as recommended by his cardiologist. Patient denied fever, night sweats, bleeding episodes, easy bruisability, and frequent infections. At evaluation, patient was found with borderline blood pressure (92/54 mmHg), sinus tachycardia, dry mucous membranes and pale conjunctiva requiring aggressive intravenous fluids for stabilization. Laboratories were significant for a normocytic normochromic anemia, thrombocytopenia and leukocytosis of 39,000. Patient was admitted to the hematology/oncology ward with a working diagnosis of suspected acute myelogenous leukemias (AML). Peripheral blood smear showed monocytosis and 41% blast cells. Subsequently, peripheral flow cytometry was performed and revealed a monoclonal population of CD34+ cells co-expressing CD19 and CD10. A bone marrow biopsy was attempted, but it resulted in a dry tap. However, immunophenotype for the peripheral smear supported the diagnosis of Mixed Phenotype Acute Leukemia (MPAL), B/myeloid. The patient underwent induction chemotherapy with cytarabine and idarubicin for one cycle. The hospital course was complicated with disseminated intravascular coagulation secondary to bacteremia but fully recovered and completed induction chemotherapy. After 1 month, bone marrow biopsy was performed and showed 2.5% blast cells, no Auer rods and 25% cellularity. There was no evidence of extramedullary disease; platelet and absolute neutrophil count were at 222,000 and 2,000 cells/mL, respectively. Patient was started on maintenance therapy with azacytidine, able to maintain adequate cell count and good tolerance. Cytogenetic analysis of bone marrow biopsy done prior to induction chemotherapy revealed t(9;22)(q34;q11.2) positive for Philadelphia chromosome. Patient was started on desatinib and currently in remission and stable. MPAL is a rare subset of the ambiguous lineage, accounting for less than 5% of acute leukemias, in which markers of more than one lineage are expressed on a single blast population (biphenotypic) or in which two distinct blast populations of different lineages are present (bilineage). We present a case of MPAL with t(9;22) which is even more unusual, accounting for less than 1% of acute leukemia. MPAL is associated with poor outcomes and we are faced with many clinical challenges in diagnosis and treatment. Fortunately, this patient has presented complete remission and he will now start on dasatinib in combination with azacitidine as consolidation therapy.

VO#18

SEVERE PULMONARY HEMORRHAGE, INFECTIOUS OR AUTOIMMUNE?

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22 y/o man with gastritis who presented with 1 week history of diffuse myalgia, fever, chills, nausea, vomiting, headache and chest pain. He sought medical attention and was given acetaminophen and sent home. Symptoms continued to progress and he developed dyspnea and jaundice. He was brought to the ER. Further inquiry elicited history that he slept in a sofa where a dead rat was found. Upon evaluation he was with tachycardia, tachypnea, febrile, adequate blood pressure, acutely ill with jaundice, and clear lungs. Laboratories were remarkable for leukocytosis, anemia, and thrombocytopenia. He was with acute kidney Injury, elevated liver enzymes, direct hyperbilirubinemia, and elevated pancreatic enzymes. He had mixed respiratory and metabolic acidosis and hypoxemia. He was breathing laboriously with accessory muscles requiring intubation. Chest x-ray showed diffuse extensive coalescent patchy opacities in both lung fields, with greater confluence in basal regions. Therefore, he was placed on lung protective measures due to evidence of acute respiratory distress syndrome. In addition patient started to cough blood through endotracheal tube. Hemoglobin continued to drop, requiring multiple transfusions. He developed refractory hypoxemia with worsening acidosis. He was started in intravenous antibiotics (ceftriaxone and doxycyclin). By this time he was hypotensive and norepinephrine drip was started. He was also placed in bicarbonate drip due to severe acidosis. Despite all efforts, patient died within 12 hours from arrival with septic shock, acute respiratory distress syndrome, disseminated

intravascular coagulation, multiple organ failure, and pulmonary hemorrhage and after two prolonged ACLS protocols. He was sent to pathology for autopsy and to the Centers for Disease Control and Prevention of Atlanta for leptospira analysis. Autopsy revealed massive pulmonary hemorrhage, interstitial nephritis, acute tubular necrosis, hepatocellular dissociation, portal inflammation, and myocarditis. Immunohistochemical analysis for leptospira was positive in all organs except the lungs. Leptospirosis is a zoonotic disease caused by spirochaetal agent. It is recognized as an emergent infectious disease with higher incidence in developing countries and tropical regions. Leptospirosis associated pulmonary hemorrhage syndrome is characterized by massive pulmonary bleeding and acute respiratory distress syndrome. Usually these patients have high amounts of leptospiral DNA in lung tissue. However this patient's immunohistochemical analysis was negative in lung tissue. This case is compatible with the literature that proposes that alveolar hemorrhage in leptospira is more of an autoimmune process rather than an infectious one. There are two phases in the clinical manifestation of leptospirosis, a septicemic and an immune one. The majority of the complications occur in the immune phase when the organisms disappear from blood stream and antibodies appear. Internists in tropical areas should be aware of leptospirosis associated severe alveolar hemorrhage. Studies with immunosupressive drugs should be conducted to treat this fatal syndrome in addition to antibiotics.

VO#19

AN UNCOMMON INFECTIOUS DISEASE MIMICKING A CEREBROVASCULAR ACCIDENT

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Progressive multifocal leukoencephalopathy (PML) is a severe demyelinating disease of the central nervous system that is caused by reactivation of the polyoma virus called JC virus. We report an interesting case of an atypical presentation of PML, mimicking an ischemic infarct. A 53 year old man with past medical history of Hepatitis C and Human Immunodeficiency Virus diagnosed on 2003, was consulted due to left sided weakness. HAART (Highly active antiretroviral therapy) was discontinued one year ago. Patient presented with left upper extremity weakness of five days of evolution after an episode of loss of consciousness and involuntary movements. Neurological examination was remarkable for right ear hearing impairment, left hemiparesis (upper more than lower) and clonus at left patellar and Achilles tendons reflexes. Head CT-Scan showed a right frontal parenchymal hypodense area with effacement of the adjacent cortical sulci, with gyriform hyperdensity of the cerebral cortex likely related to cortical laminar necrosis; findings gave the impression of subacute infarct of the right MCA territory. A Brain MRI showed a large T1 hypointense T2/Flair hyperintense white matter lesion at the right frontal lobe, involving the subcortical and right frontal centrum semiovale white matter, without grey matter involvement or mass effect. Considering that a previous Head CT-Scan with contrast did not show enhancement of this area, the aforementioned findings were consistent with PML. While patient was on HAART for 7 months, he did not present any neurological dysfunction. PML is characterized by subacute onset of progressive neurological symptoms. To our knowledge at least one case of PML presenting with acute onset has been reported. Patient's own decision to discontinue HAART for a year reactivated the JC virus. Clinical presentation was with acute neurological deficits and with changes in CT-Scan suggestive of a MCA infarct. Brain MRI, being a more sensitive study, was consistent with PML. HAART is the treatment of choice for PML. Before HAART, HIV patients infected with PML survived an average 2 to 4 months. Patients with PML on HAART clearly have a better survival, although neurological deficits often persist. MRI should be performed in all AIDS (acquired immunodeficiency syndrome) patients with neurologic symptoms considering atypical presentations of different conditions in these immunosuppressed patients. All AIDS patients should be properly informed about the importance of adherence to HAART therapy considering the risk of opportunistic infections. HAART is effective in treating PML, as in this case, and sometimes improves neurological symptoms.

VO#20

THE BUCCANEER'S SYNDROME: A LONG FORGOTTEN DISEASE

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We present the case of a 24 year old woman with history of Crohn's disease that came to our institution with generalized weakness, diffuse abdominal pain, watery diarrhea, anorexia and marked weight loss. Physical examination showed a chronically ill, unkempt woman with marked cachexia weighting 85 pounds. Laboratories exposed a severe anemia (7.3 mg/dL) and hypoalbunemia (< 1.6 mg/dL). Abdominopelvic CT scan showed active Crohn's Disease involving ileum, ileocecal valve and pancolitis with extensive perianal inflammation. The patient was admitted with Crohn's disease exacerbation with possible over imposed infectious diarrhea.

Due to the severe malnutrition she was initially started on total parenteral nutrition clear liquid diet to avoid refeeding syndrome. Diarrhea persisted even after the administration of antibiotics to treat possibility of infectious origin. Patient complained of bleeding gums. Close examination revealed that they were hypertrophic. Skin was brittle and had easily bruising with multiple echymosis. Examination of legs showed erythematous hyperkeratotic perifollicular papules and coiled hair. Patient continued to complaint of weakness, malaise, joint swelling, arthralgias and edema of extremities. She had inappropriate behavior with periods of slow mentation. Most of her symptoms could be explained by severe Crohn's activity and hypoalbuminemia but due to patient's skin and mucosal findings in combination with her poor nutritional status it became evident that she also had severe vitamin C deficiency (Scurvy). Dermatology service was consulted and they confirmed the diagnosis based on the specific clinical features. All of these lesions were photographed and biopsies were taken. They were consistent with skin changes due to nutritional deficiency. The patient was started on Vitamin C replacement. Bleeding of the gums stopped in 48 hours. After 4 days of treatment diarrhea improved. One week after starting treatment there was marked resolution of perifollicular hemorrages. After two weeks hair began to grow without curls and skin changes resolved. Comparisons were made by before and after photography of the patient's skin. Scurvy is a clinical condition widely described in the literature. It was at one time common among sailors, pirates and others aboard ships. This condition, has become increasingly rare up to a point where clinicians commonly overlook it. Vitamin C deficiency is now seen in severely malnourished individuals such as alcoholics, nursing home residents and people on extreme diets. Characteristic symptoms are gum hypertrophy with bleeding and perifollicular hemorrages with curly hair. Other manifestations are fatigue, joint pains, leg swelling, mood changes and increased skin bruisability. Diagnosis is clinical since blood ascorbic acid levels are not reliable. This case serves to remind internists about the importance of complete nutritional assessment of patients. Chronic conditions such as Crohn's disease may mask underlying vitamin deficiencies. This patient clinical status only improved after vitamin C replacement.

VP#1

NON-HIV RELATED CD4 LYMPHOCYTOPENIA IN A PATIENT WITH PULMONARY ASPERGILLOSIS

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We present a case of 76 years old man with history of arterial hypertension and gout that was brought to Emergency Room due to pruritic maculopapular rash that started two days before admission, first noted at his back, then progressively distributed throughout his body. He was taking allopurinol for gout. Physical exam revealed for an acutely ill patient, somnolent, but oriented in 3 spheres. Vital signs showed tachycardia (122 beats per minutes), tachypnea (22 breath per minutes), and borderline low arterial blood pressure (100/60mmHg). He had swelling of tongue, lips, eyelids, as well as oral ulcers. His condition deteriorates with skin detachment of 90% of whole body, presented altered mental status and hypoxemia requiring endotracheal intubation. Intravenous gammaglobulin was administered as well as 6 liters of intravenous fluids. Skin wounds were covered with appropriate dressing, and he was transferred to Intensive Care Unit. The patient was diagnosed with toxic epidermal necrolysis (TEN), confirmed by skin biopsy which shows epithelial necrosis. Unfortunately 2 days later he died. TEN is a dermatologic emergency that is characterized by an acute

epidermal necrosis. It is determined by the percent of body surface area with epidermal detachment involving greater than 30%. Up to 80% of cases of TEN are drug related. Typically occurs within 4 to 28 days after initial exposure. The offending agent induces a major histocompatibility complex-restricted immune response with clonal expansion of CD8+ Cytotoxic T Lymphocytes and production of Interleukin 2, which results in keratinocyte apoptosis. This is an exciting case of a dermatologic urgency, not commonly seen. The patient suffered from TEN secondary to allopurinol, a common etiology. The majority of drug reactions that we commonly see on emergency room are minor skin reactions or angioedema, but rarely a TEN. It is an impressive reaction that we have to treat aggressively, similar to third degree burns. Most common causes of death are from complications such as dehydration, infections and respiratory compromise.This patient deceased quickly despite aggressive management. In the United States the annual incidence 0.22 to 1.23 cases per 100,000 population. Mortality approaches to 40% - 50%. A complete history and physical exam is essential to find the causative agent. Early diagnosis is imperative in order to avoid complications and for prompt management.

VP#2

WHY IS MY PATIENT LOOSING HIS KIDNEYS UPON PNEUMONIA ANTIBIOTHERAPY?

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A 47 y/o male with past medical history of Type 2 Diabetes Mellitus and no previous record of kidney disease, hospitalized due to Health-Care Associated Pneumonia (HCAP), suddenly developed a diffuse skin macular erythematous rash, generalized edema, fever, arthralgias, eosinophilia, and Acute Kidney Injury (AKI), while receiving therapy with Cefepime. Marked elevation of serum creatinine and BUN was observed following several days of antibiotic administration. Laboratory tests showed an increasing trend of serum creatinine levels from base value of 0.8 to 7mg/dl in a period of 20 days. Fractional excretion of sodium (FeNa) reached 8.3%. The patient manifested the distinct and unusual full picture of Acute Iinterstitial Nephritis, eventually confirmed with renal function improvement after discontinuation of offending antimicrobial agent, treatment with corticosteroids, and findings of interstitial inflammatory infiltrates (lymphocytes and eosinophils) on kidney biopsy. AIN is a rare, but important, cause of reversible AKI characterized by immune-mediated tubulointerstitial damage. While incidence of solely 0.7 cases per every 100,000 individuals has been reported, early recognition of this entity and associated etiologies such as medications, infections, and autoimmune processes, still represents a defying diagnostic challenge for the evaluating Physician. Drug induced AIN has been related to the use of Beta-Lactams and Fluoroquinoles among other antibiotics. This case exemplifies the importance of identifying AIN, among the various causes of AKI in our hospitalized patients receiving therapy with Cefepime, a fourth generation Cephalosporin commonly used for HCAP.

VP#3

WHEN ANTICOAGULANT THERAPY ATTACKS: A CASE OF HEPARIN-INDUCED THROMBOCYTOPENIA PRECIPITATING WARFARIN-INDUCED SKIN NECROSIS

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We present the case of a 65 year old woman with history of coronary artery disease s/p two myocardial infarcts and two drug-eluting coronary stents, diabetes mellitus type 2, chronic renal insufficiency, and arterial hypertension who was admitted to our institution with a diagnosis of unstable angina. She was admitted on standard acute coronary syndrome therapy including dual anti-platelet therapy and high dose enoxaparin. The patient underwent left heart catheterization which was complicated with left circumflex coronary artery dissection for which she was successfully treated with a coronary artery bypass graft. The patient had an uneventful recovery and was discharged home.
Two days after discharge home the patient returned to

the hospital with retrosternal chest pain and worsening dyspnea on exertion. The physical exam revealed jugular venous distention, an S3 and bibasilar crackles on lung auscultation. Lower extremity examination revealed distal cyanosis on the toes bilaterally with absent dorsalis pedis pulses and decreased posterior tibial pulses. Labs showed thrombocytopenia (121,000) and elevated troponin levels. Lower extremity Doppler revealed absent absent dorsalis pedis blood flow bilaterally. The patient was admitted to the Intensive Care Unit with a Non ST elevation myocardial infarct, decompensated systolic heart failure and suspected heparin induced thrombocytopenia (HIT). She was started on Argatroban infusion for the HIT. The diagnosis was confirmed with positive anti heparin platelet factor-4 antibodies and serotonin assay. After two days, the patient was started on oral warfarin. Two days after starting oral warfarin therapy a large ecchymosis started to develop over the patient''s right breast with associated hemorrhagic bulla. Warfarin was discontinued due to suspicion of warfarin induced skin necrosis. Dermatology was consulted which performed biopsy and confirmed the diagnosis. Her right breast necrosis worsened and the patient became septic. The patient''s condition continued to deteriorate and eventually died of septic shock. Heparin and warfarin are among the most commonly used anticoagulant agents in the world. Besides the risks of bleeding, heparin-induced thrombocytopenia and warfarin induced skin necrosis (WISN) are well described complications associated with their use. Warfarin-induced skin necrosis has been reported to occur in 0.01-0.1% of patients taking warfarin and the co-existence of both HIT and WISN is extremely rare and provides a therapeutic challenge to physicians as warfarin is commonly used and is a cornerstone in the treatment of HIT. There are few published case reports involving the coexistence of both entities and to our knowledge this is the first case published in Puerto Rico. This case is presented to raise awareness to internists about the possibility of heparin-induced thrombocytopenia precipitating warfarin-induced skin necrosis in patients.

VP#4

NON-HIV RELATED CD4 LYMPHOCYTOPENIA IN A PATIENT WITH PULMONARY ASPERGILLOSIS

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Idiopathic CD4 lymphocytopenia was defined in 1992 as depressed CD4 levels with no evidence of HIV infection and absence of any defined immunodeficiency. The disease is so rare that some studies have been unable to find any patients that meet all the criteria for diagnosis. The rarity of this condition makes it exceedingly difficult to recall when considering all possible differential diagnosis. A 56-year-old woman with a history of hypertension came to the ER referred by her primary physician with symptoms of fever, chills, night sweats, productive cough and an x-ray which showed a mass lesion on the left lung. She was admitted to the hospital with a diagnosis of lung mass and bronchopneumonia. Upon admission, she was started on broad spectrum IV antibiotics and a sputum culture and chest CT-scan were done. Chest CT-scan revealed cavitary lesions in both upper lobes. Throughout the next few days the patient showed minimal improvement despite antibiotic treatment, therefore tests for Tuberculosis , HIV Elisa, bilateral bronchoscopy and CT-scan guided biopsy were done. All tests for TB and HIV were negative, bronchoscopy was negative for malignancy or granulomas and CT guided biopsy showed only the presence of necrotic tissue within the lesions. Finally, sputum culture came back positive for Aspergillus and she was started on treatment with Voriconazole. She had some improvement of her symptoms and was later discharged home to continue oral treatment with Voriconazole. Two weeks later she returned to the ER with symptoms of pleural chest pain, shortness of breath, tachycardia and fever. She was admitted and chest CT-scan, HIV western blot, Rheumatoid factor (RF), C-ANCA and P-ANCA were all ordered. Results of Chest CT once more showed multiple cavitary lung lesions. HIV western blot was negative and RF, C-ANCA and P-ANCA were all negative. Tests for ACE levels, Anti-scleroderma 70 and Immunoglobulin G levels were also ordered and came back within normal limits. Finally CD4 levels were ordered which returned with an absolute CD4 helper count of 290. In light of the CD4 depletion, with no serological evidence of HIV infection and an absence of any defined immunodeficiency, the diagnosis of Idiopathic

CD4 Lymphocytopenia was made. The patient continued with Voriconazole treatment as well as respiratory therapy and pain management, and was discharged home once her respiratory symptoms had improved. She continues to be closely monitored as an outpatient. This case underlines the importance of an extensive differential diagnosis. While most of the time the most obvious diagnosis is the correct one, there are some cases where a truly rare disease will surprise us. Therefore it is important to bring attention to conditions such as idiopathic CD4 lymphocytopenia and keep them in mind when evaluating possible differential diagnosis.

VP#5

PROLACTINOMA, ACROMEGALY AND PREGNANCY: IS IT POSSIBLE?

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Prolactinoma is a frequent endocrine cause of infertility in women. It usually cause infertility because of the inhibitory effect of prolactin on gonadotropin secretion. In addition, Pregnancy is a rather rare event in acromegaly because fertility is often reduced. Acromegaly results from increased growth hormone and its target insulin-like growth factor-1, most commonly due to a pituitary tumor. As it is frequently accompanied by infertility, little is known about the course of this disease in pregnancy. This is a case of 32 y/o female G0P0A0 seen at our clinic nine years ago complaining of persistent, continuous menstrual irregularities due to an elevated prolactin value, and MRI done revealed a Pituitary microadenoma. However she refused treatment. Lost to follow up, seen again at our clinic four years afterwards complaining of recurrent episode of headache. Repeated Pituitary MRI showed a Pituitary Macroadenoma (1.4 cm) with further prolactin elevations. Bromocriptine was started but unfortunately she was unable to tolerate it due to severe side effects such as nausea, vomiting and abdominal pain. Several years later early on 2011 episodes of severe headaches recurred. She was not taking any medications at this time. Another Brain MRI was again compatible with a Pituitary macroadenoma grossly unchanged from the last MRI taken. Prolactin levels were still elevated. Carbegoline treatment was initiated achieving a good medical response consisting of disappearance of clinical symptoms (headaches) and decreased pituitary adenoma size. Once more lost to follow up and on April 2012 seen at endo clinic with history of progressive hands and feet enlargement and marked prognathism. She was pregnant 24 th week of gestation. Cabergoline was discontinued once she knew was pregnant. At this time prolactin was much further elevated together with high levels of IGF-1. She showed no visual compromise during the rest of her pregnancy, however both prolactin and IGF-1 remained markedly elevated. She delivered a normal baby boy without any complications. Our case represents a rare coexistance of two endocrinopathies that usually reduces fertility and pregnancy rates. Furthermore in spite of a pituitary macroadenoma no neurological ophthalmologic complications occurred during pregnancy. The clinical, endocrine and chronological sequence with the eventual appearance of acromegaly is not an usual presentation.

VP#6

METASTATIC LYMPHOEPITHELIOMA TO THE ORBIT: AN AGGRESSIVE RARE NASOPHARYNGEAL TUMOR IN A HISPANIC PATIENT

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A 64 year-old Hispanic male patient with history of hypertension, diabetes mellitus type 2, and hypercholesterolemia presented with three month history of diminished vision and sinus congestion. The patient also reported frontal headaches, retro-orbital pain, photophobia, an occasional bloody discharge from the nose, and decreased hearing in the left ear. Prior to being transferred to our institution, the patient was treated for sinusitis by an otolaryngologist with antibiotics and a CT scan of the sinuses was ordered. The CT scan with contrast demonstrated the presence of an acute pan sinusitis with a chronic component and soft tissue inflammation causing mass effect upon the left medial and inferior rectus muscles. Upon arrival to our institution, a physical examination focused on the head demonstrated an edematous left sclerae, limited abduction of the

left eye, diplopia, periorbital edema, pain to palpation of the frontal and maxillary sinuses, and pain elicited upon left auricle retraction. A bilateral visual acuity test performed for near vision demonstrated a visual acuity in the right eye of 20/30 and in the left eye of 20/40. Laboratory tests, including complete blood cell count, serum chemistry, serum electrolytes, and sedimentation rate, were within normal ranges. Brain MRI demonstrated evidence of a T2 enhancing soft tissue lesion diffuse throughout the parasinuses with extension to the left extraconal orbital surface, and the left cavernous sinus, intracraneal extension through the cribiform plate, and dural involvement suggestive of sinonasal lymphoma. The patient underwent a left inferior orbitotomy and biopsy. A review of pathology was consistent with a sinonasal lymphoepithelial carcinoma. A PET/CT scan with F-18 Fluordeoxyglucose demonstrated scintigraphic evidence of multiple hypermetabolic lesions involving the whole ethmoid region, skeleton, lungs, liver, and extensive lymphadenopathy. The patient was started on urgent radiotherapy of the paranasal sinuses due to visual loss. After completion of radiotherapy, the patient was admitted to the hematology and oncology ward for an initial cycle of systemic chemotherapy with TPF (docetaxel, cisplatin, and fluorouracil). The patient tolerated the therapy well and was discharged to a nursing home unit with plans to continue chemo-radiation. He has since completed six cycles of chemotherapy with an adequate response. Lymphoepithelioma is a malignant tumor that rarely develops in hispanic populations. It is endemic in the Southeast Asian region. It is classified as a nasopharyngeal type III tumor. By the time symptoms present and a diagnosis is made, it is frequently advanced. Almost all cases are associated with the Ebstein-Barr virus infection. Microscopically is an aggregate of malignant epithelial cells in a lymphocytic infiltrate. Treatment consists of combined chemoradiation therapy with TPF regimens for locally advanced tumors. In conclusion, being familiar with this rare malignancy aids in the earlier detection and better outcomes for our hispanic patients.

VP#7

PREVENTIVE MEDICINE AT ITS BEST

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Internal Medicine program Hiatal hernia occurs when a part of the stomach enters the thoracic cavity through a weaken phrenoesophageal ligament. This is a condition commonly encountered in the clinical setting with a vast majority of these been a type I (95-99%), type II (5-1%), or a combination of these two types (type III, rare). It is treated with conservative measures and routine follow ups. A 54-year-old man presents to his doctor for sudden onset of acid reflux, epigastric pain, abdominal distention, increase flatulence, and weight loss. A clinical diagnosis of GERD was made and sent for gastroenterology evaluation. The patient's history was noticeable for moderate use in the past of alcohol and tobacco but denies any history of trauma, surgery, or other causes linked to GERD. On physical examination we found an adequate BMI and an unremarkable physical exam. An upper endoscopy was performed which found a large hiatal hernia with a "J" shaped stomach and erosive esophagitis confirmed by biopsy. Due to abnormal size of the hiatal hernia, an upper GI series was ordered. In addition, treatment with proton pump inhibitors and life style modifications where recommended. At follow up the patient's symptoms had improved with conservative treatment and the result of the UGI revealed a type of hiatal hernia with most of the stomach and duodenum in the thoracic cavity while the esophageal sphincter remained in the intraabdominal cavity. Although the patient reported improvement of symptoms, nevertheless, he was quickly referred for a surgical evaluation in order to prevent future complications. While most of the cases of hiatal hernias are managed conservatively and without additional work-up, we must remember the rare instances when further investigation is warranted. Most patients with this condition are not referred for surgical evaluation until medical treatment has failed. We need to be aware of the patients that are otherwise responding to treatment but are at a higher risk for grave complications like an abdominal obstruction, strangulation, or perforations and require preemptive surgical evaluation.

VP#8

PNEUMONIA IN HIV?... THINK IN KAPOSI'S SARCOMA

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Introduction Kaposi's sarcoma (KS) is a low-grade vascular tumor associated with infection with human herpesvirus 8 (HHV-8), also known as the KS-associated herpesvirus (KSHV). The clinical presentation of KS varies from indolent skin lesions to extensive visceral disease. Case Presentation A case of a 23 yo man, seropositive for human immunodeficiency virus diagnosed three weeks prior to admission and began on standard antiretroviral therapy (ART) by the same time. The patient came to the emergency room complaining of several days of fever, chills, dry cough and worsening dyspnea not resolved by oral antibiotics at home. Initial chest x ray was consistent with bilateral diffuse airspace opacities with lower lobes predominance. A computed tomography of the chest was performed which showed diffuse multifocal airspace opacities predominantly over the mid and lower lung zones with partial consolidation and air bronchograms on most of the left lower lobe. A few hours after the admission, the patient's respiratory symptoms worsened and he developed an acute hypoxemic respiratory failure requiring endotracheal intubation. Upon admission to ICU, Pneumocystis Jiroveci was ruled out by (-) sputum culture. A flexible fiberoptic bronchoscopy performed 24 hours after admission revealed diffused violaceous mucosal lesions extending from the lower third of the trachea and the right and left lung fields and segments consistent with the diagnosis of endobronchial Kaposi's Sarcoma. A few violaceous skin lesions where also noted throughout the trunk and neck. Treatment with ART was given as well as empiric antimicrobial therapy for opportunistic infections pending final Bronchoalveolar lavage reports. A skin punch biopsy was performed confirming the diagnosis. KS was initially described in approximately 6 to 20 percent of HIV-infected homosexual or bisexual men and a small number of HIV-infected patients from other risk groups. The prevalence began to decline prior to the introduction of ART, and further accelerated with the widespread use of these medications. Among patients with KS, approximately one-third will have clinically evident pulmonary disease and one-half will have pulmonary involvement detected at autopsy. Conclusion Even though Endobronchial Kaposi's Sarcoma is not so common in the ART era, this case emphasizes the importance of Flexible Fiberoptic Broncoscopy as a diagnostic tool in HIV positive patients with respiratory symptoms. Early diagnosis and treatment of HIV associated Kaposi's Sarcoma could change prognosis.

VP#9

SYSTEMIC LUPUS ERYTHEMATOSUS, "THE GREAT IMITATOR"

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Systemic Lupus Erythematosus is an autoimmune disease that most commonly affects women. It presents as a multi-system disease caused by immune complexes, autoantibodies, autoreactive lymphocytes, dendritic cells, and local factors. Its clinical manifestations are many, this represent a real challenge to physicians at the time of presentation and diagnosis. GI symptoms are usually mild, with 53% of the cases composed of nausea and vomiting; on the other hand the prevalence of malabsorption is only 9.5% leading mainly to diarrhea and weight loss. A 30-year-old man with unknown medical history arrived at the Emergency Department complaining of abdominal pain of one week duration. He reported having 3-6 episodes of diarrhea per day, 3 episodes of vomiting and unquantified fever. This discomfort had been present for about a year, but last month he went to the ER with worsening symptoms on three occasions and was discharged on oral antibiotics, without a final diagnosis. In this, his fourth visit, the patient was admitted with infectious diarrhea and moderate dehydration. With adequate hydration and IV antibiotics the patient's initial symptoms resolved. However, persistent fever was noted and laboratory evidence was significant for leukopenia, anemia, and a negative HIV test. A thorough workup was indicated due to suggestive hidden systemic disease. After performing a complete workup, remarkable findings were seen on a chest CT Scan with pleural and pericardial effusions, later confirmed by 2D echo. Further testing revealed positive ANA test, Rheumatoid factor, Anti-Smith antibody, Anti-RNP, Anti-Ro and Anti-La.

Putting all these pieces together, along with a thorough history and physical examination, a diagnosis of SLE was imminent. We had been fooled by the GI symptoms and an uncommon presentation. This case exemplifies how patients should be treated as a whole, and even though presumptive diagnoses are made, the internist's role is to investigate and go beyond what is initially obvious, considering pathologies that could frequently be missed. If we had just focused on the resolution of his GI symptoms, his life threatening pericardial effusion would have gone undetected and SLE would have won a fourth time, as the great imitator.

VP#10

AN UNUSUAL PULMONARY PATHOGEN

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Introduction Actinomycosis is an uncommon disease, usually manifested as cervicofacial infection and related to poor oral hygiene or compromised immune function. Pulmonary actinomycosis is rare; its diagnosis is difficult to obtain due to its clinical similarity with other intrapulmonary diseases. Case Presentation A 45-year-old healthy male presented with 2 months history of left upper back pain, fever, weight loss and dry cough. He works as an electricist and has a history of recent travel to Spain. Also he had a dental procedures 2 years ago without follow up. He was admitted to our hospital with heavy chest pain and shortness of breath. Physical examination was significant for tachycardia, tachypnea, decreased breath sounds and dullness to percussion. Labs on presentation showed marked leukocytosis with many bands. The chest radiograph revealed a left sided hydropneumothorax, without exclusion of empyema or mass lesion. Then chest tube was placed and patient was started on broad spectrum antibiotherapy. Computed tomogram showed a multiloculated pleural collection on the left side, with main differential diagnosis of empyema or malignancy. Cytology of sputum with transbronchial brushing and bronchoalveolar lavage were negative for malignant cells, tuberculous and fungal infection respectively. Therefore, he was referred to the thoracic surgeon for a resection through left thoracotomy with pleural decortication and drainage of empyema. Cultures of lung empyema showed growth of Actinomyces neslandi. This patient was discharged uneventfully and underwent penicillin p.o. treatment at our clinic for 2 months. He is alive and well and has had regular follow-up. Discussion Actinomycosis has the characteristic to penetrate the tissue plane, resulting in fistula or abscess formation. Pulmonary involvement is rare, accounting for approximately 15% of all patients with actinomycosis. The diagnosis of thoracic actinomycosis remains a clinical challenge, not only because it is uncommon but also because the culture of this bacterium from the sputum or bronchoalveolar secretions is technically difficult, and sometimes represents mere colonization. A reliable diagnosis of this pathogen still requires histological or microbiological examinations. Conclusion the prognosis of Actinomycosis is excellent if treatment is given in a timely manner.

VP#11

WHEN THE CURE IS WORSE THAN THE DISEASE: THE FATAL PULMONARY MANIFESTATION OF CHRONIC GRAFT VS. HOST DISEASE

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VA Caribbean Healthcare System

Case of a 31 y/o male that referred recent weight loss (16 lbs), shortness of breath, dyspnea on exertion and pleuritic chest pain. Medical history included diabetes mellitus type 2, hypertension, hyperlipidemia, hypothyroidism and nodular sclerotic Hodgkin's disease (diagnosed in 2004) for which he received initial ABVD chemotherapy without adequate response. Our patient developed hypogammaglobulinemia (s/p IV gamma globulin infusion) and underwent autologous hematopoietic stem cell transplant (HSCT) with subsequent relapse for which he received chemotherapy with Gemcitabine/Cisplatin and involved field radiation. The patient later underwent matched unrelated allogenic HSCT in 2006, were he developed afterwards chronic graft vs. host disease (GVHD) with renal, skin and pulmonary involvement. Chronic immunotherapy included oral prednisone, mycophenolate and sirolimus. Patient was last seen at Hematology/oncology clinics during September where his prednisone was tapered down to 5mg daily. In early January, the patient traveled to Nashville Tennessee to his Bone Marrow Transplant Unit for a follow up appointment. Pet/CT scan for restaging purposes was performed which reported negative for malignancy recurrence. Chest CT

scan revealed small right and moderate size left pleural effusions with a hydropheumothorax for which he was sent back to Puerto Rico for further evaluation. Small chest tube catheter was placed for drainage. Pleural fluid was exudative in nature and cytological analysis was negative for malignancy. Patient was diagnosed with progression of Chronic GVHD and suspected bronchiolitis obliterans syndrome (BOS) for which prednisone therapy was increased. Chronic Graft vs. Host disease is a multisystem immune-mediated disorder characterized by immunosuppression and immune dysregulation. It is a severe and debilitating complication following an allogenic HSCT were the transplanted immune cells attack host's body cells. Most common reported risk factors include increased recipient age, HLA disparity, use female donors for male recipients, use of mobilized peripheral blood stem cells and use of donor lymphocyte infusion. Historically chronic GVHD referred to any symptoms developing after post-transplant day one hundred. Manifestations range from inflammatory/acute changes such as edema, rash, mucositis, diarrhea and transaminitis to fibrotic/chronic changes such as sclerotic, lichen-planus skin changes, fasciitis, sicca syndrome, joint contractures, esophageal strictures and bronchiolitis obliterans. While pulmonary manifestations ranges from 40-60% of transplant cases, bronchiolitis obliterans is a less common manifestation particularly of long term survivors of chronic GVHD (5-10%). Bronchiolitis Obliterans is a non-reversible chronic obstructive lung disease caused by fibrous obliteration of the lumen of respiratory and membranous bronchioles. Complications include pneumothorax caused by airleak. It is a diagnosis of exclusion showing persistent obstruction patter in pulmonary function tests and biopsy (surgical open lung > transbronchial biopsy). BOS in this setting is associated to poor prognosis due to lack of definitive treatment and low survival rates. Constant monitoring / screening is imperative since recognition of this irreversible disease is important.

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