Proceedings from the 2011 Annual Meeting of the American College of Physicians, Wisconsin Chapter

The Wisconsin Chapter of the American College of Physicians held its annual meeting in Wisconsin Dells, September 9-11, 2011. Internal medicine residents from each of Wisconsin's 5 residency programs presented their research and/or unusual clinical experiences via posters and vignettes.

PRESENTED POSTERS

Effect of Hyperglycemia on Outcomes in Acute Exacerbations of Chronic Obstructive Pulmonary Disease

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Background: Hyperglycemia is associated with adverse health outcomes independent of its associated metabolic disease states. However, little evidence exists concerning hyperglycemia and outcomes associated with acute exacerbations of chronic obstructive pulmonary disease (AECOPD). This study examined blood glucose (BG) during AECOPD hospitalization and clinical outcomes. We hypothesized that increased BG is associated with worse clinical outcomes.

Methods: We retrospectively studied a cohort of 215 hospitalized patients (40 to 80 years of age) with physician-validated AECOPD from January 1, 2004 to December 31, 2008. Inclusion criteria for this study were a diagnosis of AECOPD at admission and discharge, and BG obtained within 6 hours of hospital presentation. Regression analyses accounting for repeated BG measurements during hospitalization were performed to estimate the odds ratio (OR) for daily mean BG and length of hospitalization, hospital readmission, and 90-day all-cause mortality.

Results: Mean length of hospitalization was 3 days. Adjusting for age and diabetes, decreased BG was associated with longer length of hospitalization (OR, 0.72, 95% CI, 0.54-0.96, $P=0.03$). Forty-one patients (19%) were readmitted to the hospital within 30 days of discharge from index hospitalization. Adjusting for previous covariates and length of hospitalization, BG was not associated with 30-day hospital readmission (OR, 0.82, 95% CI, 0.54-1.22, $P=0.32$). Nine patients (4%) died within 90 days of their index hospitalization. Adjusting for previous covariates and readmission, decreased BG was associated with increased odds of 90-day all-cause mortality (OR, 0.30, 95% CI, 0.11-0.86, $P=0.02$).

Conclusion: Decreased BG levels were associated with a longer hospitalization and 90-day all-cause mortality, suggesting that BG during hospitalization may be indicative of overall health and therefore may be a useful prognostic tool. Blood glucose response (or lack thereof) in light of hyperglycemic agents (96% of cohort received corticosteroids during hospitalization) may be a proxy for a patient's overall physiological status.

Eosinophilic Esophagitis: An Escalating Epidemic?

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Background: Eosinophilic Esophagitis (EE) is a relatively "new" clinicopathological entity characterized by chronic esophagitis and dense eosinophilia of the esophageal mucosa. We sought to determine the incidence of EE, observe the incidence trends between 1995-1997 and 2005-2007, and evaluate the temporal relationship between onset of atopic dermatitis (AD) and EE diagnosis.

Methods: A retrospective cohort study was conducted in a population-based cohort. Esophageal biopsy reports from 1995-1997 and 2005-2007 were screened using SNOMED (Systematized Nomenclature of Medicine) to identify patients with pathologic confirmed or suspected EE. Histopathology reports in which EE could not be excluded and those with features suggestive of EE were reviewed. Cases of esophagitis due to chemicals, drugs, infections, inflammation, and structural abnormalities (tumors, strictures, ulcers) were excluded. A single pathologist blinded to clinical, endoscopic features, and histopathology diagnosis reviewed 373 tissue specimens. Medical records of confirmed EE cases were reviewed to determine associated atopic dermatitis based on American Academy of Dermatology (AAD) criteria, clinical presentation, macroscopic findings on endoscopy, and site of biopsy.

Results: Twenty-seven cases of EE were positively confirmed: 20 adults and 7 children. Median age at diagnosis was 32.1 years. Though 9 patients had some features of AD, none met all the major criteria set by AAD. There was a significant increase in the incidence rates of EE in the study population from 1995-1997 compared to 2005-2007 (2.76 vs 13.6 cases per 100,000 person years). Similarly increased incidence rates were observed in both female (1.91 vs 11.4 cases per 100,000 person years) and male (4.37 vs 18.2 cases per 100,000 person years) populations.

Conclusions: Given the stability of demographic conditions and health care access, our study demonstrates an increase in

incidence of EE from 1995 to 2007 in a population-based cohort that cannot be attributed to misclassification or misdiagnosis. There was no significant association between atopic dermatitis and EE. These findings suggest that EE may be more common than previously realized. Identifying factors that contribute to this increased risk should be subject to further investigations.

Long-term Glycemic Control in Diabetes Mellitus Patients Started on U-500 Regular Insulin

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Background: Glycemic control in types 1 and 2 diabetes mellitus has become more challenging with the rising obesity epidemic. In patients who require insulin doses exceeding 200 units/day, using U-100 regular insulin may not provide adequate glycemic control because of either poorly absorbed subcutaneous depositions or unreliable absorption patterns.

Methods: This study's purpose was to test the hypothesis that switching from U-100 regular insulin to U-500 regular insulin improves long-term glycemic control in diabetic patients who have not attained glycemic control. A retrospective review was conducted for these patients with U-500 begin dates between January 2005 and December 2010.

The primary measure of long-term glycemic control is a long-term reduction in hemoglobin A1C (Ha1c). This is defined at a time point greater than 8 months post U-500 initiation and ending either when the patient discontinued the use of U-500 insulin or at the latest available date. Secondary endpoints studied included change in body mass index (BMI) after initiation of U-500 insulin and change in 6-month Ha1c (collected between 4 and 8 months post U-500 initiation).

Results: The mean change in Ha1c for long-term analysis (n=68) was -1.11±1.95 with *P* value of <0.001 (95% CI: -1.58 to -0.64). The mean long-term follow-up was 35.78±22.62 months with minimum of 9.17 and maximum of 93.99. The mean change in Ha1c after approximately 6 months (n=44) was -1.32±1.66 with a *P* value of <0.001 (95% CI, -1.82 to -0.81); mean change in BMI at 6 months was 0.67±2.42 ($P = 0.082$) and 1.55±5.39 ($P = 0.021$) at the latest date.

Conclusion: U-500 may improve glycemic control, both in the short term and long term for those patients in whom glycemic control is not achieved with U-100 insulin. There does appear to be a small increase in BMI in the long term. One needs to take this into account when deciding whether or not to use U-500. However, this alone should not deter a clinician from considering the use of U-500.

Working Beyond the Duty Hour Rules

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Background: The Accreditation Council for Graduate Medical Education (ACGME) recently announced new guidelines that will allow occasional exceptions to the duty hour rules in very limited circumstances. This study assessed the frequency and circumstances in which house staff might use these exceptions.

Methods: We conducted a cross-sectional survey study of internal medicine house staff at a single academic tertiary care hospital. The anonymous survey asked about the 2 prior weeks of ward service and whether participants would have used the anticipated exceptions, if allowed. Participants also were asked to provide brief descriptions of situations.

Results: Fifty-nine percent of the surveys were returned. Interns and residents each accounted for 50% of the total. Sixty-nine percent indicated they had wanted to stay longer than current duty hour rules allowed. Of those, 55% would have broken the 24+6 hour rule; 33%, the 10-hour rule; and 12%, the 80-hour rule. Continuity for an unstable patient was the most common reason cited for wanting to stay. Humanistic attention for the family or patient and educational opportunities also were cited frequently. Descriptions of these situations illustrated several themes, including concerns for workload, patient acuity, critical decision points in patient care, and doctor-patient communication.

Conclusions: Nearly 70% of house staff identified at least 1 time in the preceding 2 weeks that they wanted to exceed current duty hours. The majority involved providing continuity for an acutely ill patient; however, the doctor-patient relationship, humanistic attention to patients, and workload also were commonly cited. We conclude that after July 1, situations will routinely arise during which house staff will want to stay beyond duty hours, and this may occur more frequently than anticipated by the ACGME.

Resident-Driven Quality Improvement

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Background: There are more than 51,000 deaths in the United States each year from colorectal cancer (CRC) and more than 500,000 patients receiving treatment for end-stage renal disease. Early diagnosis and prevention of both CRC and chronic kidney disease (CKD) leads to better outcomes for patients, making these optimal areas of concentration for quality improvement (QI) initiatives. Using the Wisconsin Collaborative for Healthcare Quality (WCHQ) as a guide for the development and measurement of residents' QI interventions, the Internal Medicine residency program at the Medical College of Wisconsin (MCW) formulated academic, year-long projects to improve outcomes in both CRC screening and health markers in CKD.

Methods: For the CRC project, chart review of clinic patients identified those appropriate for a targeted QI intervention. Different clinic sites implemented strategies for their specific populations and residents' interventions, including reminder letters and patient information pamphlets on the importance of CRC screening. Chart review also was performed to identify patients with at least Stage III CKD. Interventions included frequent follow-up for blood pressure (BP) monitoring, increased low-density lipoprotein (LDL) control, and increased testing for proteinuria. Changes to the electronic medical

record also were introduced to facilitate appropriate interventions for patients with CKD. Outcomes for CRC screening and BP/LDL goals in CKD patients were measured before and after the interventions.

Results: Initial data from the 2009-2010 academic year QI project showed that residents' comfort using QI measurement to improve their clinical skill increased from 52% to 85% after the educational intervention. For the CRC project, evaluation by remaining residents 1 year post-intervention showed increased CRC screening rates across all clinic sites. This includes colonoscopies and other CRC screening modalities. Less data is available for the ongoing CKD project. Mid-intervention review reveals that blood pressure and cholesterol control have improved.

Discussion: Overall, residents have responded positively to the program and have been enthusiastic about implementing the interventions. For both QI projects, resident education on quality improvement as well as on the specific clinical disease being targeted was integral to the program's success. The CRC QI project clearly improved screening rates. Initially, it appears that residents are identifying and treating chronic kidney disease more appropriately.

Omega-3 Polyunsaturated Fatty Acids Decrease Caveolin Expression in Cardiac Fibroblasts: One Possible Mechanism of Fish Oil's Cardiac Benefits

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Background: Heart failure is the leading reason for hospital admissions and is the most costly Medicare expenditure. About half of heart failure cases are due to diastolic dysfunction. One of the main causes of diastolic dysfunction is cardiac fibrosis. Previous study demonstrated that Omega-3 polyunsaturated fatty acids (ω-3 PUFAs, eicosapentaenoic acid [EPA], and docosahexaenoic acid [DHA]) prevent overload-induced cardiac fibrosis and cardiac dysfunction by blocking transforming growth factor β1-induced phospho-Smad2/3 nuclear translocation through activation of the cyclic guanosine monophosphate (cGMP)/protein kinase G (PKG) pathway in cardiac fibroblasts. Previous study also demonstrated that in cardiac fibroblast, EPA and DHA increase cGMP levels by increasing phospho-eNOS and eNOS protein levels and nitric oxide production. Caveolin is the principal structural protein in caveolae, which interacts with endothelial NOS (eNOS) and leads to eNOS inhibition. Therefore, we tested the hypothesis that EPA and DHA decrease caveolin expression in cardiac fibroblasts.

Methods/Results: Confluent cultures of adult mouse cardiac fibroblasts in 6-cm collagen-coated plates were incubated in the presence or absence of the indicated control, DHA or EPA for 24 hours. Western Blot analysis was carried out to determine protein levels of caveolin and glyceraldehyde-3-phosphate dehydrogenase (GAPDH). GAPDH was used as the internal control. Compared with control, DHA (10 mM) and EPA (10 mM) significantly reduced caveolin/GAPDH ratio in cardiac fibroblasts (72% and 65% reduction, respectively $P < 0.05$)

Conclusions: DHA and EPA decrease caveolin expression in cardiac fibroblasts. This study suggests that EPA and DHA increase intracellular levels of eNOS by decreasing caveolin expression in cardiac fibroblasts. Future study is warranted to examine whether over-expression of caveolin in cardiac fibroblast attenuate the EPA- and DHA-induced eNOS activation.

DISPLAYED POSTERS

Testicular Mesothelioma?

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Introduction: Malignant mesothelioma of the tunica vaginalis testis is an aggressive and rare neoplasm, representing less than 5% of all malignant mesothelioma. There are fewer than 200 cases reported to date. It presents as a hydrocele or an intrascrotal mass, and most diagnoses are made from post-operative histopathology. Previous asbestos exposure is reported in 30% to 40% of reported cases.

Case: A 40-year-old African-American man with a past medical history of hypertension and hyperlipidemia presented with left testicular swelling and dull aching pain of 4 months. He had generalized fatigue and unintentional weight loss of 20 pounds in the last 4 months. He denied any trauma to his scrotal area, history of asbestos exposure, or family history of cancer.

On physical examination, he appeared well with stable vital signs. There was no palpable lymphadenopathy. Lung and cardiac examinations were unremarkable. There was no gynecomastia. The abdomen was nontender, and the liver and spleen were not palpable. Left hemiscrotum was markedly enlarged and firm, nontender, and without discrete mass. The right scrotum was normal in size without tenderness or indurations, and he exhibited no extremity edema. Hemogram, liver, and renal function tests and testicular tumor markers were normal. Computed tomography (CT) study showed partially visualized left testicular mass and hydrocele without retroperitoneal, intra-abdominal pelvic laparoscopy. The remainder of the chest, abdomen, and pelvis were normal. Following a diagnosis of left hydrocele, hydrocelectomy showed a nodular swelling along the testis. Histopathology and immunohistochemical report from the paratesticular mass and hydrocele sac was signed out as papillary mesothelia lesion that showed microscopic early invasion. After the histopathology, definitive treatment with left orchiectomy and hemiscrotectomy was done. The patient subsequently was treated with adjuvant chemotherapy with 2 cycles of Alimta and cisplatin. Due to his deteriorating creatinine clearance, cisplatin was switched to carboplatin. Twenty months after diagnosis, the patient was free of metastasis.

Conclusion: Our patient had an unusual neoplasm, mesothelioma of tunica vaginalis testis primarily involving the testes. Because of this clinical scenario's rarity, treatment recommendations are not standardized.

Applying the principles derived from experience with the treatment of mesothelioma of the lung and from limited experience with the management of testicular mesothelioma, we can devise an adjuvant chemotherapy regimen and follow-up modality that may offer good long-term survival. We also recommend post-hydrocelectomy histopathological analysis.

Neutrophilic Eccrine Hidradentis in a Patient with Myelodysplastic Syndrome Receiving G-CSF

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Introduction: Skin rashes are a common and frequently nonspecific finding with varying clinical significance. They are often a manifestation of an underlying process such as infection, autoimmunity, malignancy, or medication reaction. For many clinicians, these findings pose a diagnostic challenge and it may be difficult to determine the exact etiology.

Case: A 54-year-old man with a history of myelodysplastic syndrome was admitted for fever. On admission, his white blood cell (WBC) count was 1.25 K/uL with an absolute neutrophil count (ANC) of 0.490 K/uL. In addition to fever, he complained of right upper quadrant pain. Imaging was negative for acute abdominal pathology. However, he was started on ertapenem for a suspected intra-abdominal infection. Over the course of 3 days his abdominal pain improved but his low-grade fever persisted. On day 4, he spiked a fever of 40°C, and his ANC dropped to 0.08. As a result, he was given granulocyte colony stimulating tactor (G-CSF). Due to continued fever and dropping ANC, on hospital day 6, he was given another dose of G-CSF. That same day, he was found to have developed a nonpruritic, erythematous, maculopapular rash that involved primarily his chest, abdomen, legs, and arms. Skin biopsies were obtained and results were consistent with a diagnosis of neutrophilic eccrine hidradenitis (NEH).

Discussion: NEH is an extremely rare inflammatory skin reaction commonly seen in patients undergoing chemotherapy for hematologic malignancies. It also has been reported in healthy patients, patients with solid malignancies, infections, and in association with certain medications. The eruptions are often seen in neutropenic patients presenting with fever. It is characterized by the sudden onset of erythematous papules and plaques that can affect the trunk, arms, legs, and face including the periorbital region. Lesions are typically asymptomatic but can be tender and pruritic. A biopsy is required for diagnosis, and histology classically reveals neutrophilic infiltration of the eccrine glands with accompanying necrosis. The pathophysiology is not understood entirely but thought to be due to the direct toxic effect of the offending agent in the sweat glands. Another theory is that NEH is part of the spectrum of neutrophilic dermatoses. NEH is self-limiting and resolves spontaneously within 1 to 2 weeks without any long-term sequelae. Steroids, nonsteriodal anti-inflammatory drugs (NSAIDs), and antibiotics have been used for symptom control and to decrease duration. Dapsone also has been suggested for prevention of recurrent NEH.

Not Just Another Viral Syndrome

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Introduction: Acute disseminated encephalomyelitis (ADEM) is a disorder characterized by a monophasic inflammatory demyelination of the central nervous system (CNS). Most cases have been identified in children and usually follow one of the exanthematous diseases, but it also may present with similar clinical features in adult patients.

Case: A 23-year-old woman with no significant past medical problems presented with persistent fever and neck/back pain. She had been evaluated at an outside hospital 2 weeks prior to the current presentation and was treated for aseptic meningitis based on inconclusive imaging and cerebrospinal fluid (CSF) analysis. Pertinent physical exam findings were pain with cervical flexion, bilateral lower extremity weakness, and central visual field defect of the left eye. Her laboratory evaluation revealed leukocytosis, antinuclear antibody negative, rheumatoid factor positive, and elevated serum antistreptolysin-O titer and C-reactive protein. Brain magnetic resonance imaging (MRI) showed new areas of supratentorial white matter signal intensities and bilateral optic nerve enhancement. CSF findings were significant for high opening pressure, lymphocytic pleocytosis, low glucose/high protein, but negative oligoclonal bands. As the hospital course progressed, the only other significant laboratory findings were the positive IgG and IgM *Mycoplasma* serologies. Given the patient's improvement with steroids, MRI findings, and the otherwise negative infectious workup, she was given the working diagnosis of ADEM. A course of systemic corticosteroids, azithromycin, and ciprofloxacin were completed, and the patient made a full recovery.

Discussion: ADEM typically presents with an acute onset of focal neurological signs within days to weeks of an initial nonspecific viral illness or vaccination. It usually follows a monophasic course, and this allows ADEM to be differentiated from multiple sclerosis (MS). However, recently reported adult cases have demonstrated multiphasic presentations; consequently there has been increased reliance on MRI for diagnosis. The radiographic patterns generally are multifocal asymmetric lesions that mainly involve the supratentorial white matter. Key differentiating factors between ADEM and MS are atypical clinical symptoms of MS, absence of oligoclonal bands in CSF, and eventual gray matter involvement. Successful management strategies include corticosteroids, plasma exchange, and intravenous immunoglobulin. Outcome of ADEM is generally favorable in the pediatric population but mortality levels in adults can be high, especially in patients requiring intensive care unit admission or presenting with multiphasic forms.

A Rare Complication Associated with Graves' Disease

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Introduction: Graves' disease is an autoimmune disease that results in an overactive thyroid gland. Autoantibodies act to stimulate the thyroid stimulating hormone (TSH) receptor ultimately leading to an excessive production of T_3 and T_4. Several autoimmune diseases like Graves' disease are known rarely to be associated with neutropenia.

Case: A 33-year-old African-American woman presented with a 1-year history of palpitations, poor appetite, weight loss, lightheadedness, and heat intolerance that had worsened acutely 2 weeks prior to admission. She had a history of Graves' hyperthyroidism that was diagnosed 2 years prior. At the time of diagnosis, she was started on methimazole, but she discontinued the medication about 6 months prior to admission because she felt it was no longer controlling her symptoms. On physical exam, her pulse was 130. She appeared flushed and mildly diaphoretic. She had mild exophthalmos but no lid lag. Her thyroid gland was tender to palpation and markedly enlarged. Her reflexes were hyperactive. On admission, her TSH was undetectable, free T_3 >32.6 pg/ml, and free T_4 >7.77 ng/ml. She also was found to be leukopenic with a white blood cell count of 2600/cu ml and an absolute neutrophil count of 670/cu ml. The patient was admitted with severe thyrotoxicosis secondary to Graves' disease. Her leukopenia and neutropenia were thought to be due to an autoimmune process rather than methimazole. She was started on propylthiouracil and prednisone for her hyperthyroidism and propranolol for symptom control. She was referred to endocrine surgery for definitive management of her Graves' disease.

Discussion: The association between Graves' disease and neutropenia is thought to be due to the production of antineutrophil autoantibodies. It also is speculated that the autoantibodies against the TSH receptor may cross react with thyrotropin binding moieties on neutrophils leading to neutrophil destruction. The treatment for neutropenia secondary to Graves' disease is regulating thyroid function. In addition, methimazole rarely causes agranulocytosis resulting in neutropenia; but in the case described above, this was very unlikely as the patient had been off methimazole for months. It is important to recognize this rare complication associated with Graves' disease and to promptly treat the underlying thyroid dysfunction.

Relationship Between Body Composition and Glomerular Filtration Rate Estimates in the General Population

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Background: Differences in body composition, (ie, lean mass or lean mass percentage) may be responsible for imprecision in estimated glomerular filtration rate (eGFR) estimates from serum creatinine. In this study, we examined the relationship between the eGFR and anthropometric and body composition measures in a large cohort.

Methods: We analyzed data from a cross-sectional study on bone health comprising 1630 randomly selected community-dwelling adults 30 to 86 years old. The Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations were used to calculate eGFR from IMDS-standardized serum creatinine. Body mass index (BMI) and body surface area (BSA) were calculated from measured height and weight. Body composition was determined by dual-energy x-ray absorptiometry, and grip strength was measured. Linear regression models adjusted for age, hypertension, diabetes, and smoking were used to examine the association between eGFR and the variables of interest.

Results: In the fully adjusted models in women, eGFR-MDRD was inversely associated with height ($\beta = -0.08$; $p = 0.012$), lean mass percentage ($\beta = -0.06$; $p = 0.047$), and grip strength ($\beta = -0.15$; $p < 0.001$), and eGFR-CKD-EPI was inversely associated with grip strength ($\beta = -0.08$; $p = 0.001$). In men, there was an inverse association between eGFR-MDRD and lean mass percentage ($\beta = -0.10$; $p = 0.013$) and grip strength ($\beta = -0.12$; $p = 0.022$) and between eGFR-CKD-EPI and lean mass percentage ($\beta = -0.07$; $p = 0.018$). However, there was no association between eGFR calculated using either of the 2 equations and weight, BMI, BSA, lean mass, or fat mass.

Conclusions: The inverse relationship between eGFR and measures of muscle mass and muscle strength suggest that incorporation of these variables might improve eGFR prediction from serum creatinine in the general population.

Spontaneous Hemorrhage into the Mediastinum from a Parathyroid Adenoma

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Introduction: Extracapsular hemorrhage of a parathyroid adenoma is extremely rare yet should be considered in a patient presenting with spontaneous bleeding in the neck and mediastinum. The etiology of this occurrence is currently unknown. Elevated PTH (parathyroid hormone) and calcium levels with specific radiological findings are useful in diagnosis.

Case: A previously healthy 56-year-old female presented with a 3-day history of progressive intermittent left neck pain and dysphagia. She denied fever, chills, weight loss, recent trauma, history of hyperparathyroidism, anticoagulation, or NSAID use. On physical examination, the patient was afebrile with fullness over the left lower neck without ecchymosis. CT of the chest and neck was suggestive of an inflammatory process involving the superior and

posterior mediastinum and an ill-defined, enhancing mass in the left tracheoesophageal groove, starting at the midportion of the posterior aspect of the thyroid.

Laboratory studies showed WBC 4.9 x 10^3/uL, hemoglobin 12 g/dl, serum calcium 11.1 mg/dl (normal 8.5-10.3 mg/dl), and ionized calcium 6.5 mg/dl (normal 4.7-5.5 mg/dl). PTH was elevated at 101 pg/ml (normal 7-53 pg/ml). Her hemoglobin dropped to 8.9 g/dl over the next 3 days although she remained hemodynamically stable. MRI of the chest and neck showed a diffuse process within the lower neck extending into the superior mediastinum suggestive of a hematoma with bilateral pleural effusions. Left neck exploration showed an enlarged left superior parathyroid adenoma with surrounding blood clot and fibrin. Symptoms resolved postoperatively with normalization of PTH and serum calcium levels. A subsequent chest x-ray revealed complete resolution of the pleural effusions.

Discussion: Spontaneous hemorrhage of a parathyroid adenoma is extremely rare. Hemorrhage may be confined to the capsule or extend, as in this case, extracapsularly. Symptoms depend on the size of the adenoma and hematoma and may include a neck mass, swelling, pain or discomfort, bruising, ecchymoses, dysphagia, hoarseness, or dyspnea. Predisposing factors include trauma, use of anticoagulants or NSAIDs, and the imbalance between the growth of the adenoma and available vascular supply. Diagnosis of spontaneous rupture of a parathyroid adenoma without provoking factors is challenging. A high index of clinical suspicion is required in order to make an accurate diagnosis.

Propylthiouracil: Suppressing More Than Thyroid Hormone

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Case: A 56-year-old woman with a past medical history of Graves' disease presented with a chief complaint of fever, chills, nonproductive cough, and general malaise for 4 weeks. Her symptoms began immediately after initiation of propylthiouracil (PTU) therapy for recurrence of hyperthyroidism, though she failed to report this until the day before admission. She was diagnosed with Graves' disease in 1996 and initially treated with methimazole. However, she did not tolerate this and was switched to PTU. She received this therapy for 2 years, after which time it was stopped due to remission of her disease. At this presentation, the patient had a temperature of 100.3°F, rigors, exudative tonsil lesions, and an erythematous pharynx. She had a mild normocytic anemia (hemoglobin 9.2 g/dL) and thrombocytopenia (platelet count 123 e3/uL), but more substantially her white blood cell count (WBC) was 1.3x10^9/L with an absolute neutrophil count of zero, TSH was 0.015 µU/mL. PTU was discontinued after consultation with hematology affirmed concern for PTU-induced pancytopenia. She was not started on granulocyte colony stimulating factors (GCSF) since little evidence suggested a benefit in PTU-induced agranulocytosis. The patient had recovery of neutrophils on hospital day 10 to 1.8x10^9/L. Her neutrophils remained above 1.5 x10^9/L during the remainder of the hospital stay, and she had a WBC of 4.8 x10^9/L, hemoglobin 11.8g/dL, and platelet count of 265e3/uL on the day of discharge. She underwent radioactive iodine ablation (RAI) for definitive treatment.

Discussion: Thionamides (PTU and methimazole) are first-line options for treatment of Graves' disease, with methimazole being preferred in nonpregnant patients since it is more effective with fewer side effects. Agranulocytosis is a rare, serious complication of thionamides occurring in 0.3% of patients, with pancytopenia being even more rare. Therefore, physicians and patients must be aware of symptoms of agranulocytosis, discontinue the medication, and perform further evaluation immediately. Routine monitoring is not recommended since agranulocytosis develops suddenly, though typically within the first 3 months of therapy. The median time to resolution of agranulocytosis is 10 to 14 days. Case reports and a small prospective study have not shown an improvement in recovery times with G-CSF. Instead, discontinuation of the thionamide and supportive treatment with antibiotics for neutropenic fever is recommended. Then either RAI or thyroidectomy should be pursued for definitive treatment.

Another Great Masquerader

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Introduction: Human immunodeficiency virus (HIV) is an increasingly prevalent disease, and early diagnosis is important to prevent the spread of infection and to begin prompt treatment. Acute retroviral syndrome (ARS) describes the clinical signs and symptoms of primary HIV infection, which includes the period from initial HIV infection to HIV seroconversion.

Case: A 19-year-old man with a past medical history of chronic constipation and seasonal allergies presented with complaints of rectal pain for 1 week along with fever, chills, and malaise. Prior to presentation, he had been evaluated at an outside hospital and underwent a rectal exam under anesthesia with no identification of abnormalities. On presentation at our institution, physical exam was significant for a low-grade fever, maculopapular rash on his torso, and perianal mucosal ulcerations. Initial lab evaluation was significant for elevation of hepatic transaminases and thrombocytopenia. He was admitted for further treatment and evaluation, and ceftriaxone was initiated to cover for Gram-positive bacterial infections, including sexually transmitted diseases. Rectal swabs were negative for herpes simplex virus (HSV) and bacteria, including group A streptococcus and *H. ducyeri.* Further laboratory workup was negative for viral hepatitis, syphilis, gonorrhea, and chlamydia. Initial HIV antibody assay also was negative, but serum HSV serologies (IgG and IgM) were positive. When informed of his HSV infection, the patient admitted to having 13

male sexual partners in the last year, which prompted concern for an acute retroviral infection. HIV RNA polymerase chain reaction (PCR) was ordered and revealed an HIV viral load of over 700,000. The patient was discharged home with outpatient infectious disease clinic follow-up. As an outpatient, antiretroviral medications were started, and the patient's HIV viral load eventually became undetectable after 6 months of therapy.

Discussion: The initial presenting signs and symptoms of acute retroviral syndrome are often nonspecific. The most common presentation is an acute mononucleosis-like illness characterized by fever, sore throat, and lymphadenopathy. Other symptoms include lethargy, malaise, myalgias, weight loss, headache, and a diffuse maculopapular rash. Acute retroviral syndrome also can involve multiple organ systems. Muscosal ulcerations of the oropharynx, esophagus, and the genitalia have been reported to occur in 28%, 17%, and 6% of patients respectively. Involvement of the gastrointestinal system can include vomiting and diarrhea along with pancreatitis, colitis, and epiglottitis. Hepatitis is a common presentation that often resolves as the host's immune system gains control over the initial viral replication. Other laboratory abnormalities include anemia, leucopenia, and thrombocytopenia. Neurologic involvement most commonly includes headaches but also can include aseptic meningitis or encephalitis. The signs and symptoms of ARS usually begin within 2 to 4 weeks of initial HIV infection and last approximately 2 to 3 weeks. During the primary HIV infection, the viral load is very high and the patient is highly infectious. Early identification is important, not only for initiation of antiretroviral therapy to preserve the host's immune responses, but also to decrease transmission through patient education and therapy. Clinicians should have a high index of suspicion of ARS in patients with generalized mononucleosis-like symptoms and risk factors for HIV infection.

Fulminant Pseudomembranous Colitis

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Introduction: Clostridium difficile is a cause of pseudomembranous colitis that commonly presents as diarrhea after antibiotic use. Diagnosis of this disease may be difficult in patients with other chronic gastrointestinal disease and may lead to increased morbidity and mortality.

Case: A 45-year-old woman with celiac disease presented with diarrhea, vomiting, abdominal pain, laryngitis, rhinitis, and fever. She had not been adhering strictly to a gluten-free diet, and she recently had undergone treatment with cephalexin for a toenail infection. She also was exposed to sick contacts through her employment at an assisted living facility. Initially, she was started on zanamivir for likely influenza infection, and she returned home. The next day her symptoms became worse and she reported to a different clinic where she was referred to the emergency department (ED) due to dehydration and an acutely tender abdomen. On examination, her abdomen was soft but tender in the periumbilical region with guarding. Abdominal CT revealed pancolitis but no free air. Her white blood cell count was 18,100/mm3, and her stool *C. difficile* nucleic acid amplification test (NAAT) was positive. She felt significantly better the next day after receiving intravenous (IV) hydration, oral vancomycin, and antiemetics. She was discharged home on metronidazole and recovered to her baseline over the next 3 days. She then had a recurrence of symptoms 11 days later and reported to the ED. She again tested positive for *C. difficile* and was started on oral vancomycin and IV metronidazole. Her abdomen was soft but more tender than before. On hospital day 2 her abdominal pain and diarrhea worsened significantly. Surgery was consulted and an exploratory laparotomy was deemed necessary. She underwent total colectomy with end colostomy. Her condition improved after surgery, and the rest of her hospital stay was uneventful.

Discussion: C. difficile is a spore-forming Gram-positive rod that produces 2 exotoxins (A and B) and typically causes infections in the setting of antibiotic use and immunosuppression. It is believed that alterations in the normal flora caused by antibiotics and immune dysfunction allow *C. difficile* competitive and selective advantage in the gut flora. Exposure to the bacteria at the time of antibiotic use is not always necessary due to its presence in the normal flora of 2% to 5% of the general population. The clinical presentation can range from a few days of mild diarrhea to life-threatening pseudomembranous colitis. Although *C. difficile* is a well-known cause of diarrhea, diagnosis in patients with other gastrointestinal diseases sometimes may be missed.

My Blood Gets Too Thin with Warfarin

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Case: An 85-year-old man presented to the hospital with shortness of breath and coughing up blood. He had been admitted just 2 weeks prior for non-ST Segment Elevation Myocardial Infarction (NSTEMI), atrial fibrillation with rapid ventricular rate (RVR), bilateral pneumonia and was discharged on warfarin 4mg per day for atrial fibrillation and moxifloxacin for pneumonia. International normalized ratio (INR) on discharge was 1.3. After discharge, INR was monitored closely due to drug interaction between warfarin and moxifloxacin. He did well, but a few days later had to stop taking warfarin due to supratherapeutic INR. He then started developing progressive shortness of breath followed by nose bleeds and hemoptysis for which he presented in the TEC and was found to be hypoxic with Pa02 of 49.7 on 3L. INR was noted to be >9 and partial thromboplastin time (PTT) was 67.3. Direct visualization of nasopharynx with a rigid scope revealed areas of scabbing and old bleeding sites in the left anterior naris. Vitamin K and multiple units of fresh frozen plasma (FFP) were given; INR dropped to 1.6 but climbed up again requiring additional doses of vitamin K.

Patient had not taken more warfarin than recommended nor was there evidence of him taking super warfarin or brodifacoum. Brodifacoum levels were checked and were negative. Wafarin levels checked during his hospital stay revealed warfarin level of <1 despite an INR of 2. He was tested for VKORC1 and CYP450 2C9 and found to have genetic polymorphism involving both genes resulting in decreased production of an enzyme that metabolizes the active isomer of warfarin to inactive products and also decreased availability of vitamin K, making him very sensitive to warfarin.

Does Size Matter? Uncemented Total Hip Arthroplasty in Obese vs Non-Obese Patients: An 18- to 27-Year Follow-up Study

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Introduction: This study's purpose was to evaluate the incidence of aseptic loosening with use of an uncemented tapered femoral component in obese vs nonobese patients at 18 to 27 years (mean 23.5 years).

Methods: Between 1983 and 1987, 285 consecutive uncemented total hip arthroplasties were performed with use of a tapered stem. The patients were divided into 2 groups, obese and nonobese, as determined by their body mass index (BMI). There were 105 obese patients (119 hips, BMI ≥ 30) and 156 nonobese patients (166 hips, BMI < 30). The outcome of every femoral component with regard to stem fixation, revision, or retention was determined for all 285 hips. Complete follow-up was obtained on the 97 patients (111 hips) surviving a minimum of 18 years (range 18 to 27 years).

Results: Of the 119 hips in obese living and deceased patients, 1 stem (1%) had been revised for aseptic loosening and one was loose by radiographic criteria. In the 55 surviving hips, none had been revised for aseptic loosening and one was loose.

Of the 166 hips in nonobese living and deceased patients, none had been revised for aseptic loosening and one was loose by radiographic criteria. In the 56 surviving hips, none had been revised for aseptic loosening and one was loose. No significant difference between the 2 groups with regard to clinical outcome or perioperative complications was found.

Conclusion: Uncemented tapered stems provide excellent fixation in obese and nonobese patients out to 27 years.

Unraveling the Mystery: A Patient with Dancing Feet

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Introduction: Painful legs and moving toes (PLMT) syndrome is a rare medical disorder characterized by involuntary movements of the toes or the whole foot and pain in lower limbs.

Case: A 63-year-old man presented with complaints of involuntary movements in both legs over the last 8 to 10 years. These movements could be momentarily suppressed by voluntary action and did not persist during sleep. He also described a deep, aching, burning pain with fluctuating intensity in both legs. Electrodiagnostic, laboratory, and imaging studies were normal. Physical exam revealed semi-rhythmic flexion-extension and occasional abduction of the phalanges in both feet, especially the great toes, characteristic of PLMT syndrome.

Discussion: Spinal cord and cauda equina diseases, neuropathies, radiculopathies, drugs, and other systemic diseases are the main causes of this syndrome, although many cases still are idiopathic. The involuntary movements appeared bilaterally in the toes in our patient, which suggests that central reorganization (especially in the spinal level) is the cause of PLMT. Electromyogram (EMG) and nerve conduction studies have proven helpful in demonstrating spontaneous arrhythmic bursts of affected muscles and the underlying neuropathy in some patients.

Conclusion: Physicians should be aware of this rare debilitating condition. Though much progress has been made in elucidating its etiology, its exact mechanism still remains a mystery. It is important to consider PLMT in a patient with painful legs and/or restless leg syndrome without any significant history of neurological disease or trauma. Diagnosis is essentially clinical, and treatment is complex, including different combinations of drugs and invasive techniques with a poor outcome.

Lactic Acidosis and Confusion After a Fall

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Introduction: Confusion is a common reason for patients seeking urgent medical care. The causes are numerous with many that are potentially life-threatening, including toxic ingestions.

Case: A 52-year-old male presented with confusion and loss of coordination 24 hours after a fall with a binge drinking episode. During evaluation at an emergency department the evening of his fall, a head CT and basic metabolic panel were unremarkable. At breakfast his wife noted he was experiencing slowed and inappropriate speech and difficulty coordinating his gait. By the time he was admitted, his neurologic exam had become unremarkable. Initial laboratory evaluation showed an increase in creatinine to 1.11 from 0.76 mg/dl and a decrease in bicarbonate to 16 from 28 mg/dl the day prior. An arterial blood gas showed an anion gap metabolic acidosis with respiratory compensation. His serum lactate also was elevated markedly at 23 mmol/L. Urinalysis revealed occasional calcium oxalate crystals. Upon further questioning, the patient admitted to an attempted suicide prior to his fall by consuming 1 cup of ethylene glycol. Ethylene glycol level subsequently returned at 135 mmol/L. He was started on a fomepizole and bicarbonate drip and his anion gap acidosis resolved within 24 hours.

Discussion: Ethylene glycol is a widely available chemical found in industrial products. It is responsible for dozens of deaths in the United States annually. While ethylene glycol itself is relatively nontoxic, it is bro-

ken down into calcium oxalate and other harmful metabolites that can cause oliguric or anuric acute kidney injury. Usual presentations include development of mild central nervous system (CNS) effects such as inebriation and sedation, which are exacerbated with coingestion of ethanol. Other neurologic symptoms include cranial nerve palsies, tetany, and cerebral herniation in large doses. Renal manifestations are oliguria and hematuria due to crystal deposition. Workup in suspected poisonings should include basic chemistries, arterial blood gas, serum osmolality, and electrocardiogram (ECG). It also is important to rule out coingestion and establish the level of ingestion. Treatment in mild to moderate levels of ingestion consists of competitively inhibiting alcohol dehydrogenase and normalizing the patient's pH, with bicarbonate drip if necessary. More profound ingestions may require acute hemodialysis for the removal of this toxic and often lethal chemical.

A Case of Strongyloidiasis Unmasked by Corticosteroids

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Introduction: Most cases of strongyloidiasis in the United States are subclinical. They may occur seldom in debilitated or immunocompromised patients, and immunosuppressive agent recipients. We describe an unusual case of strongyloidiasis with intestinal and pulmonary manifestations in a Puerto Rican immigrant. His disease was unmasked after receiving high dose corticosteorids for pneumonitis.

Case: Our patient was a 75-year-old Puerto Rican man with multiple admissions over the past 3 months for progressive shortness of breath of uncertain etiology. He was diagnosed with asthma exacerbation and treated with corticosteroids, antibiotics, and bronchodilators. Prior to receiving corticosteroids, he had modest peripheral eosinophilia. Extensive workup led to a diagnosis with acute respiratory distress syndrome of unknown etiology with diffuse alveolar damage on biopsy. High-dose corticosteroids did not lead to clinical or radiological improvement. He started complaining of lower abdominal pain. Colonoscopy revealed superficial ulcerations and erythema in the ascending colon. Fusiform-shaped larva were noticed on the cecal biopsy. A positive repeated stool ova and parasite indicated *Strongyloides stercoralis.* A 2-day regimen of ivermectin was given, corticosteroids dose decreased. He returned 4 days later with progressive shortness of breath and was found to have pneumothorax and persistent diffuse bilateral lung infiltrates. His condition deteriorated with respiratory failure and failure to thrive. At that point, the patient and family opted to discontinue treatment. He was eventually discharged to hospice care and expired shortly after.

Discussion: Strongyloidiasis in immunocompetent hosts is asymptomatic, often limited to incidental finding of peripheral blood eosinophilia. However, in immunocompromised hosts, it often causes disseminated disease. Our patient most likely acquired the infection in Puerto Rico where he worked as a farmer. He was asymptomatic until he received high dose corticosteroids, which unmasked the diagnosis.

Spontaneous Upper Extremity Myonecrosis Secondary to Clostridium Septicum: Clue to Colonic Malignancy

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Introduction: Clostridium septicum can be differentiated from other *Clostridium* species by causing nontraumatic gas gangrene in tissues. Once culture is positive for *Clostridium septicum* in gangrenous tissue, suspicion of colorectal malignancy should be high. By hematogenous spread, *Clostridium septicum* will cause nontraumatic gas gangrene in immunocompromised patients with colorectal malignancy. The case report will portray a need for workup for underlying malignancy in the setting of spontanous nontraumatic gangrenous *Clostridium septicium* myonecrosis.

Case: A 49-year-old man with no significant past medical history presented to the emergency department (ED) with left-sided upper abdominal pain of 1 day duration with emesis, bloody diarrhea, right upper arm pain, and cramping. On physicial exam, he was diaphoretic, tachycardic, afebrile. Right upper arm, shoulder, and forearm and lateral chest wall were significant for swelling and mottling of skin with moderate tenderness and crepitence. X-ray showed extensive subcutanous emphysema. Antibiotics were started. Emergency surgical debridement and fasciotomy were performed. The arm was not salvagable and amputation was performed. Postoperatively, patient developed septic shock and was on mechanical ventilation. The culture from debridement was positive for *Clostridium septicum*. Abdominal CT did not show any masses. After resolution of septic shock and weaning from ventilation the patient underwent colonoscopy, which showed a 3-cm ascending colon mass; pathology report presented as tubulovillous ademona with intramural adenocarcinoma. Patient underwent hemicolectomy and was staged as IIIa (Dukes C).

Discussion: This case represents the importance of association between rare cases of *Clostridium septicum* nontraumatic gangrenous myonecrosis and occult malignancy. It emphasizes the need for extensive workup to exclude malignancy, especially colorectal cancer.

Recurrent, Reversible Acute Kidney Injury: Puzzles, Pointers, and the Allure of Internal Medicine

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Introduction: Sarcoid, noncaseating granulomatous interstitial nephritis (GIN) is an underrecognized entity of a well-known disease. Although first described in 1933 by Garland and Thomson, less than 50 case reports exist in literature. In 1 autopsy series, 20% of patients with sarcoidosis were noted to have GIN.

Case: We report a 76-year-old man who was referred for nonoliguric acute kidney injury

(AKI) (baseline creatinine of 1.3 mg/dL in September 2009 and 2.2 in September 2010) in the background of hypertension on fosinopril, atrial fibrillation on warfarin therapy, prostatic adenocarcinoma (prostate-specific antigen 11.42ng/mL, T2a Gleason grade 3+3/10), pulmonary sarcoidosis quiescent since 2006, and gastroesophageal reflux disease on omeprazole. Clinical exam was noncontributory.

In the absence of other abnormal laboratory parameters, failure to recover on withholding fosinopril, increasing creatinine 3.6 mg/dL, and expressed unwillingness to proceed with a kidney biopsy given warfarin use, the patient was advised to discontinue omeprazole and consider an empiric trial of prednisone for possible omeprazole-induced vs sarcoid interstitial nephritis. In 4 weeks, his renal indices recovered to 2.3 mg/dL and steroids were discontinued. However, he returned in 3 months with a recurrent episode of AKI (creatinine 5.6 mg/dL), evidence of mild hypercalcemia (10.7 mg/dL), normal intact parathyroid hormone (iPTH) and polyuria. The clinical pointer led to a kidney biopsy in the absence of pulmonary evidence of active sarcoidosis and a differential of metastatic prostatic carcinoma. It confirmed noncaseating granulomatous involvement, without acid-fast bacilli or evidence of vascular involvement. He was restarted on steroids, with dramatic improvement in renal indices (creatinine 2.3 mg/dL, Ca 8.8, iPTH 70 in 4 weeks of treatment).

Conclusion: In addition to highlighting all facets of sarcoidosis and renal GIN, this case demonstrates the relevance of recognizing the uncommon and sometimes subtle, extrathoracic pointer (hypercalcemia, past response to empiric steroid trial) of a relatively common disease. Furthermore, it underscores the allure of conundrums in medical practice that are not only challenging but also profoundly satisfying. This patient clearly had an eminently curable disease that was otherwise relentless and destined to saddle him with dialysis and its antecedent morbidity.

Papillary Thyroid Cancer in Monozygotic Twins

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Introduction: Numerous studies have demonstrated a slightly greater concordance for cancer in monozygotic twins. Also, in studies comparing familial with sporadic papillary thyroid cancer, some investigators have reported higher rates of multicentric tumors, lymph node metastasis, vascular invasion, and local invasion in familial forms. Two case reports published in 1955 and 1988 emphasized the role of genetic factors in twins with papillary thyroid cancer and we are reporting one more case diagnosed incidentally in a set of 37-year-old monozygotic twins.

Case: The first twin was referred to us by her OB/GYN for an incidentally discovered thyroid mass. Ultrasound-guided fine needle aspiration (FNA) cytology of the mass revealed papillary thyroid carcinoma; pathologic diagnosis at the time of total thyroidectomy indicated multifocal disease with metastases to local lymph nodes.

The second twin, healthy and completely asymptomatic, was referred to us by her sister for screening. Thyroid ultrasound showed bilateral small thyroid nodules, one of which was confirmed by FNA to be papillary carcinoma. Interestingly, she too was found to have metastatic disease at the time of surgery. Post ablation total body radioiodine scan detected persistent activity in the thyroid bed—not an uncommon finding. Within the following 6 months, the patient discovered new left neck lymphadenopathy. Lymph node mapping by ultrasound followed by FNA confirmed bilateral metastatic papillary carcinoma. The patient was referred for elective neck dissection; postoperative thyroglobulin level and imaging results are pending.

Discussion: Although the genetic basis for familial papillary thyroid cancer is yet to be completely understood, screening with ultrasound and FNA is warranted in monozygotic twins, as this report provides further evidence that the familial form of papillary carcinoma of the thyroid may exhibit aggressive behavior.

An All-Consuming Case

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Case: A 44-year-old man with a history of incarceration presented with 2 weeks of headache, fever, and night sweats. He reported progressive breathlessness, a 30-pound weight loss over 4 months, and photophobia. His admission temperature was 104°F. Chest x-ray demonstrated diffuse bilateral pulmonary interstitial nodular opacities that were concerning for miliary tuberculosis. His serum Quantiferon tuberculosis (TB) test was positive. Histoplasma, blastomyces, Pneumocystis carinii, cytomegalovirus (CMV) and HIV assays were negative. Bronchoscopy with bronchoalveolar lavage was performed, but sputum acid-fast bacilli smears were negative. Empiric antituberculosis chemotherapy was initiated with isoniazid, rifampin, pyrazinamide, and ethambutol. His headache and photophobia worsened. Cerebrospinal fluid (CSF)analysis showed 85 WBC with 9% lymphocytes, protein of 70mg/dL, glucose of 47mg/dL and a negative acid-fast bacillus (AFB) smear. Brain MRI showed innumerable supra and infratentorial 3-6 mm ring enhancing lesions with surrounding edema, consistent with tuberculomas. The final diagnosis was miliary tuberculosis with intracranial tuberculomas. Dexamethasone was added to his antituberculosis chemotherapy, with rapid resolution of his headache and fevers. He was discharged on directly observed therapy and prednisone. After discharge, his sputum cultures grew Mycobacterium tuberculosis.

CNS tuberculosis occurs in 1% of all TB cases in immunocompetent individuals. It carries a 15% to 40% mortality. Tuberculomas are extremely uncommon in the West, but they account for 20% to 30% of intracranial space occupying lesions in children in India and Asia. Classic CSF findings include low glucose and high protein and cell counts (with lymphocytic

predominance). Serial CSF AFB smears greatly improve the diagnostic sensitivity. TB CSF polymerase chain reaction (PCR) has 55% sensitivity and 95% specificity. Typically, isoniazid, rifampin, ethambutol, and pyrazinamide are used for 2 months, with isoniazid and rifampin being continued for a total of 12 months (18 months with tuberculomas). Multiple randomized control trials have demonstrated decreased mortality in patients who receive steroids in the treatment of TB meningitis.

A Tale of 2 Granulomas

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Introduction: Wegener's granulomatosis and blastomycosis are both granulomatous diseases that are difficult to diagnose, especially if both simultaneously affect the lung. Accurate diagnosis is important as it has therapeutic implications.

Case: We describe a 74-year-old man, ex-smoker, who presented with a 2-week history of bilateral conjunctivitis with left dacroadenitis. He was seen by ophthalmology 1 week prior to admission, when he was diagnosed with bilateral conjunctivitis and presumptively treated with antibacterial eye drops. However, the conjunctivitis worsened warranting a hospital admission, during which chest radiography demonstrated an area of lobar consolidation. The patient initially was treated for community-acquired pneumonia and bilateral conjunctivitis with IV antibiotics without improvement in either the lung consolidation or conjunctivitis/left dacroadenitis. Initial and repeat eye cultures were negative. Bronchoscopy with washing and biopsy of the lung lesion demonstrated numerous inflammatory cells without malignant cells. Subsequently, the patient underwent a CT-guided core biopsy with the same results aforementioned. He was continued on IV antibiotics without improvement. Given that his conjunctivitis also was not improving, biopsy of the lacrimal duct was performed and demonstrated granulomas. Subsequent, serologic testing was positive for cytoplasmic antineutrophil cytoplasmic antibodies (c-ANCA) and anti-proteinase 3 (PR3) antibodies. Also at this time, fungal culture from bronchoaveolar lavage grew a slow-growing mold, later identified as blastomycosis. Ultimately, the patient was diagnosed with both Wegener's granulomatosis without renal involvement and blastomycosis, and was treated for both with IV cyclophosphamide, prednisone, and itraconazole. Follow-up chest radiography showed improvement of the lung lesions with clinical improvement of the conjunctivitis.

Discussion: Wegener's granulomatosis and blastomycosis are 2 rare granulomatous diseases, one being an autoimmune disease process and the other a fungal infection. Diagnosis of either can be challenging, and diagnosing both at the same time can be a diagnostic dilemma. Part of diagnosing either is based on a good history. However, there can be atypical presentations, which require more focus on serology and histology.

VIGNETTES

Anaplasmosis as a Mimicker of Thrombotic Thrombocytopenic Purpura

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Introduction: Anaplasmosis is an illness endemic to the upper Midwest transmitted by *Ixodes scapularis.* It can mimic thrombotic thrombocytopenic purpura (TTP) insofar as it presents with thrombocytopenia, fevers, altered mental status, and acute kidney injury, but without microangiopathic hemolytic anemia. Early recognition in endemic areas can prompt rapid resolution and proper utilization of health care resources.

Case: A 59-year-old man with coronary artery disease (CAD) presented with 2 days of confusion, fevers, unsteady gait, and nonbloody diarrhea. Upon presentation, he was febrile, hypotensive, and disoriented. His exam was significant for the lack of hepatosplenomegaly, lymphadenopathy, or petechiae/purpura and was otherwise unremarkable. His complete blood cell count (CBC) revealed WBC 5.4, Hb 14.6 and platelets 35. His creatinine was 4.3 mg/dL indicating acute kidney injury and his lactate dehydrogenase (LDH) was 619 U/L. His smear revealed numerous burr cells but very few schistocytes. Hemolysis labs were negative. He was admitted to the intensive care unit (ICU), volume resuscitated, and started on broad-spectrum antibiotics. Given his constellation of symptoms, there was concern for TTP hemolytic uremic syndrome (HUS), so plasmapheresis was begun. His mental status began to improve before plasmapheresis was started however, and further history revealed that the patient bred horses in rural Wisconsin and admitted to multiple tick bites. Subsequently, *Anaplasma* and *Ehrlichia* DNA PCR tests, Lyme screen, and *Babesia* smear were collected. Doxycycline was started for empiric treatment of tick-borne illness. The patient's clinical condition, kidney function, and platelet count improved in the first 36 hours. *Anaplasma phagocytophilum* DNA returned positive 3 days later and his ADAMTS13 activity returned normal, further proving that he did indeed have anaplasmosis and not TTP-HUS. He required no further interventions and was discharged in stable condition with a 3-week course of doxycycline.

Discussion: Anaplasmosis and other tick-borne illnesses can present similarly to TTP-HUS, however there is no evidence of microangiopathic hemolytic anemia in the former. Tick-borne illnesses should be added to the differential depending on season and geographic location. This patient's initial improvement can be attributed to prompt treatment with antibiotics and not due to the plasmapheresis he received. Prompt recognition and treatment of anaplasmosis by internists and ED physicians can help avoid potentially unnecessary and expensive interventions such as plasma exchange, dialysis, and admission to the ICU.

An Unusual Case of Cardiac Tamponade

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Case: A 19-year-old man presented with a 1-week history of diffuse myalgias, arthralgias, subjective fevers, and initial sore throat. At the time of admission, he also had developed chest pain and dyspnea. Exam revealed a pericardial rub and sinus tachycardia. Lab findings included leukocytosis (WBC peak of 43.70, 91.3% granulocytes), anemia, and thrombocytopenia. Chest x-ray was significant for a left lower lobe (LLL) infiltrate. Transthoracic echocardiogram (TTE) revealed a trivial pericardial effusion without tamponade. Patient was started on NSAIDs for pericarditis and IV ceftriaxone and azithromycin for presumed community-acquired pneumonia.

On hospital day 2, he developed right upper quadrant (RUQ) pain, and an abdominal CT was significant for hepatosplenomegaly and retroperitoneal/mesenteric lymphadenopathy. On hospital day 3, he developed increased chest pain and dyspnea and repeat TTE was suggestive of impending tamponade. He was intubated secondary to acute respiratory failure, and an emergent pericardial window was placed. Chest x-ray revealed diffuse infiltrates. Bronchoscopy/BAL were unrevealing. The patient then developed a diffuse maculopapular rash and became febrile to 102.4°F with prior low-grade fevers. Infectious disease was consulted and extensive work-up was completed with negative cultures and testing for HIV, Epstein-Barr virus, CMV, influenza, enterovirus/coxsackie, adenovirus, parvovirus, Lyme, anaplasma/ehrlichia/rickettsial panel, tularemia, chlamydia, brucella, fungal antibody panel. Anti-histoplasma Ab was positive. Itraconazole was initiated.

Due to a largely negative infectious work-up, lack of clinical improvement, and concern for adult-onset Still's disease (AOSD), rheumatology was consulted. Ordered labs all were negative with the exception of a significantly elevated ferritin of 11,888 ng/ml, C-reactive protein (CRP) 29.5 mg/dl, and erythrocyte sedimentation rate (ESR) 83 mm/hour. Patient was started on high-dose steroids and began to clinically improve. He was discharged on prednisone and itraconazole. The working diagnosis was AOSD vs disseminated histoplasmosis. Follow-up testing for histoplasma Ab was negative. The patient's final diagnosis was AOSD.

Discussion: Adult-onset Still's disease is a rare inflammatory disorder with yet unclear etiology. Diagnosis may be guided by the Yamaguchi criteria. The major criteria include intermittent fever of at least 39°C for > 1 week, arthralgias for > 2 weeks, characteristic skin rash, leukocytosis with > 80% granulocytes. The minor criteria include sore throat, lymphadenopathy, hepatosplenomegaly, abnormal liver function tests, and negative antinuclear antibody (ANA)/ rheumatoid factor (RF). Significantly elevated ferritin levels also are seen in up to 70% of patients with AOSD.

Diabetic Myonecrosis: Diagnostic and Therapeutic Pitfalls

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Introduction: Diabetes and consequent end organ damage of retinopathy, nephropathy, and neuropathy are well recognized. However, Diabetic Myonecrosis (DMN), a relatively rare, potentially life- and limb-threatening complication is underrecognized and often misdiagnosed.

Case: A 43-year-old morbidly obese man with poorly controlled diabetes (HbA1C 10.8% - 17.5%) presented with a subacute history of a very painful thigh of approximately 10 to 12 weeks duration. He denied any history of trauma, fever, or chills. Musculoskeletal exam revealed a profoundly swollen, tender distal right thigh without skin breakdown, erythema, or crepitus, and a range of motion limited by pain. Anterior and posterior thigh compartments were soft without evidence of elevated compartment pressures. Peripheral pulses were palpable, reflexes mildly diminished, and a left diabetic foot ulcer was noted. Labs revealed anemia (7.9g/dL), mild leukocytosis, and elevated CRP (19.3 mg/dL). A Doppler ultrasound ruled out deep venous thrombosis. A presumptive diagnosis of cellulitis with edema was made.

Four days later, in the absence of objective improvement and new onset acute kidney injury (AKI, creatinine 2.6 mg/dL), he was noted retrospectively to have subacute persistently elevated creatinine kinase ranging from 564 to 369 IU/L). A urinalysis revealed diabetic proteinuria (2.54 g/mg) with a benign sediment. A diagnosis of DMN was made and confirmed by MRI with gadolinium. It revealed profound edema in the subcutaneous fat, perifascial, multifocal enhancement of the quadriceps and adductor muscles, in addition to an extensive area of absent enhancement within the right vastus medialis suggesting muscle necrosis. He subsequently was dialyzed temporarily to remove gadolinium. A muscle biopsy was consciously withheld to avoid infection. Conservative therapy with bed rest, analgesia, and short-term immobilization resulted in improvement. Most recent creatine kinase (CK) was 88 U/L.

Conclusion: Heightened awareness for the occurrence of DMN as a complication of diabetes so frequently observed in clinical practice would facilitate prompt recognition, avoid invasive diagnostic interventions, and prevent iatrogenic morbidity. Institution of conservative management may in all likelihood culminate in improved outcomes. This case also highlights the role of MRI as a diagnostic tool and the role for prophylactic temporary hemodialysis to decrease risk for nephrogenic systemic fibrosis in the background of gadolinium exposure and AKI.

Myxedema Madness, Stertor, and Rhabdomyolysis

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Introduction: The clinical presentation of thyroid hormone deficiency is diverse, subtle, and nonspecific. We describe a case of

a patient with myxedema presenting with unusual clinical features of stertor and muffled voice.

Case: A 59-year-old man presented with 1-month history of shortness of breath, stertor, and 2 days of visual hallucinations. He was diagnosed with hypothyroidism 4 days prior to presentation and was prescribed levothyroxine 100 mcg once daily. Physical examination showed temperature 97.6°F, blood pressure 144/80 mm/Hg and pulse 76 bpm. He was alert and oriented with stertorous breathing pattern. His voice was muffled and skin was thick, coarse, and dry. There were no palpable thyroid nodules. Lower extremities showed nonpitting pretibial edema.

Emergency fiberoptic laryngoscope was performed showing upper airway narrowing with mucosal thickening. Laboratory studies were significant for thyrotropin (TSH) 54.69 uIU/ml, CK 21963 U/L, aspartate aminotransferase 625 U/L, sodium 106 mmol/L, and chloride 75 mmol/L. Ultrasound of neck showed diffuse, multinodular goiter. Treatment was initiated with nasopharyngeal airway, continuous positive airway pressure (CPAP), hypertonic saline 3%, IV, hydrocortisone, and thyroid hormone replacement. Hydrocortisone was discontinued when the results of cortrosyn stimulation test showed normal response.

Discussion: Our case highlights the multisystem clinical manifestations of myxedema. Stertor refers to heavy snoring sound heard during respiration. Stertor and muffled voice, as seen in patients with myxedema, are due to the deposition of connective tissue component in pharyngeal tissue causing airway obstruction. Psychiatric manifestations include cognitive dysfunction, affective disorders, psychotic features, or so-called myxedema madness. Failure to recognize and promptly initiate therapy with thyroid hormone replacement is associated with mortality as high as 60%. Hydrocortisone should be administered until the results of the cortisol levels are known since failure to treat in the presence of adrenal insufficiency could result in adrenal crisis.

Pulmonary Nodules and Fever in an Immunosuppressed Patient

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Introduction: Histoplasmosis is a fungal infection that presents as a flu-like illness. It is typically self-limited in healthy patients and resolves without intervention. In immunocompromised patients, histoplasmosis is more likely to progress to fulminant disease without intervention. The nonspecific presentation of histoplasmosis in immunocompromised patients challenges clinicians by fostering a broad differential diagnosis. The potential for early progression to fulminant disease in immunocompromised patients lends to the importance of an aggressive work-up and early treatment.

Case: A 73-year-old white woman with a 30-year history of Crohn's disease presented to her internist with a 3-day history of intermittent fevers, chills, night sweats, weakness, and arthalgias. The patient did not have any respiratory symptoms upon presentation, however, her history was significant for a productive cough that spontaneously resolved 1 week prior to developing fevers. The patient's medication regimen included nightly total parenteral nutrition (TPN) infusions, infliximab, rifaximin, and moxifloxacin. Initial ambulatory work-up was unremarkable for an infectious or neoplastic etiology. On subsequent ambulatory work-up, chest CT revealed multiple pulmonary nodules with mediastinal and hilar lymphadenopathy. The patient was admitted and underwent bronchoscopy, which did not yield a diagnosis. The patient's symptoms continued to progress. On hospital day 5, mediastinoscopy yielded specimens containing Histoplasma capsulatum. Subsequent serology and antigen studies were negative suggesting nondisseminated disease. The patient was treated with fluconazole and her symptoms resolved after 7 days. Serial CT scans at 14 and 24 weeks showed a favorable response to treatment with a reduction in the size and number of pulmonary nodules.

Discussion: Histoplasma capsulatum is a dimorphic fungi often present in soil. It is endemic to the Ohio and Mississippi River valleys. Infection occurs through direct inhalation of microcondidia. Primary manifestations depend on the degree of exposure and the immune status of the host. Approximately 10% of immunocompetent patients develop a self-limited flu-like illness characterized by fevers, chills, night sweats, cough, and myalgias. Chronic pulmonary and disseminated infections occur most frequently in immunocompromised patients. Serology and antigen studies are highly sensitive and specific for differentiating between isolated pulmonary infections and disseminated disease. Effective treatment of progressive or chronic infections includes amphotericin B, fluconazole, and itraconazole. Immunocompromised patients may require lifelong treatment to prevent recurrence.

Diagnosed Skin Deep

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Introduction: Pyoderma gangrenosum (PG) is most often associated with inflammatory bowel disease (IBD); however, rare subtypes may be associated with underlying malignancy.

Case: A 64-year-old white man presented from an outside facility with a 6-week history of a warfarin and catheter-directed thrombolysis-resistant deep vein thrombosis and a 2-week history of two progressively enlarging ulcerations on his left leg. These lesions were initially dime-sized, but by the time of transfer, had progressed to diameters of 20 cm and 25 cm. His physical examination was significant for left lower extremity edema and exquisite tenderness. Skin biopsy showed a dense, diffuse, neutrophilic infiltrate in the superficial and deep dermis consistent with PG. Tissue cultures were negative for bacterial and fungal elements. Initial labs were significant for an isolated anemia with hemoglobin of 8.0 g/dL, which had been stable throughout his hospitalization. However, repeat assay revealed pancytopenia with WBC 4.6 x 10^3/uL, hemoglobin

6.9 g/dL, and platelets 158 x 10^3/uL. Blood smear revealed 2% unclassifiable cells. In the context of pancytopenia and unclassifiable cells on the peripheral smear, a bone marrow biopsy was obtained to evaluate for myeloid malignancy. The aspirate contained 33% blasts with a hypercellular core biopsy, which confirmed the diagnosis of acute myelogenous leukemia (AML). The patient was started on treatment with oral prednisone, but his hospital course was complicated by an episode of atrial fibrillation with rapid ventricular response and acute kidney injury. Due to these comorbid conditions, he was not a candidate for induction chemotherapy, and after initiating hemodialysis, he developed acute respiratory failure. Following a goal-setting discussion, his family chose to proceed with comfort measures only. The patient died on hospital day 18.

Discussion: PG is a rare disease often associated with inflammatory bowel disease. However, it has been described in other disorders, including acute myelogenous leukemia (AML). PG primarily affects young to middle-aged adults, but it has been described in all age groups. The type of PG described in patients with underlying hematological malignancy is usually the superficial bullous subtype of PG. It appears as an aggressive, painful, necrotic lesion with superficial bullae that break down to form an ulcerated lesion with undermined edges. The surrounding skin has pathognomonic violaceous borders. The course of the skin lesion parallels the hematological disorder. The presence of PG is an ominous sign with one study citing 23 cases with only 4 patients living past 8 months. Treatment usually consists of steroids for the PG and treatment of the underlying malignancy or disorder. As described above, outcomes generally are poor when associated with PG.

Curse of the Caribbean

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Case: A 74-year-old woman with rheumatoid arthritis treated with hydroxychloroquine developed 1 episode of mild gastroenteritis of 1 to 2 days duration while on a week-long vacation in the Caribbean. Six weeks later, the patient was admitted to a local hospital with gradual worsening of her chronic back pain, generalized weakness, frequent falls, and episodes of confusion. She was afebrile with stable vitals and had marked back pain with movement. Palpation tenderness was present in the paraspinal region of her lower back. Head CT and x-ray of lumbar spine was unrevealing. Blood cultures grew *Salmonella* serotype Enteritidis. The patient received IV levofloxacin for 5 days, and with clinical improvement, she was discharged with an additional 5 days of oral levofloxacin.

Three weeks later, the patient was readmitted to the same hospital with complaints of persisting back pain, weakness, and confusion. She had a fever of 104.2°F with midline lumbar tenderness. After transfer to our hospital for further care, we performed an MRI of the spine that showed L4-L5 diskitis. Blood cultures and disc space aspirate cultures grew *S. enteritidis*. Abdominal CT showed a 2-cm saccular mycotic aneurysm of the distal abdominal aorta. While on ceftriaxone, patient underwent aneurysmectomy with aortic reconstruction using autologous spiral saphenous vein graft. Tissue culture from the resected aneurysm also grew *S. enteritidis.* She was continued on ceftriaxone for a total of 6 weeks. Her pain improved and she was doing well when seen 2 months later at follow-up in clinic.

Discussion: Mycotic aneurysm is a rare but serious complication of nontyphoidal *salmonella* bacteremia, occurring most commonly in the abdominal aorta. This case demonstrates the importance of clinicians' awareness that adults with a relapse of *salmonella* sepsis often have a serious endovascular infection. This risk is increased in patients above 50 years of age with atherosclerosis. Anti-*salmonella* antimicrobial therapy should be started and a CT or MRI with contrast should be performed on an emergency basis. Following diagnosis, surgical resection of the aneurysm with in situ graft revascularization, the procedure of choice, should be done as soon as possible. Postoperative antimicrobial therapy for 6 to 8 weeks based on ESR and clinical response is recommended.

Early Lung Cancer Presenting as Hoarseness

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Introduction: Hoarseness is a symptom with numerous causes, including malignancy. Rapid determination of its source is necessary to identify serious but potentially curable etiologies.

Case: A 42-year-old white man with a 25-pack-year smoking history presented with a complaint of 4 weeks of hoarseness. On further interview, the patient also had dyspnea, productive cough without hemoptysis, and weight loss of 50 pounds over 3 months. Besides mild tachypnea and anxious appearance, the patient's vital signs and physical exam were normal. Similarly, his complete blood count and basic chemistry panel were within normal range, and a urine drug screen was negative. His chest x-ray revealed densities superimposed over the left upper lobe, thought to represent either a deformity of the left 3rd rib or a pneumonic infiltrate. Chest CT with contrast was obtained to further evaluate this finding and revealed a 2.8-cm left upper lobe mass accompanied by ipsilateral hilar adenopathy involving the aorto-pulmonary window (through which the left recurrent laryngeal nerve courses). In follow-up, bronchoscopy with biopsy showed non-small cell lung cancer, ultimately staged as T2N1M0 (IIB). He was thereafter scheduled for video-assisted thorascopic surgery-based resection of the neoplasm.

Discussion: Lung cancer remains the primary cause of cancer death in the industrialized world, and diagnosis at an earlier stage is more amenable to potentially curative surgical intervention. In the primary care setting, historical details shown to be independently associated with a diagnosis of lung cancer include hemoptysis, dyspnea, cough, anorexia, weight loss, and cigarette use. Hoarseness is less often associated with pulmonary neoplasia but

still caused by extra-laryngeal malignancy 13.5% of the time, and by lung cancer most often among these (6.6%). Therefore, given the grave nature of lung cancer, it is important to consider it as an etiology when assessing the complaint of hoarseness, especially when accompanied by the listed independently associated symptoms. Although the primary diagnostic modality in evaluating hoarseness is laryngoscopy, neck and chest CT should be considered when laryngoscopy is normal or identifies vocal cord paralysis of uncertain cause.

Recurrent Acute Myocardial Infarction in a Patient with Immune Thrombocytopenic Purpura

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Case: A 58-year-old white woman with medical history of immune thrombocytopenic purpura (ITP) (but no known coronary artery disease history) was admitted with shortness of breath and chest pain. ECG and cardiac biomarkers demonstrated an acute ST-elevation myocardial infarction (STEMI). Coronary angiography was performed urgently and revealed thrombosis in the mid-left anterior descending (LAD). Aspiration thrombectomy of the LAD was performed successfully. No lesions were detected in the LAD or other coronary arteries that required stenting. Heparin, eptifibatide, aspirin, and clopidogrel were instituted prior to thrombectomy. The patient developed recurrent chest pain with new ST-segment elevations and cardiogenic shock in the following 18 hours. Another coronary angiogram showed repeat extensive thrombosis of the LAD with distal embolization. Large clot burden was painstakingly extracted but distal perfusion remained suboptimal. Hypercoagulable state was suspected due to recurrent thrombosis without anatomical lesions, and extensive coagulation work-up was done that turned out negative. The patient was placed on anticoagulation, aspirin, and clopidogrel without bleeding complications or thrombocytopenia. To reduce the risk of thrombocytopenia bivalirudin instead of glycoprotein IIb/IIIa antagonists were used for the second myocardial infarction. Prednisone was continued for maintenance treatment of ITP.

Discussion: ITP predominantly causes bleeding but also may be associated with thrombotic events. The mechanism of arterial thrombosis in ITP patients is still unclear, but several hypotheses exist. Thrombolytic therapy is contraindicated in acute myocardial infarction in ITP patients. Primary percutaneous coronary intervention (PCI) can be safe in this setting. During and post PCI procedure, glycoprotien IIb/IIIa inhibitors and anticoagulation should be used cautiously. Dual antiplatelet therapy can be well tolerated in some patients. Another consideration that needs to be pointed out is that the major goal for treatment of ITP is to provide a safe platelet count rather than correcting the platelet count to normal levels.

A Case of Atypical Adenoma and Papillary Thyroid Carcinoma

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Introduction: Atypical parathyroid adenoma is a rare etiology for primary hyperparathyroidism. These neoplasms share some histologic characteristics with parathyroid cancer but do not meet the rigorous criteria of cancer. One such case and a discussion of the differential diagnosis of primary hyperparathyroidism are presented here.

Case: A 79-year-old woman with a history of cholelithiasis was brought to the ED for generalized weakness following a flight. Associated symptoms included weight loss, constipation, and decreased mental acuity. Physical examination revealed significant muscle wasting of the thenar eminence and a thyroid nodule. Lab work was significant for calcium of 18.0 and PTH 1558. Initially, she was treated with pamidronate and hydration. Ultrasound of the thyroid showed mass in the left thyroid lobe and a soft tissue lesion interposed between the superior left thyroid lobe and common carotid artery. Further imaging revealed the nodule had intense sestamibi and mild iodine activity, suggestive of a thyroid cancer with a closely associated parathyroid neoplasm. She received definitive therapy with total thyroidectomy, node dissection, and parathyroidectomy. Histopathology showed papillary thyroid carcinoma of follicular variant, and an atypical parathyroid adenoma. The parathyroid mass did not clearly fit criteria for malignancy, but the local invasion and presence of coagulative tumor necrosis led to treating this as a parathyroid carcinoma. Patient tolerated the surgery well and was discharged from the hospital on calcitriol and close follow-up.

Discussion: Parathyroid carcinoma, atypical parathyroid adenoma, and parathyromatosis account for about 2% of cases of primary hyperparathyroidism (PHPT). This patient's nonspecific clinical course, and extremely elevated serum calcium and parathormone are typical findings of parathyroid carcinoma. The concomitant finding of associated thyroid cancer is very rare, only having been reported 5 times before. The long-term treatment plan will necessarily involve close surveillance for recurrence as the patient does not clearly need radio or chemotherapy.

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