Proceedings from the 2010 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 10-12, 2010. 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

Phlegmasia Cerulea Dolens Involving the Left Extremity

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Introduction: Deep Vein Thrombosis (DVT), postphlebitic syndrome and recurrent venothromboemboloism is a major health concern leading to considerable morbidity and mortality. Identifying acquired or inherited thrombophilic and structural factors leading to thrombosis is important in order to provide appropriate treatment and prevent complications.

Case: A 49-year old woman presented with a 10-day history of left buttock and thigh pain and a 2-day history of marked swelling and bluish discoloration of the left leg. Ten days prior to presentation, she underwent a vaginal hysterectomy for menorrhagia and dysmenorrhea. Doppler ultrasound of the left leg at the time of presentation was negative for DVT. Computed tomography (CT) of the abdomen and pelvis showed extensive thrombus within the left common iliac, internal iliac, and external iliac venous system and compression of the left iliac vein by the right iliac artery consistent with May-Thurner syndrome. Patient underwent a left lower extremity venogram confirming iliac vein compression, Trellis phannacomechanicallysis/thrombectomy, and angioplasty and stent placement in left common iliac vein. She also received warfarin to maintain international normalized ratio (INR) 2-3 for 3 months. Follow-up Doppler ultrasound examination of left lower extremity and iliac veins showed no evidence for thrombosis.

Discussion: DVT is the most common cause of unilateral leg swelling. Phlegmasia cerulean dolens is a severe form of DVT caused by proximal venous outflow obstruction estimated to occur in 2% to 5% of patients who undergo evaluation of lower extremity venous disorder. Location and extent of the thrombus as seen in our patient should raise suspicion of congenital structural abnormalities such as May-Thurner syndrome or iliac compression syndrome. This condition occurs predominantly in middle-age women and is caused by the compression of left common iliac vein by the right common iliac artery. Because the artery has greater pressure than the vein, it compresses the vein against the pelvic rim, causing venous stasis, which predisposes to thrombus formation. Diagnosis is made by Doppler ultrasound, CT, or venogram. Anticoagulation therapy without correction of the structural abnormality will not prevent thrombotic complications. The approach to treatment should include prevention of thrombosis propagation, pulmonary embolism, and restoration of venous outflow in the lower extremity.

Conclusion: May-Thurner syndrome should be considered with patient presentation of left lower extremity swelling and iliac vein thrombus. Treatment involves thrombolysis and stent placement followed by anticoagulation therapy. Prompt therapy is important in order to prevent venous gangrene.

Metastatic Pancreatic Small Cell Carcinoma Presenting as Acute Pancreatitis

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Case: A 77-year-old woman was found to have pancreatitis based on abdominal pain and an elevated amylase and lipase level. An abdominal CT scan revealed an ill-defined 2.2-cm mass in the pancreatic head and bilateral 4-cm adrenal masses. An endoscopic ultrasound redemonstrated the pancreatic and adrenal mass lesions; fine needle aspirations of both were performed, revealing small cell carcinoma by cytological examination. Immunohistochemistry was performed, and thyroid transcription factor-1 (TTF-1), synaptophysin, and chromogranin were positive, confirming the diagnosis. The patient did not have any respiratory complaints but was a long-time smoker. A chest CT demonstrated enlarged axillary, mediastinal, and hilar lymph nodes as well as a solitary 8-mm sclerotic lesion in the midthoracic spine but was notably negative for pulmonary nodules or masses. A brain CT showed brain metastases. The patient declined chemotherapy and succumbed to her disease within 2 months after the initial diagnosis.

Background: Small cell carcinoma of the pancreas is a very rare and aggressive tumor with a high metastasis rate. Approximately 1% of all primary pancreatic neoplasm are small cell carcinomas; 4% of all small cell carcinomas have an extra-pulmonary origin. In a review of all published cases of small cell carcinoma of the pancreas, 91% of cases were in a metastatic stage at time of the initial diagnosis. Bilateral adrenal metastases from a primary small cell carcinoma of the pancreas as described in this case is exceedingly rare and has only been described on 1 other occa-

sion. The main treatment option in small cell carcinoma of the pancreas is chemotherapy. However, no consensus exists due to the limited number of cases. Survival seems to be worse than in small cell carcinoma of the lung, with a median survival of 1 month with symptomatic treatment alone, 2 months with chemotherapy alone, and 4 months with chemotherapy and local treatment.

An Uncommon Presentation to a Common Diagnosis

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Case: A 63-year-old white man with a history of psoriasis was admitted from an outside hospital with hypercalcemia. He was followed by nephrology for a urethral stricture with routine labs and told to go to the emergency department (ED) because of a calcium level of 13.5. The patient had not seen a doctor for many years until 1 month prior. He complained of a mild "smoker's cough" and generalized malaise. His exam revealed psoriatic lesions throughout his body but was otherwise unremarkable. Parathyroid hormone was appropriately low, and an extensive malignancy workup was negative. Chest CT showed no pulmonary nodules, a thickened interstitium, and peribronchial thickening. After finding an elevated angiotensin converting enzyme level, sarcoidosis was considered. Dermatology was consulted to biopsy a lesion on his thigh that did not appear consistent with psoriasis; it showed noncaseating granulomas, confirming the diagnosis of sarcoidosis.

Discussion: Sarcoidosis is a multisystem inflammatory disease characterized by noncaseating granulomas commonly affecting the lungs, liver, skin, and eyes. In the United States, we commonly think of young, healthy African American women presenting with respiratory symptoms and hilar adenopathy, but worldwide, Scandinavians have the highest prevalence rates, are often asymptomatic, and have a second peak in incidence in those over age 50. By remembering that sarcoid affects all ages, ethnicities, and has a variable a presentation, we may be able to diagnose patients sooner and affect patient outcomes.

The clinical picture of sarcoidosis often depends on ethnicity, duration of the disease, organs involved, and the activity of the granulomatous process. Ninety percent of patients will have lung involvement, while the diagnosis can be difficult without obvious pulmonary involvement. Hypercalcemia, due to increased conversion of Vitamin D 25-OH to 1,25-OH by the granulomatous marcrophages leading to increased intestinal absorption of calcium, may only occur in 2% to 10% of patients with sarcoid. Hypercalciuria and an elevated angiotensin-converting enzyme (ACE) level are other biochemical markers of disease, but not specific to sarcoidosis. Therefore, it is imperative to obtain tissue for a definitive diagnosis. Skin, superficial lymph node, salivary gland, or renal biopsies are an option when lung pathology is not present. Thus, it is important to consider sarcoid in nonparathyroid homorone-related hypercalcemia with a negative malignancy workup, because it is a disease that affects all individuals of different ages and commonly presents in an uncommon manner.

Holy Macro: Hypopituitarism Due to Mass Effect

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Introduction: Recognizing hypopituitarism can be difficult due to the nonspecific presenting symptoms, which can be as unimpressive as a simple headache or fatigue, if there are any presenting symptoms at all. However, identifying hypopituitarism early is essential as many of the causes may be catastrophic including primary or metastatic tumors, and outcomes are dependent upon timely initiation of treatment.

Case: A 78-year-old man with past history significant for prostate and colon cancer, diabetes mellitus, and coronary artery disease, presented to the ED with a 2-week history of progressive headache, weakness, and vision changes. During his initial presentation at the onset of symptoms, a head CT was performed. No acute processes were identified to explain his symptoms. He was discharged home with plans for supportive care, but his symptoms progressed to include anorexia, nausea, and vomiting. Upon re-evaluation, magnetic resonance imaging (MRI) revealed a posterior pituitary macroadenoma with extension into the right cavernous sinus. Further workup noted hypocortisolism, hypothyroidism, and decreased testosterone levels. Treatment with steroids and radiation therapy were initiated, and his fatigue, weakness, and vision improved significantly. Given his prior oncologic history, a more aggressive evaluation was pursued, and he was found to have concurrent mantle cell lymphoma and diffuse large cell lymphoma in mediastinal lymph nodes. The patient was discharged home but had increasing difficulty caring for himself and subsequently required readmission to the hospital. Shortly thereafter, prior to beginning treatment for his lymphoma, he passed away.

Discussion: Hypopituitarism consists of the deficiency of many or all (panhypopituitarism) of the pituitary hormones. Clinical manifestations of hypopituitarism are dependent upon which hormone is deficient and to what degree. Therefore, presenting symptoms are fairly nonspecific and may include fatigue, headache, weight changes, dry skin, cold intolerance, loss of sex drive, loss of pubic or body hair, decreased appetite, and hypotension. Headaches and vision disturbances may accompany any of the above symptoms if a mass lesion is present. In addition to masses, which are the most common cause of hypopituitarism and can be primary or metastatic (rare), other etiologies of hypopituitarism include surgery, radiation, infection, pituitary infarcts, and genetic diseases. Treatment of hypopituitarism is dependent upon the cause and range from hormone replacement to chemoradiation and surgery.

Long-Term Outcomes in Patients with *Borrelia burgdorferi* Reinfection

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Background: Reinfection with *Borrelia burgdorferi* is recognized increasingly, but long-term outcomes are described incompletely.

Methods: We conducted a retrospective outcome study of patients with Lyme

reinfection, characterized by recurrent erythema migrans (EM) lesions, and matched controls with a single episode of early Lyme disease. Long-term outcomes were assessed by chart review, a survey consisting of a 36-item short form health survey (SF-36), and a standardized 10-item symptom questionnaire.

Results: From a population of 404 patients diagnosed with definite Lyme disease during 2000-2004, reinfection was identified in 24 patients (6%). Sixteen patients had complete long-term follow-up data available and were matched to 48 controls. One patient had 2 documented episodes of reinfection. Patients with reinfection were treated with oral doxycycline for a median duration of 14 days (range 5-28). SF-36 scores of patients with reinfection were similar to matched controls. There were no significant differences between patients with reinfection vs controls with regards to pain (78.9 vs 77.1, $P=0.747$), role limitations due to physical health (84.4 vs 73.6, $P=0.248$), general health (72.0 vs 65.5, $P=0.230$), social functioning (93.8 vs 89.1, $P=0.403$), vitality (60.6 vs 56.4, $P=0.515$), role limitations due to emotional problems (83.3 vs 85.1, $P=0.829$), emotional well-being (79.3 vs 81.0, $P=0.650$), or physical functioning (84.4 vs 74.5, $P=0.177$). Additionally, there were no significant differences between the 2 groups on the 10-item symptom-based questionnaire.

Conclusion: Lyme reinfection is relatively common in patients from endemic areas. Long-term outcomes were similar to outcomes of patients with a single episode of early Lyme disease. The clinical features and long-term outcomes of patients with recurrent EM lesions are consistent with reinfection etiology and not persistent *B. burgdorferi* infection.

An Unusual Case of Pancreatitis Caused by *Ascaris*

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Case: A 62-year-old Filipino woman visiting the United States presented with a 2-day history of severe abdominal pain, nausea, vomiting, and chills. She denied any history of alcohol consumption or cholelithiasis. Initial vital signs showed blood pressure (BP) 147/103, heart rate 120, temperature 99.3°F, and SaO_2 of 94%. Physical exam revealed distended abdomen with epigastric tenderness; otherwise unremarkable. Chemistry panel showed amylase 2521, lipase 9058, white blood cell (WBC) of 18.8, normal liver function tests (LFTs) and bone morphogenetic protein (BMP). Gallbladder ultrasound showed prominent thickening of the gallbladder wall and pericholecystic fluid. Abdominal CT scan showed pancreatitis and linear filling defects within the small bowel consistent with intestinal parasites. Stool was positive for *Ascaris lumbricoides.* Subsequent endoscopic retrograde cholangiopancreatography (ERCP) directly visualized the worm. Patient was kept NPO, hydrated, and started on albendazole. Clinical course became complicated with hemodynamic instability, respiratory failure, and acute renal failure (ARF). She was intubated and put on pressors and Meropenem. Patient recovered and was extubated successfully. Upon discharge, patient was stable; her symptoms resolved; amylase, lipase, and kidney functions were normal. Repeated stool microscopy was negative.

Discussion: Most cases of acute pancreatitis in the United States are attributed to alcohol consumption and gallstones, but in 10% of patients miscellaneous causes such as parasitic infections, viruses, and bacteria are responsible. While *Ascaris* is a well-recognized cause in underdeveloped countries, its exact incidence in the United States is unknown. Several cases were reported in recent immigrants or travelers to endemic areas. Abdominal ultrasound and CT have high diagnostic accuracy (80%). However, the diagnostic method of choice is ERCP, which shows not only the exact site but the number of parasites, and also is considered the treatment of choice for extracting parasites. The diagnosis of parasitic pancreatitis is difficult in disease-endemic areas, and even more so in nonendemic areas. This case illustrates that pancreatic ascariasis should be considered even in nonendemic countries, and it may resolve with anthelminthic treatment.

Level of Scientific Evidence Underlying Recommendations Arising from National Comprehensive Cancer Network Clinic Practice Guidelines

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Purpose: The level of scientific evidence on which the National Comprehensive Cancer Network (NCCN) guidelines are based has not been investigated systematically. We describe the distribution of categories of evidence and consensus (EC) among the 10 most common cancers with regard to recommendations for staging, initial and salvage therapy, and surveillance.

Methods: We obtained the latest versions (as of July 6, 2010) of relevant guidelines. The NCCN definitions for EC were Category I (high level evidence with uniform consensus), Category IIA (lower level of evidence with uniform consensus), Category IIB (lower level of evidence without a uniform consensus but with no major disagreement), and Category III (any level of evidence but with major disagreement).

Results: Of the 1023 recommendations found in the 10 guidelines, the proportions of Category I, IIA, IIB, and III EC were 6%, 83%, 10%, and 1%, respectively. Recommendations with Category I EC were found in kidney (20%), breast (19%), lung (6%), pancreatic (6%), non-Hodgkin lymphoma (6%), melanoma (6%), prostate (4%), and colorectal (1%) guidelines. Urinary bladder and uterine guidelines did not have any Category I recommendation. Eight percent of all therapeutic recommendations were Category I. Guidelines with the highest proportions of Category I therapeutic recommendations were breast and kidney cancers (30% and 28%, respectively). No Category I recommendation was found on screening or surveillance.

Conclusions: Recommendations issued in the NCCN guidelines are developed largely from lower levels of evidence but with uniform expert opinion. This underscores the urgent need and available opportunities to expand evidence base in oncology.

Recurrent Rib Fractures

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Case: A 57-year-old white man was evaluated in April 20l0 for recurrent rib fractures and lumbar and proximal femur bone mineral density (BMD) T-score of -5.2 and -3.4 respectively. Past medical history was notable for chronic obstructive pulmonary disease (COPD), coronary artery disease, dyslipidemia, and HIV since 1989. Medications include lamivudine-zidovudine and lopinavir ritonavir since 2006; aspirin, clopidogrel, omeprazole, pravastatin, and niacin. Fluticasone/salmeterol 250/50 mcg bid was introduced in September 2007 for severe COPD. Physical examination showed centripetal adiposity, pronounced pink abdominal and inguinal striae, multiple echymoses and rib tenderness. Complete blood cell count (CBC), renal and hepatic function, electrolytes, calcium, phosphate, intact parathyroid hormone, 25-OH-VitD, prolactin, serum and urine protein electrophoresis, and serum free light chains were normal. Random morning cortisol was 0.5mcg/d (4-24 mcg/dl), 24 hours urine-free cortisol <7.2 mcg, late-night salivary cortisol <10 ng/dl (< 100 ng/dl) and DHEA <30 mcg/dl (40-310 mcg/dl) all were very low. One hour post-corticotropin (ACTH) serum cortisol was 7.1mcg/dl (expected >20 mcg/dl). Serum ACTH was 32 pg/ml (0-46 pg/ml). Pituitary MRI was normal. Biochemical markers did not reveal accelerated bone turnover. Chest radiographs confirmed numerous rib fractures. This patient has iatrogenic Cushing's syndrome and adrenal suppression secondary to the potentiated systemic glucocorticoid effect of inhaled fluticasone by ritonavir. Patient's ritonavir was discontinued and he was placed on raltegravir. He was started on physiological and tapering doses of hydrocortisone and teriparatide. His cushingoid features have since receded and he has no further fractures.

Discussion: Ritonavir is a potent inhibitor of the cytochrome P450 3A (CYP3A4) enzyme activity. Fluticasone is potent inhaled corticosteroid with a long elimination half-life and prolonged glucocorticoid receptor occupancy and is also a substrate for CYP3A4 pathway. Fluticasone is most suppressive of HPA axis and has higher propensity for systemic accumulation when used with agents that inhibit CYP3A4 like ritonavir.

Reactive Hemophagocytosis: Is This Condition Underdiagnosed?

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Case: A 79-year-old woman, HIV negative on long-term steroids, presented with T (CD4) cell lymphopenia and cytomegalovirus (CMV) viremia associated with CMV, *Pneumocystis jiroveci* pneumonia (PCP), and *Aspergillus* pneumonia. She was receiving steroids for a diagnosis of cold agglutinin hemolytic anemia. The patient fulfilled 5 out of 8 criteria required for diagnosis of hemophagocytic syndrome: (1) fever for more than 7 days, (2) bicytopenia with low platelet count of 90 and hemoglobin of 8 without any bone marrow hypoplasia, (3) hypertriglyceridemia with tryglycerides of 400 mg/dl, (4) hyperferritinemia >500 at 9000, (5) natural killer (NK) cell activity low with count at 7. She did not fulfill the following hemophagocytic syndrome criteria: splenomegaly; increased soluble CD 25 levels, which were not checked; and bone marrow biopsy, which essentially was normal and did not show hemophagocytosis.

We considered the patient's syndrome to be associated with the CMV infection; there appeared to be little consensus for a diagnosis of hemophagocytic syndrome among the experts. The patient received 4 doses of intravenous immunoglobulin, which has been used previously for CMV-associated hemophagocytic syndrome. This treatment was chosen because it is relatively safer compared to etoposide. The patient also received the following for her infections: ganciclovir for CMV, TMP/SULFA for PCP and possible nocardia, and voriconazole for *Aspergillus.* She was continued on steroids both because she had been on them chronically and to prevent inflammatory changes with PCP treatment.

Hematology initially saw the patient, and did not see clear evidence of hemolysis. The measured amplitude of the cold-reactive antibody was low (1+), although Coombs C3 was positive, Direct Coombs positive. Current anemia was thought related more to inflammation/infection, thrombocytopenia consumptive, related to acute illness. However, the patient developed full-blown acute respiratory distress syndrome and remained ventilator dependent. In keeping with her advanced directive, her goals of care were transitioned to comfort, and life support was discontinued.

Not a Textbook Case of Headache

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Introduction: Giant cell (temporal) arteritis (GCA) is a chronic vasculitis involving both large and medium vessels. It is characteristically a systemic illness with widespread vascular involvement, but the cranial braches of the aortic arch are affected most often.

Case: An 82-year-old woman with a past medical history of atrial fibrillation, hypertension, and hyperthyroidism presented with a 3-month history of occipital headache radiating around her head and to her neck. A head CT was negative for acute intracranial abnormality except left sphenoid sinusitis. She was treated with antibiotics for sinusitis, but later returned with complaints of a global, unrelenting headache, followed by abrupt onset of jaw claudication with right-sided scalp tenderness. During these symptoms, the patient's physical exam was normal, including 2+ bilateral temporal pulses. Her basic laboratory studies were unchanged from previous values, including a white blood count of 13,000/uL, erythrocyte sedimentation rate (ESR) of 79 mm/hour and C-reactive protein 5.4 mg/dl. She was treated empirically with oral prednisone while arranging temporal artery biopsy. After just 1 day of treatment, the patient had almost complete resolution of her symptoms. Her bilateral temporal artery biopsies subsequently were found to be consistent with giant cell arteritis.

Discussion: GCA is seen rarely in patients <50 years old; the mean age of diagnosis is 72 years. Clinical manifestations are variable and include fever, fatigue, weight loss, new headache, jaw claudication, visual symptoms, and polymyalgia rheumatica. The classic GCA headache occurs in the temporal regions, but it may occur in the occipital or frontal areas and also may be generalized. The American College of Rheumatology diagnostic criteria include the following: age > 50 years; localized, new-onset headache; tenderness or decreased pulse of temporal artery; ESR >50 mm/h; and biopsy revealing necrotizing arteritis with a predominance of mononuclear cells or granulomatous process with multinucleated giant cells. The presence of 3 of 5 criteria is associated with 94% sensitivity and 91% specificity for the diagnosis of GCA. Temporal artery biopsy is the gold standard for GCA diagnosis, and the treatment of choice is oral glucocorticoids. Resolution of the inflammatory infiltrate in GCA occurs slowly after the start of treatment, thus it is possible to make an accurate diagnosis several weeks after the start of prednisone therapy. Thus, scheduling biopsy should not interfere with the start of treatment.

Hemophagocytic Lymphohistiocytosis (HLH)

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Case: A 64-year-old white man was transferred from an outside hospital with presumable diagnosis of pancreatitis and septic shock. He initially presented several months earlier with abdominal pain misdiagnosed with cholecystitis and underwent laparoscopic cholecystectomy. He had continuous decline with progressive weight loss (50 lbs/4 mo), nausea, vomiting, continued abdominal pain, pancytopenia, elevated liver enzymes, and high creatinine. Initial CT showed diffusely enlarged retroperitoneal and peripancreatic lymph nodes, enlarged, "inflamed" pancreatic head. He continued to deteriorate and was admitted and treated for sepsis and pancreatitis. Initial bone marrow finding of mild histiocytosis and hemophagocytosis was considered to be secondary to sepsis. He continued to deteriorate in spite of treatment, required ventilator and pressor support, and was transferred to Aurora St. Luke's for further management. At this point, he developed progressive multiorgan failure including respiratory failure, pancytopenia, elevated liver enzymes with jaundice (total bilirubin >25), renal failure requiring dialysis, coagulopathy with multiple factor deficiencies, hypoglobulinemia, hypertriglyceridemia hyperferritinemia, and elevated factor VIII. Imaging studies showed mild pleural and pericardial effusion, spleenomegaly, ill-defined hepatic mass, enlarged pancreatic head, mild lymph node enlargement, and DVT. Liver biopsy showed nonspecific inflammation. A second bone marrow biopsy revealed extensive lymphohistiocytosis and erythrophagocytosis suggestive of hemophagocytic lymphohistiocytosis (HLH). Although he received intensive care support including mechanical ventilation, pressors, continuous veno-venous filtration (CVVH), intravenous immunoglobulin (IVIG), steroid treatment, and multiple broad-spectrum antibiotics, progressive multi-organ failure eventually led to the patient's demise.

Discussion: HLH is a rare but fatal disorder that results from infiltration of various organs and tissues with lymphocytes, natural killer cells, and hemophagocytic histiocytes, and reflects a highly stimulated yet ineffective immune response triggered by various stimuli. This case shows complexity of HLH diagnosis due to septic shock-like manifestations. Early diagnosis is essential to start appropriate treatment achieving a better outcome. However, this is often very difficult due to varied and nonspecific presentation.

DISPLAYED POSTERS

Common Presentations of an Uncommon Disease: Clinical Aspects of Cardiac Sarcoidosis

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Case: A 51-year-old African American man with history of ventricular arrhythmias, atrial fibrillation on anticoagulation and hypertrophic cardiomyopathy (based on prior ECG) presented to the ED with 2-day history of intermittent chest pain, dyspnea, palpitations, and lightheadedness. On examination he was tachycardic with no jugular venous distention, cardiac murmurs, or edema. Laboratory studies revealed therapeutic INR and troponin of 0.16 but otherwise were within normal limits. Electrocardiogram (ECG) showed supraventricular tachycardia with rate of 172 beats per minute. His tachycardia did not respond to metoprolol, diltiazem, and adenosine. Elective cardioversion was performed, during which the patient went into asystole and was revived with 2 to 3 seconds of cardiopulmonary rescuscitation (CPR). Diffuse patchy enhancement on cardiac MRI suggested an infiltrative process, most likely sarcoidosis. ACE levels and serum protein electrophoresis were within normal limits. Chest CT scan did not show any lymphadenopathy but showed bilateral lung nodules.

Discussion: Most common in Japanese and Scandinavian populations, cardiac sarcoidosis (CS) is clinically apparent in only 5% of the patients but is detected at autopsy in at least 25% of the patients with sarcoidosis. It accounts for 13% to 25% of death from the disease. Presentations include arteriovenous (AV) or bundle branch block, atrial and ventricular tachycardias, congestive heart failure, left ventricular aneurysm and sudden death (SD). SD is responsible for 24% to 65% of all deaths related to CS in the United States. Though endomyocardial biopsy remains the gold standard for diagnosis, it is a high risk procedure with a very low sensitivity. With early and late gadolinium enhancement images, sensitivity and specificity of MRI for CS is reported to be 75% and 77% respectively. Steroids are the mainstay of treatment. Implantable cardioverter-defibrillator (ICD) placement is recommended in patients with sustained ventricular tachyarrhythmias and syncope, ECG abnormalities, or wall motion abnormalities attributed to CS. Cardiac transplantation is the definitive treatment in patients with intractable arrhythmias or

end-stage heart failure. The patient presented, subsequently had an ICD implantation, and was started on steroids.

The Tick Made Him Nervously Sick

Leslie Harris, MD, Craig Cole, MD; Gundersen Lutheran, La Crosse, Wis

Introduction: Myasthenia gravis is the most common neuromuscular transmission disorder. A myasthenia gravis crisis can be triggered by infections, exertion, excitement, or numerous other stressors. We report a case of myasthenia gravis crisis due to ehrlichiosis.

Case: An 86-year-old white man with history of well-controlled myasthenia gravis presented to the ED with weakness and dyspnea that had been worsening progressively over the past several days. Due to impeding respiratory failure, the patient required intubation within minutes of presentation. Thus, initial history was limited. Exam revealed a weak, septic patient with a maculopapular rash on the bilateral forearms. Lab work was remarkable for thrombocytopenia and transaminitis. Peripheral blood smear revealed morulae inside several neutrophils. The patient was diagnosed with myasthenia gravis crisis due to sepsis from ehrlichiosis. He was treated with doxycycline, plasmapheresis, and IVIG. Later, the patient was extubated and reported a history of tick exposure. After 1 week, the patient recovered well enough to be discharged from the hospital.

Discussion: Many stressors have been associated with causing myasthenia gravis crises but to date there are no other cases of ehrlichiosis-induced myasthenia gravis crisis reported in the literature. This case demonstrates that patients who present with myasthenia gravis crisis can be critically ill, but can quickly recover if their inciting event is identified and treated.

An Illusive Presentation of Upper Extremity DVT

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Case: The patient is 29-year-old white woman with no significant past medical history who presented with 1 week left arm and shoulder pain. Pain started first at the back of the shoulder and progressed to the arm with restriction of range of movement and noticeable superficial vein dilatation on upper extremity. Patient denied fever, recent weight loss, chest pain, shortness of breath or dyspnea on exertion. There was no trauma to upper extremity and no personal or family history of DVT. Physical examination included the following: blood pressure 127/86, pulse rate 94, respiratory rate 16 and temperature 96.4°F. Lungs were clear to auscultation. Left shoulder was tender to palpation, and dilated veins were noted on surface of left arm. Labs showed normal basic metabolic panel and CBC; WBC 8.1, hemoglobin 11.6, hematocrit 34.8 and platelet count 330, prothombin time (PT) 10.4, partial thromboplastin time (PTT) 31 and INR 1. Doppler ultrasound of left extremity showed thrombosis in left axillary and subclavian veins. CT chest with contrast showed a 4.5 homogeneous soft tissue mass in the anterior mediastinum. Pathology report of excisional biopsy done by CT surgery confirmed primary mediastinal diffuse B cell lymphoma. Patient was treated with 4 cycles of R-CHOP followed by radiation therapy. She was anticoagulated with LMH and coumadin as an outpatient and continued to do well without development of complications such as SVC syndrome, pulmonary embolism (PE), or chronic venous insufficiency.

Discussion: Upper extremity DVT accounts for 2% to 3% of all venous thrombosis of which approximately one-third is primary idiopathic. Secondary causes are related to central venous catheters, cancers, and hormone replacement therapy (HRT). Primary mediastinal lymphomas are associated with SVC syndrome. There is little data describing upper extremity DVT in patients with B cell lymphomas.

An Uncommon Cause of Dancing ECG

Pravachan Hegde, MD, Ronald Go, MD, FACP; Gundersen Lutheran Medical Foundation, La Crosse, Wis

Case: A 54-year-old woman with a history of chronic lymphocytic leukemia with progression to prolymphocytic leukemia in remission was admitted with chest pain, exertional shortness of breath, and low back pain. Her vitals were stable and physical examination was unremarkable. An ECG showed electrical alternans and a chest x-ray demonstrated enlargement of the cardiac silhouette with clear lung fields. A transthoracic echocardiogram (TTE) revealed a large infiltrating mass involving the right ventricle, right atrium and atrial-ventricular groove. The tumor involved the root of the aorta and main pulmonary artery. The patient was noted to have a large circumferential pericardial effusion without evidence of tamponade. Pathology from endomyocardial biopsy of right ventricle was consistent with a low-grade B-cell lymphoma positive for CD20 and negative for CD3. CT scan showed disease involving the heart, mediastinal and paraspinal regions, bilateral kidneys, distal superior mesenteric artery, mesentery and pericardium. She was initiated on fludarabine, cytoxan, and rituxan (FCR) chemotherapy to which she initially responded well. However, she was readmitted 2 weeks later with recurrence of the effusion and was subsequently initiated on etoposide, doxorubicin, vincristine, cyclophosphamide and prednisone chemotherapy with rituximab (EPOCH-R). A repeat TTE showed that the effusion as well as the right ventricular outflow area of tumor burden had decreased in size with symptomatic improvement. She is now being followed closely in hematology clinic.

Discussion: This is a very rare and unusual presentation of an aggressive non-Hodgkin lymphoma arising out of prior B-cell prolymphocytic leukemia involving the heart. We initially treated the patient on FCR chemotherapy as her B prolymphocytic leukemia had responded to FCR and was in remission. But she did not respond to FCR chemotherapy. She was later switched over to EPOCH regimen as there is some evidence that EPOCH may produce more cell kill than CHOP-based regimens in untreated B–cell lymphomas (*Blood.* 2002; 99:2685-2693). The prognosis and optimal treatment is uncertain as it has not been reported previously in the literature.

Lymphocytic Esophagitis Presenting as Chronic Dysphagia

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Objective: Recognize lymphocytic esophagitis as a cause of chronic esophageal dysphagia

Case: A 60-year-old diabetic woman with stage IV chronic kidney disease and a lichen planus history presented with chronic intermittent dysphagia to solids for 7 years, which had worsened during the last 1 year. She had associated abdominal discomfort but denied any other gastrointestinal symptom. She had been treated with lansoprazole and famotidine with minimal improvement. The examination was unremarkable. Significant laboratory findings included blood urea nitrogen 58mg/dl, serum creatinine 5.7 mg/dl (baseline), total calcium 8.9 mg/dL, phosphates 4.9 mg/dL, estimated glomerular filtration rate (GFR) 8.2 mL/min, thyroid stimulating hormone 2.56 uIU/mL and hemoglobin ll.l g/dL. Chest radiography was normal and barium swallow showed normal swallowing with non-specific ringing. A follow-up esophagogastroduodenoscopy (EGD) revealed diffuse full-length esophageal ringing and furrowing with no other anomalies. Multiple biopsies were taken and lower esophageal sphincter dilatation done. Histology revealed multifocal peripapillary intraepitheliallymphocytic infiltrates involving the esophageal mucosa consistent with lymphocytic esophagitis. No eosinophilic component was observed. In absence of a standard treatment, a trial of fluticasone was initiated to be followed with sequential EGD. She also continued taking famotidine.

Discussion: Lymphocytic esophagitis is characterized by infiltration of the epithelium by inflammatory T lymphocytes. It is thought that chronic mucosal insult causes infiltration of T-lymphocytes thereby propagating an inflammatory process, leading to esophageal dysmotility, hence dysphagia. No data on prevalence, gender or age distribution exists, but 43 % of lymphocytic esophagitis patients present with dysphagia (*Am J Clin Path.* 2008;130[4]:508-513). Patients can be asymptomatic or have an underlying reflux esophagitis (most common), esophageal infections, radiation, allergy, and autoimmune disease like Crohn's disease or lichen planus. Histology shows extensive infiltration by intraepitheliallymphocytes around peripapillary fields, with CD3, CD4, and CD8 stains dominant. Biopsy findings in absence of structural or neurological causes make this the likely etiology. A proven treatment is unknown but a trial of topical steroids and anti-acid therapy can be given. This is extrapolated from eosinophilic esophagitis data; a familiar but different entity.

Bulging Eye: A Severe Complication of Acute Sinusitis

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Case: An 81-year-old white man was admitted with severe, acute right facial pain; bulging and redness of the right eye for the past day. He developed fulminant symptoms while on therapy with oral doxycycline for presumed acute sinusitis – sinus congestion and pain 2 days prior to presentation in the ED. Physical examination of the right eye showed ptosis and edema of the periorbital area. Right proptosis was present and ocular motility was limited in all 4 directions to about 80% normal. Vision in both eyes was 20/50 and pupils were symmetrical and pinpointed. The right cornea was clear, intraocular pressure was 22. He had leukocytosis of 22,000; CT scan of the orbits and sinuses revealed thrombosis of the superior ophthalmic vein and right-sided paranasal sinus disease with obstruction of osteomeatal units. MRI on the same day confirmed the superior ophthalmic vein thrombosis but no extension to cavernous sinuses.

Patient initially was treated with piperacillin/tazobactam, vancomycin and heparin drip. After 2 days of therapy with no clinical improvement, repeated MRI showed progression to bilateral superior ophthalmic vein thrombosis and cavernous vein thrombosis with persistent paranasal sinuses obstruction. Patient underwent endoscopic sphenoidotomy and maxillary antrostomy, which resulted in rapid clinical improvement. Cultures obtained intraoperatively grew *Streptococcus alpha hemolytic;* blood cultures grew *Streptococcus intermedius.* Antibiotics were adjusted to ceftriaxone, metronidazole. The patient subsequently was discharged on these antibiotics and warfarin therapy after almost total resolution of his symptoms.

Discussion: This case shows importance of evaluation of patient suffering from sinusitis for any ocular symptoms. It may indicate rare but serious complication of thrombosis in cavernous sinuses that carries high risk of mortality and warrants aggressive IV antibiotic treatment and surgical sinus drainage.

Fevers in an HIV Patient

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Introduction: The incidence of infective endocarditis (IE) is estimated to be 4 cases per 100,000 person-years. Of these, an estimated 3% is the result of a HACEK bacteria. While an uncommon diagnosis, HACEK endocarditis should be recognized as part of the differential in individuals presenting with fevers of unknown origin.

Case: A 43-year-old HIV-positive man with a history of drug abuse presented with fevers for 3 weeks. The patient was in the ED 3 weeks prior also for fevers. At that time, chest x-ray was negative. He was swabbed for H1N1 and discharged home with tamiflu. Since then, the patient reported continued temperatures. Physical exam was unremarkable. Initial laboratory studies were notable for leukocytosis of 11.6, a positive urine drug screen for cocaine and opiates, and an unremarkable LP. A head CT showed subtle areas suspicious for acute infarcts. A source of infection was sought with blood cultures, HIV RNA load, CD4 count, and a multitude of urine and respiratory studies. Temperatures consistently were elevated but responded to acetaminophen. Infectious disease was consulted and IV vancomycin and piperacillin-tazobactam were started. On hospital day 2, preliminary blood cultures showed gram negative bacilli. A transesophageal echocardiography revealed mitral valve vegetations. By day 3, the organism was identified as *Haemophilus parainfluen*zae, sensi-

tive to ceftriaxone. A peripherally inserted central catheter (PICC) was placed, and the patient was discharged home to complete 6 weeks of IV ceftriaxone.

Discussion: Although IE is associated typically with a history of cardiac lesions or injection drug use, it is important to recognize the diagnosis as part of the fever differential even without such histories. The HACEK group is a rare cause for IE but is not an uncommon cause of native-valve endocarditis in individuals without injection drug use. The recognition and identification of endocarditis is important to be prepared for its numerous complications, such as heart failure, which affect a significant portion of patients.

Severe Bleeding from an Uncommon Disorder

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Introduction: Acquired factor inhibitors present with severe spontaneous bleeding in adults. Here we describe a case of acquired factor V (FV) inhibitor with pelvic and soft tissue bleeding in a renal transplant patient, likely related to an occult infection.

Case: A 44-year-old man presented with an extensive right pelvic, gluteal, and thigh hematoma and hemoglobin 7.7 g/dL. His medical history was significant for renal failure secondary to Alport syndrome requiring renal transplantation in 1994. He required transplant nephrectomy of the rejected allograft in 2006, and later received a second renal transplant in 2009.

CT imaging demonstrated a 16 x 9-cm hematoma. Coagulation studies were obtained: prolonged partial thromboplastin time (PTT) 65.1 sec (nL 26-34 sec) and INR 2.0 (nL ≤1.1); thrombin time, fibrinogen, and platelet function assay were normal. Liver function tests and platelets (311 K/µL) were normal; a mixing study was negative. Factor X and VIII activities were normal, and FV activity was decreased at 19% (nL 70-135). A FV inhibitor assay was negative (0.2 Bethseda Units). A lupus anticoagulant panel detected a prolonged dilute Russell venom viper time, indicating the presence of a weak FV inhibitor.

As FV-specific concentrates are not available, fresh frozen plasma (FFP) and platelets (which contain ~20% of circulating FV) were given to replete FV. Steroids were given to suppress inhibitor production, and later rituximab was initiated as an immunodulatory agent. The patient had an appropriate response with FV activity >50% and stabilization of bleeding. Two weeks following hospital discharge, he was found deceased at his home. An autopsy showed a 4 x 3 x 3-cm abscess involving the right psoas muscle. Within the abscess cavity were sutures and staples from within the transplant nephrectomy site. No acute hematoma or occult bleeding were found at autopsy.

Discussion: FV activity levels have poor correlation with bleeding risk. Hemophilia patients experience spontaneous bleeds with factor activity levels <5%, but patients with FV activities of ≤20% may experience bleeding. An acquired FV inhibitor should be suspected in the setting of prolonged PTT and INR and clinical bleeding. Empiric therapy with factor replacement (FFP and platelets) and high-dose steroids should be considered while the diagnosis is being confirmed.

Itching for a Diagnosis

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Introduction: Cutaneous T-cell lymphomas (CTCLs) should be considered in any patient with chronic dermatitis that does not respond to conventional treatments. The most common CTCLs are mycosis fungoides (MF) and Sezary syndrome (SS) with initial presentation with skin manifestations and pruritis.

Case: A 66-year-old African American woman with a history of eczema was admitted for increasing pruritis. She was diagnosed with eczema 6 years ago. It initially began as nummular lesions on her extremities relieved with over-the-counter (OTC) medications. Over the years, the lesions became eczematous with pink pigmentation. The past few months it became generalized to her entire body with increasing pruritis. She tried OTC vaseline and various topical medications with no relief. Past biopsies taken 4 times were unremarkable. She denied any fevers, chills, weight loss, recent travels, changes in medications, or allergies. The patient was admitted for triamcinolone wraps and further evaluation. On admission, vitals were stable and physical exam was unremarkable except for diffuse hyperkeratotic skin lesions with patchy hyperpigmented areas and eczematous changes, thickened hyperkeratosis on palms and soles, and small, pink, firm nodules predominantly on her back. Skin biopsy showed hyperplastic epidermis with Pautrier's micro-abscesses consistent with MF. Flow cytometry of the peripheral blood showed peripheral T cell clone consistent with SS. Chest/abdomen/pelvis CT showed axilla and inguinal lymphadenopathy. Biopsy of cervical node showed benign thyroid tissue. Based on these findings, a diagnosis of CTCL Stage IV A1 with SS was made. The patient was started on photophoresis and IFA.

Discussion: Cutaneous T-cell lymphomas (CTCLs) should be considered in any patient with chronic dermatitis that does not respond to conventional treatments. CTCLs are uncommon and represent 2.2% of all lymphomas. They increase with age and are 2 times more common in men and in African Americans. The etiology is unclear. MF generally presents with skin patches/plaques, eczematous-like lesions, or erythroderma with pruritis. Sezary syndrome is a more aggressive variant with peripheral blood involvement by malignant T cells. Often, multiple skin biopsies are required for diagnosis.

Metastatic Pulmonary Calcification Secondary to Primary Hyperthyroidism

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Objectives: Metastatic pulmonary calcification (MPC) has been described in a variety of benign and malignant diseases. Differentiation of primary hyperparathyroidism (PHP) from other causes of hyper-

calcemia (HCa) in the setting of MPC and subacute renal failure is important in order to expedite appropriate management.

Case: A 67-year-old man with a past history of hypothyroidism treated with levothyroxine (LT) 300 mcg daily, and cryptogenic cirrhosis presented with 1-week history of bilateral leg pain self-treated with aspirin 325 mg 6-7 tablets daily. He reported taking 2 tablets of β-carotene (βC) daily. Both medications were discontinued 1 week prior to presentation. He denied vitamin D or herbal supplementations, long periods of inactivity, weight loss, chills, or night sweats. Chemistry evaluation was significant for total calcium level (TLC) 14.7 mg/dl (8.5-10.3), PTH (parathyroid hormone) intact 47 pg/mL (N=11-67), ionized calcium (iCa) 7.6 mg/dl, phosphate 5.2 mg/dl (2.2-4.5), BUN 105, Cr 6.8, TSH 0.01 uIU/mL (0.40-5.70), free T4 2.9 ng/dl (0.6-1.2), thyroglobulin (0.6 ng/ml <3.0), free retinol 423 uglL (325-780), 1,25-hydroxyvitamin D 48 pmol/L (39-193), angiotensin converting enzyme 26 U/L (30-80), normal serum protein electrophoresis and skeletal survey. Fungal panel was negative for histoplasmosis, blastomycosis, coccidiomycosis, quantiFERON-TB. Urinalysis was normal without Bence Jones protein. He received vigorous hydration and diuretics with resolution of HCa and normalization of iCa. Repeat chemistry found PTH 231 pg/mL. Chest radiograph showed small nodular densities in the upper lobes. Chest CT showed multiple small calcified nodules. Neck ultrasound showed a hypoechoic parathyroid nodule posterior to the left thyroid gland. Parathyroid SPECT/CT revealed parathyroid adenoma. He underwent successful radioguided parathyroidectomy with PTH control.

Discussion: Metastatic calcification refers to the deposition of calcium salts in normal tissue due to conditions causing HCa, hyperphosphatemia, and local alkaline environment. MPC in the setting of PHP is an uncommon medical condition. It has been described in such diverse conditions as chronic renal failure on hemodialysis, hyperparathyroidism, bone osteolytic bone tumors and granulomatous diseases. PHP and malignancy are the most common causes of HCa. Other contributing factors leading to HCa in our patient include exogenous hyperthyroidism and βC consumption. As found in our patient, parathyroid adenomas are not completely autonomous, and PTH secretion may be partially suppressed by elevated Ca levels.

The Use of Plasmaphoresis in the Treatment of Wegener's Granulomatosis: A Case Report

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Background: Wegener's granulomatosis is a form of vasculitis that causes rare cases of renal-pulmonary symptoms. While predominantly treated with corticosteroids, the use of plasmapheresis may be beneficial in severe cases involving pulmonary hemorrhage.

Case: A 72-year-old man with a past medical history significant for hypertension and gout presented with a 2-week history of progressive shortness of breath. He initially was diagnosed with acute otitis media in an outpatient setting and prescribed a 10-day course of amoxicillin. During his antibiotic course, the patient's shortness of breath worsened and he developed diarrhea and oliguria. Patient first went to an outside hospital where he was noted to have significant abnormal kidney functioning with creatinine of 10.2 and serum urea nitrogen (BUN) of 100. Hemoglobin was 7.2; ESR was 107; chest x-ray showed pulmonary edema. Patient was admitted for acute renal failure and placed on dialysis. He also was treated with broad-spectrum antibiotics for possible multilobar pneumonia. Autoimmune antibody tests were conducted and C-ANCA was positive. Patient was given a working diagnosis of Wegener's granulomatosis and started on pulse solumedrol and referred to our hospital for confirmatory testing and initiation of plasmapheresis.

On exam, patient was noted be afebrile, nontachycardic, nonhypertensive. He appeared dyspnic with respiratory rate of 16 and oxygen saturation of 92% on 15L oxygen. On pulmonary exam, he had diffuse coarse crackles bilaterally and decreased breath sounds along both lung bases. Cardiac, abdominal, and neurologic exam was within normal limits and noncontributory. Labs on admission showed an elevated WBC of 15.3, low hemoglobin of 8.8, C-reactive protein (CRP) of 13.3, BUN of 133, and creatinine of 9.8. Chest x-ray demonstrated bilateral infiltrates, suggestive of pulmonary hemorrhage. Patient was started on broad-spectrum antiobiotics, hemodialysis, and plasmapheresis. Kidney biopsy was obtained later confirming the diagnosis of Wegener's granulomatosis.

Discussion: This case explores the treatment modalities for a patient with severe ANCA-positive vasculitis. Plasmapheresis is theorized to help remove ANCAs from the bloodstream and, in retrospective studies, has been suggested to be beneficial for patients with severe renal disease and pulmonary hemorrhage. In 2 randomized clinical trials, patients receiving plasma exchange along with immunosuppressants had a greater likelihood of recovering renal function after initially being placed on dialysis vs patients treated with immunosuppressants alone. Plasma exchange has the potential to be a more prominent treatment adjunct in Wegener's granulomatosis and other vasculitis syndromes, but more studies are necessary before such recommendations can be made.

VIGNETTES

Valvular and Nonthrombotic Neurologic Sequelae from Antiphospholipid Antibody Syndrome: A Case Report

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Background: Antiphospholipid antibody syndrome (APS) is a relatively common cause of acquired thrombophilia and recurrent pregnancy-related complications. While less well-known, its non-criteria manifestations can also have clinical significance.

Case: A 43-year-old man with dementia, epilepsy, and suspected APS was referred to the rheumatology clinic for further evaluation. In addition to seizures, he had expe-

rienced progressive cognitive decline and recurrent headaches. Prior labs revealed high titer anticardiolipin antibodies and positive lupus anticoagulant. An earlier electroencephalogram (EEG) demonstrated posterior slowing. Positron emission tomography (PET)/CT had revealed hypometabolism of bilateral mesial temporal lobes. Review of systems was negative for rash, photosensitivity, oral ulcers, arthritis, serositis, venous/arterial thromboses, or stroke. Family history was negative for thrombotic events or recurrent miscarriages.

On exam, his thought process was slightly slowed. Cardiac exam revealed no regurgitant murmur and no evidence of synovitis; skin exam without livedo reticularis or rashes. Cranial nerves were intact. Treatment was begun with baby aspirin, hydroxychloroquine, and rituximab. Repeat EEG demonstrated generalized background slowing in the high-theta band. Neuropsychologic testing showed borderline/mildly impaired results in multiple cognitive domains. Transthoracic echocardiogram (TTE) revealed mild-moderate mitral regurgitation plus mildly thickened leaflet tips. Transesophageal echocardiogram (TEE) later showed a nonmobile mass on the anterior mitral leaflet measuring 1.3 x 0.7 cm, concerning for Libman-Sacks endocarditis.

This case highlights 2 noncriteria manifestations of APS—neuropsychiatric disease and Libman-Sacks endocarditis. The spectrum of neurologic abnormalities is varied, ranging from behavioral changes to seizures. Libman-Sacks endocarditis involves sterile, nonbacterial lesions that most commonly affect the mitral valve. While often clinically silent, they can predispose to complications such as severe valvular regurgitation and thromboembolic events. This case also illustrates the use of hydroxychloroquine and rituximab as novel treatments for APS. Multiple case reports suggest clinical improvement in APS patients treated with these agents. Further validation of their efficacy through randomized controlled trials is necessary before they become standard treatment options.

Ski Trip Results in Paralysis

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Case: A 20-year-old Chinese man presented to the ED with progressive paralysis. He was skiing earlier that day, and in the evening he developed diffuse muscle cramping and woke up later that night with profound muscle weakness, mainly in lower extremities. The symptoms progressed over a couple hours to the point when he was "unable to move." Patient denied trauma during skiing and had no difficulty breathing or swallowing. Past medical history was significant for hyperthyroidism diagnosed 10 years prior; patient was taken off the medications for about a year. Review of systems revealed weight loss of 10 pounds in 1 year and occasional palpitations. Exam found a tachycardic (pulse 120) anxious patient, with systolic flow murmur, muscle strength 0/5 in both upper and lower extremities bilaterally, absent patellar, axilles, biceps, and brachioradialis reflexes. Neurological examination revealed intact cranial nerves. Initial laboratory work was only significant for hypokalemia. ECG indicated sinus tachycardia and first-degree atrioventricular block. Further testing was significant for elevated T3 and T4 as well as low thyroid-stimulating hormone. Initial diagnosis of thyrotoxic periodic paralysis was made. Treatment was initiated with potassium chloride supplementation and nonselective beta-blockers. Symptoms of quadriplegia completely resolved within 48 hours. The patient was started on antithyroid treatment for the diagnosis of Grave's disease.

Discussion: Thyrotoxic periodic paralysis is a rare and dramatic complication of hyperthyroidism. It is more common in Asian population, predominantly men. Precipitating factors like strenuous exercise and large carbohydrate load are frequently identified. Signs of hyperthyroidism are commonly subtle. Hypokalemia and muscle weakness result from intracellular shift of potassium. Early diagnosis and treatment with potassium supplementation prevent possible complications of cardiac arrhythmias and respiratory failure. Nonselective beta-blockers can help ameliorate the symptoms and prevent future attacks. Definite treatment of hyperthyroidism abolishes thyrotoxic periodic paralysis.

Not Your Typical Chest Pain

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Introduction: Pernicious anemia is the most common cause of Vitamin B12 deficiency, secondary to autoantibodies against parietal cells and intrinsic factor. Indentifying pernicious anemia is important to prevent neurologic complications, correct underlying hematologic abnormalities, and identify associated autoimmune conditions.

Case: A 47-year-old African American man with a history of throat cancer, now in remission, presented with a chief complaint of substernal chest pain and shortness of breath over 2 weeks. In addition, he reported weight loss, fatigue, and weakness. On initial exam, he had pallor of his lips, conjunctiva, and palms, and the rest of his exam was normal. In the ED, ECG demonstrated normal sinus rhythm without ischemic changes. Initial cardiac enzymes were normal but CBC demonstrated pancytopenia with platelet count of 144, white count of 3.7, hemoglobin of 7.0 gm/dL, hematocrit of 21 and a mean corpuscular volume (MCV) of 134. Peripheral blood smear was significant for megaloblastic changes with hypersegmented neutrophils and Holly-Jolly bodies. Work-up of his pancytopenia demonstrated a Vitamin B12 of <30, normal folate , thyrotropin (TSH) elevated to 14.45 and Free T4 of 0.61. Anti-parietal cell antibody was negative but intrinsic factor blocking antibody was positive, leading to the diagnosis of pernicious anemia. The patient was discharged on intramuscular (IM) Vitamin B12 injections as well as levothyroxine 100µg.

Discussion: Pernicious anemia is the most common cause of Vitamin B12 deficiency. Autoantibodies against intrinsic factor and parietal cells are useful markers for pernicious anemia, with 73% sensitivity and 100% specificity when used together. Approximately 90% of patients with pernicious anemia have antiparietal cell antibod-

ies and 60% have intrinsic factor blocking antibodies. Vitamin B12 deficiency can result in megaloblastic changes and pancytopenia, as in this patient, as well as subacute combined degeneration of the spinal cord that is often irreversible even after Vitamin B12 supplementation. Neurologic deficits include loss of vibratory sensation, proprioception, dementia, and psychosis. Pernicious anemia also often presents with numerous constitutional symptoms, as in this case. As pernicious anemia is an autoimmune disease, it is often associated with other autoimmune diseases including Grave's disease, autoimmune thyroiditis, vitiligo, and hypoparathyroidism. At the initial diagnosis, it is important to screen for these other autoimmune diseases to also appropriately treat these conditions as supplementation of Vitamin B12 is initiated.

Waiting with Wegener's

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Background: Wegener's granulomatosis is a necrotizing vasculitis involving small- and medium-sized blood vessels that commonly affects the respiratory tract and kidney. The gradual onset of symptoms often results in delayed diagnosis, thus recognition of the systemic effects is important for timely diagnosis and treatment.

Case: A 23-year-old man presented to his primary physician complaining of shortness of breath, hemoptysis, and bilateral foot purpura. He related a 10-month history of intermittent epistaxis and 2-month history of persistent cough, rhinorrhea, and nasal congestion. Chest radiograph showed bilateral pulmonary infiltrates and chest CT showed bilateral infrahilar consolidation and interstitial infiltrates. Bronchoscopy revealed nucleated cells and blood. Urinalysis was positive for red blood cells and protein, and his ESR was elevated. He received a working diagnosis of Goodpasture's syndrome and was referred to multiple specialists for further workup. He subsequently developed sharp earache, left-sided hearing loss, diffuse arthralgias, and lower extremity edema, prompting hospital admission. On exam, his vital signs were stable with oxygen saturation at 94% on room air. His lungs were clear with decreased breath sounds bilaterally, and he had 0.5 cm palpable purpura on his lower extremities. A complete blood cell count (CBC) showed normocytic anemia. Further testing found positive cytoplasmic antineutrophil cytoplasmic antibodies (C-ANCA) and serum proteinase 3 antibodies. Nasal mucosal biopsy showed neutrophilic vasculitis and acute granulation. He was diagnosed with Wegener's granulomatosis and started on high-dose steroids and cyclophosphamide. The patient stabilized and was discharged 2 days after admission.

Discussion: Wegener's granulomatosis is a necrotizing vasculitis involving small- and medium-sized blood vessels predominantly affecting middle-aged men. Common manifestations include sinusitis, mastoiditis, hemoptysis, and hematuria. American College of Rheumatology diagnostic criteria are as follows: nasal or oral inflammation; abnormal chest radiography showing nodules, fixed infiltrates or cavities; abnormal urinary sediment; and arterial or perivascular granulomatous inflammation on biopsy. Two or more of the 4 criteria yields a sensitivity of 88% and a specificity of 92%. C-ANCA, especially anti-proteinase 3 antibodies, are also present in the serum of up to 95% of patients and can support the diagnosis. The average time from symptom onset to diagnosis is 3 to 12 months, with patients seeing an average of 4.4 physicians before diagnosis. The delay typically is due to the gradual onset of symptoms over time. It is important to recognize the clinical manifestations of Wegener's granulomatosis so as to not delay diagnosis and treatment. Untreated, the course is malignant and 80% of patients die within 1 year. Standard treatment is a combination of high-dose corticosteroid and cyclophosphamide, which induces remission in at least 85% of patients within 6 months.

Hip Pain in a Patient with Systemic Lupus Erythematosis and Tuberculosis

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Case: A 48-year-old woman who recently emigrated from Mexico presented to urgent care with a chief complaint of right hip pain. The pain had been constant for 8 months and was described in the trochanteric bursa and groin region. Physical exam revealed intact range of motion with some limitation on internal rotation. She had a past medical history significant for systemic lupus erythematosis treated with high doses of prednisone for 3 years. A hip x-ray showed osteoarthritis with blood tests revealing anemia and leukocytosis. A quantiferon gold test for tuberculosis (TB) was positive. MRI showed evidence of either synovitis or a complex joint effusion. Therefore, a hip athrocentesis was performed to more clearly delineate the etiology of the pain. The results were bacterial and fungal culture negative and acid-fast baccilus (AFB) smear and culture negative. Suspicion for septic arthritis with TB remained high. Three months later, the patient underwent a second hip arthrocentesis. Pathology from the synovium revealed granulomatous inflammation, and AFB culture positive. At that time she also complained of 2 weeks of cough. A chest x-ray revealed multinodular disease in the lungs suspicious for military TB. She was admitted to the hospital and started on isoniazid, rifampin, pyrazinamide, ethambutol, and moxifloxacin. Her pulmonary nodules resolved on x-ray but her hip pain had not resolved.

Discussion: This case illustrates the potential risk of unregulated use of immunosuppressive drugs in a patient with an already impaired immune system who is also in a high-risk area for TB exposure. It raises the discussion of whether the benefits of immunosuppressive therapy outweigh the potential side effects in this type of scenario.

Dietary Polyherbacy and the Problem of a Didn't Ask, Don't Tell Attitude

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Introduction: Recent national surveys reveal that at least 1 in 3 patients use a dietary supplement, and the average patient uses 3

to 5 dietary supplements, usually containing multiple active ingredients—a practice termed polyherbacy akin to polypharmacy.

Case/Discussion: A 79-year-old man with COPD reported increasing weakness for a month to the point of collapsing prior to admission. He was alert and oriented, in no acute distress, registering elevated systolic blood pressures of 170 -180 mmHg, a heart rate of 65 bpm, a respiratory rate of 18/min and an O_2 saturation of 97% on room air. Examination was unremarkable except for features of mild COPD. He did not have any muscle tenderness nor was he cushingoid. He was noted to be profoundly hypokalemic, 2.1 mmol/L (normal 3.4-5.1 mmol/L), had a bicarbonate of 37 mmol/L (normal 22-28 mmol/L) and a creatinine of 0.9 mg/dL. Dietary history confirmed adequate potassium intake. The transtubular potassium gradient of 14 (normal < 10) with urinary potassium-creatinine ratio of 8 in the face of severe hypokalemia (normal < 3mEq/mg creatinine) confirmed renal potassium wasting raising a differential diagnosis of primary hyperaldosteronism or adrenal tumor. Abdominal CT was unremarkable and AM cortisol was 28 ng/dl. Unexpectedly, the plasma aldosterone was very low, < 2.5ng/dL (normal 3-34), plasma renin was low normal, 0.24ng/mL/h, which led to the diagnosis of an Apparent Mineralocorticoid Excess state.

Following repeated inquiry, the patient's wife brought in a respiratory herbal supplement—"Second Wind," which he had been taking for 6 weeks. Content review revealed among other things, licorice root extract, 250 mg per serving size of vegetable capsule. He recovered 2 weeks after discontinuation of the supplement, with aggressive potassium replacement.

Conclusion: Despite growing knowledge of the widespread use of dietary supplements, many patient-physician encounters are "didn't ask, don't tell" when it relates to use of dietary supplements. This clinical vignette, in addition to showcasing a Syndrome of Apparent Mineralocorticoid Excess, highlights the unintended consequences of polyherbacy, the urgent need to deconstruct the myth that herbal and dietary supplements are "all natural, all pure, and therefore free of harm." It stimulates us to consider a concerted effort for a public health policy and clinical practice guideline to address a burgeoning problem.

ANCA + Vasculitis Presenting as Diabetes Insipidus

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Introduction: Wegener's granulomatosis is a necrotizing granulomatous vasculitis associated with antineutrophil cytoplasmic antibodies that typically involves the upper and lower respiratory tracts and the kidneys. It can affect any organ system and many patients will have neurologic involvement at some point in the course of their disease. However, central diabetes insipidus (DI) as the first symptom of Wegener's is extraordinarily rare.

Case: A 66-year-old man presented with a 2- to 3-week history of polyuria and thirst. The symptoms developed gradually with progression to hourly urinary frequency. The patient denied hesitancy, urgency, dysuria, or hematuria. He noted migrating myalgias and arthralgias occurring over the preceding 2.5 years. He also reported a dry cough. Physical exam was unremarkable. Serum osmolality was mildly elevated at 309 with urine osmolality low-normal at 106. A water deprivation test was conducted with findings consistent with partial central diabetes insipidus. The patient was started on nasal DDAVP with appropriate decrease in urine output and increase in urine osmolality. MRI of the brain and sella turcica demonstrated absence of the "normal pituitary bright signal," which was thought to suggest an infiltrative process in the posterior pituitary gland. A chest CT demonstrated multiple pulmonary nodules bilaterally with necrotic centers. Biopsies of these nodules revealed inflammatory changes with giant cells, microabscesses, and some granulomatous features, with patchy surrounding interstitial fibrosis with centrilobular predilection, favoring a diagnosis of Wegener's granulomatosis. P-ANCA was positive but c-ANCA and myeloperoxidase (MPO) were negative. Renal function was normal. PCR for TB was negative.

Approximately 5% of patients with Wegener's granulomatosis will be p-ANCA positive, though the majority are c-ANCA positive. As with this patient who had no renal impairment, approximately one-fourth of cases of Wegener's granulomatosis will occur as a "limited" form with clinical findings isolated to the upper respiratory tract or lungs. Other organ systems that may be involved include the joint, skin, eyes, and nervous system. Central DI associated with Wegener's granulomatosis is rare, with only approximately 22 cases reported in the literature. Fewer cases exist of central diabetes insipidus as the presenting symptom of Wegener's granulomatosis.

Not a Drop of Blood: Managing a Jehovah's Witness with Cardiac Disease and Gastrointestinal Blood Loss

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Case: A 62-year-old woman with a past medical history significant for persistent coronary artery disease despite bypass, breast cancer, and diverticulosis presented to Aurora Sinai Medical Center because of bright red blood per rectum. Initial hemoglobin was 10.3 g/dL. The patient was a Jehovah's Witness and clearly stated she would accept no blood product because of her beliefs.

Six hours after admission, the patient became acutely symptomatic from her blood loss with dizziness and chest pain. Repeat hemoglobin was 7.0 g/dL. The patient was transferred to the intensive care unit where she was started on fluid resuscitation and erythropoetin. A nuclear medicine study was performed, which confirmed ongoing bleeding. The patient was embolized by interventional radiology. The next day, her hemoglobin continued to drop, to 4.0 g/dL. She developed altered mental status and severe chest pain. An ECG demonstrated evidence of ischemia. The patient was transferred to Aurora St. Luke's Medical Center for possible hyperbaric oxygen therapy.

After transfer, the patient was reevaluated and had improved mental status. Hemoglobin was 2.9 g/dL. Because of

improving symptoms, hyperbaric treatment was deferred and patient was managed supportively. Two weeks later, the patient was clinically improved and discharged with hemoglobin of 4.0. On follow-up a month after the inciting event, her hemoglobin was 11.9 and she was completely asymptomatic.

Discussion: This case highlights some of the difficulties in treating patients without blood products, and some of the strategies used to provide adequate tissue oxygenation in this setting. This case also represents 1 of the lowest survived hemoglobin ever recorded in a patient without blood transfusion, and the lowest reported in a patient with coronary disease.

Monoclonal Antibody Therapy for Recurrent Abdominal Pain?

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Background: Recurrent abdominal pain can be a challenging diagnosis for clinicians, especially in elderly patients with chronic pain who have previously had extensive evaluations. Abdominal pain associated with cytopenias deserves thorough evaluation, as a potentially treatable underlying diagnosis can be uncovered. To demonstrate this, we present a case of previously unidentified paroxysmal nocturnal hemoglobinuria (PNH) causing repeated admission for abdominal pain that was successfully treated with eculizumab.

Case: An 86-year-old woman with history of chronic back pain, abdominal surgeries, and pancytopenia attributed to a myelodysplastic syndrome (MDS) was admitted to the hospital for abdominal pain and emesis. She had 4 hospital admissions within the preceding 8 months for abdominal pain attributed to opioid-induced ileus and partial small bowel obstructions (SBO). A previous enteroscopy had shown only small bowel inflammation, and workup of her anemia several years earlier showed a relatively small fraction of her blood cells with an immunophenotype consistent with PNH; however, she had no prior evidence of active hemolysis. She had been receiving intermittent transfusions for anemia and thrombocytopenia. Her presentation on admission was consistent with recurrent SBO and subsequent CT scan revealed multiple focal segmental areas of small bowel wall thickening as well as dilatation of proximal jejunal small bowel loops. Laboratory evaluation on admission showed hemoglobin of 9.6, platelets of 71, white blood cell count of 8.5, and total bilirubin of 0.9, all stable from previous testing. Enteroscopy with biopsy showed severe jejunal ulceration and venous thrombus formation consistent with ischemic jejunitis. Magnetic resonance angiography (MRA) was negative for mesenteric venous thrombus, and thrombophilia workup was also negative but reevaluation of the patient's anemia revealed a positive urine hemosiderine, low haptoglobin, and elevated lactate dehydrogenase (LDH) consistent with hemolysis. Immunophenotype testing showed loss of GPI-anchored proteins on both granulocytic (58% of total granulocytes) and erythroid (8% of total erythrocytes) cells consistent with PNH. Treatment with eculizumab was initiated, and at 3 months she had not required a single transfusion or had recurrence of her abdominal pain.

Discussion: PNH is a treatable disorder occurring in the setting of MDS in 5% to 9% of cases that should be considered in all patients with recurrent abdominal pain. As demonstrated by this case, proper diagnosis and treatment can result in decreased hospital admissions and improved quality of life.

Metastatic Angiosarcoma Presenting as Diffuse Pulmonary Hemorrhage

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Introduction: The syndrome of diffuse pulmonary hemorrhage (DPH), which includes hemoptysis, anemia, and bilateral pulmonary infiltrates, has a broad differential diagnosis. Establishing the specific cause of DPH can be challenging. Hemoptysis can be a feature of metastatic angiosarcoma, but these patients often have an established diagnosis of angiosarcoma from their primary tumor. We report a case of metastatic angiosarcoma presenting as diffuse pulmonary hemorrhage, a rare presentation for this uncommon disease.

Case: A 32-year-old white man with no significant past medical history presented with hemoptysis for 6 weeks. He reported dyspnea and palpitations for 3 weeks. He had a 10-pack/year history of tobacco abuse and also reported binge alcohol use and smoking marijuana. He denied intravenous drug use. His physical exam was normal except for pallor. Laboratory studies revealed hemoglobin of 6g/dL. His ESR and C-reactive protein were elevated. Tests for HIV, fungal infection, autoimmune disease, and TB were negative. Chest radiograph revealed diffuse ground glass appearance. Chest CT revealed innumerable clusters of micronodules in the peripheral distribution in upper and lower lobes bilaterally. Nodular lesions also were noted in the liver and spleen. Percutaneous liver biopsy showed malignant cells with extensive necrosis, but a definitive diagnosis could not be made. Bronchoscopy with lavage and fine needle aspirate of the lymph node was negative for malignant cells. Video-assisted thoracoscopic surgery (VATS) with wedge biopsy of lung was performed, and the specimen showed extensive intravascular involvement of malignant cells consistent with metastatic angiosarcoma. The patient received paclitaxel with resolution of the hemoptysis and lung lesions and was doing well 6 months after initial presentation.

Discussion: Metastatic angiosarcoma should be included in the differential diagnosis of DPH. Bronchoscopy may not be a reliable method for diagnosing angiosarcoma presenting as DPH as the pathological findings can be obscured by hemorrhage. A more definitive diagnostic procedure such as VATS-guided lung biopsy needs to be considered.

AML with Blast-Negative CNS Involvement

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Introduction: Central nervous system (CNS) involvement in acute myelogenous leukemia (AML) is less common than in acute lymphoblastic leukemia (ALL). CNS leukemia can present as headache, nausea, vomiting, cranial nerve palsies, or seizures. However, CNS leukemia cannot be confirmed reliably by detection of blasts in the cerebrospinal fluid (CSF). CNS deficits in a previously diagnosed AML patient should be considered recurrence of disease unless proven otherwise.

Case: A 28-year-old man with a diagnosis of AML achieved complete remission with 7+3 induction chemotherapy with cytarabine and daunorubicin. Months later, he presented with right facial droop, left ptosis, and diplopia. Physical exam was remarkable for right facial nerve palsy and left third cranial nerve palsy. Laboratory studies revealed a white cell count of 1.0, absolute neutrophil count of 0, hemoglobin 8.8 g/dL, platelets 452. The CSF had 2 white blood cells (WBC), glucose 120, protein 26. CSF bacterial and fungal cultures, viral serologies, and Lyme titers were negative. Six separate CSF collections were negative for blasts. MRI of the brain was unremarkable. Bone marrow aspirate revealed 88% blasts. The patient was diagnosed with recurrent AML with CNS involvement despite blast-negative CSF.

Discussion: CNS involvement is less common in AML than ALL and also is less common in adults than children. Since high-dose cytarabine—which penetrates the CNS—has been incorporated into AML treatment, the incidence of CNS leukemia has decreased. However, CNS AML does occur in 3% to 5% of patients and it cannot always be confirmed by blasts in the CSF. Despite clinical CNS involvement, the CSF may be blast-negative on serial collections. Expert consensus dictates that if clinical evidence of CNS involvement is present, the patient should be treated for CNS leukemia, which typically includes systemic and intrathecal chemotherapy.

Palatal Eschar in Sinusitis: Scan Them Early, Treat Them Swiftly

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Introduction: Sinusitis is a common and relatively benign diagnosis in office practice and zygomycetes are an extremely unusual cause of sinusitis in immunocompetent individuals. However, these ubiquitous fungi can quite literally transform into a bone-erosive, life-threatening species, particularly in the context of diabetes with ketoacidosis or other immunocompromised states.

Case: We report a 38-year-old obese white woman, with diabetes, who presented with 1 week history of severe right-sided facial pain, a several month history of sinusitis that had failed to respond to augmentin and fluroquinolones. Earlier that morning in urgent care, she was recommended to start moxifloxacin and prednisone for sinusitis. Later that night in the ED, she was tachycardic (heart rate 146 bpm), tachypneic (respiratory rate 26/min) had a BP of 150/105 mmHg. Her exam was remarkable for severe right facial tenderness, periorbital ecchymosis, and a painful black eschar on the palate. Her chemistries revealed blood glucose of 592 mg/dl, sodium of 120 mEq/dL, bicarbonate of 6 mEq/dL, anion gap of 32, and an arterial blood pH of 7.08. Urinalysis was remarkable for dipstick ketones, albuminuria, and glucosuria. CT of the head and paranasal sinuses revealed large, localized, complete opacification of the right maxillary antrum, and mucosal thickening in the right and left ethmoid sinuses without any intracranial abnormality. She was initiated on aggressive hydration, IV insulin therapy, with amphotericin B. Intraoperatively at emergency surgery she was noted to have necrotic tissue with the eschar extending from the lateral edge of the alveolar rim to the midline of the hard palate and involving the right incisor all the way to the last molar. Partial right maxillectomy along with excision of floor of right nasal cavity and debridement of necrotic tissue was performed. Cultures from that necrotic tissue grew *Rhizopus* species. She subsequently required further debridement, micafungin, and posaconazole therapy with recovery over 4 months.

Discussion: Rhinocerebral mucormycosis typically manifests with sequential involvement of the nasal cavity, sinuses, eyes, internal carotids, brain, and often is complicated by seizures and hemiplegia. The mortality rate (50% to 85%) is very high. Nasal ulcerations occur in half the patients, and a painful black eschar on the palate or nasal mucosa is a classic but nonspecific sign. Awareness of the disease, a high index of suspicion, early imaging and diagnosis, emergent surgical resection, and aggressive medical management are cornerstones in preventing a fatal outcome.

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