Proceedings from the 2012 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, 2012 Internal medicine residents from each of Wisconsin's 5 residency programs presented their research and/or unusual clinical experiences via posters and vignettes. Vignettes will be published in the next issue of *WMJ.*

DISPLAYED POSTERS

Assessing Efficacy of Nonpharmacological Intervention in Older Hospitalized Patients with Insomnia

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Introduction: Insomnia is a common problem affecting 67% of hospitalized seniors. In acute care settings, 60% of patients receive sedative hypnotic drugs for insomnia. Sedatives may have serious adverse effects on older adults. Many nonpharmacologic sleep interventions have been proposed but have not been researched in depth. The goal of our study was to evaluate the efficacy of nonpharmacological vs pharmacological interventions for seniors hospitalized with insomnia.

Methods: We conducted a quality improvement project with 2 phases to adults 60 years and older admitted to our facility November 2009 to March 2011. We included all patients with acute sleeping problems without prior diagnosis of insomnia or patients with chronic insomnia on pharmacological treatment. Excluded were those who required frequent nursing monitoring due to acute illness, severe pain/immediate postoperative, unable to follow direction due to delirium/dementia, anosmia, hearing deficits, sleep apnea on continuous positive airway pressure (CPAP), allergies to lavender oils. After the completion of phase I with hypnotics/sedatives as standard of care, the second phase used the sleep kit, which included massage therapy, lavender aromatherapy, relaxing music, and warm blankets as standard. Outcome measurements were total hours and quality of sleep, wake-times after sleep onset, feeling after waking up in the morning. T-test, chi-square or Fisher exact test was used for univariate analysis. Multivariable logistic regression analysis was used to assess the association between sleep quality (good/very good/excellent vs fair/poor) and sleep intervention (sleep kit vs sleep aid), while adjusting for age, sex, race, difficulties falling asleep, difficulties staying asleep, duration of sleep problem, and nap during the day. Statistical analyses were performed using SAS 9.2.

Results: There were 64 patients in the sleep aid group and 60 patients in the sleep kit group, and no significant difference in age, sex, race, and sleeping problems between the groups. Following intervention, there was no difference in hours of sleep, however the group with sleep kit (78%) reported significantly better quality of sleep than the sleep aid group (52%). Multivariable regression showed that sleep kit was significantly associated with better quality of sleep (adjusted odds ratio [OR]=3.72, P=0.002).

Conclusion: By using the nonpharmacological intervention, patients can improve their sleep quality while avoiding adverse effects from using sleep aids and thus enhance rest and sleep in hospital setting.

Infective Endocarditis Caused by *Cardiobacteruim Valvarum*

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Introduction: Cardiobacterium valvarum is a newly recognized human pathogen related to infective endocarditis (IE). However, cardiobacterium species are rarely the etiology of IE. We present a case of *C valvarum* IE affecting normal native mitral valve in a patient with no history of recent dental procedure that was detected by broad-range polymerase chain reaction (PCR) and 16S rRNA gene sequencing.

Case: A 49-year-old woman presented with sudden loss of left central vision, 2 months history of fever, chills, and 40-lb weight loss. Temperature was 102°F, blood pressure (BP) 110/80, heart rate (HR) 72. Physical examination showed loss of left central visual field, with signs of retinal artery occlusion, and 2/6 systolic murmur at the apex. Laboratory data showed hemoglobin (Hb) 9.2, white blood cell (WBC) 7.1, C-reactive protein (CRP) 7.6 mg/dl. Transthoracic echocardiography (TTE) revealed vegetations on the posterior mitral valve (MV) leaflet. Blood culture grew *C valvarum* that was confirmed by 16S rRNA gene sequencing. Patient was treated with ceftriaxone for 4 weeks. A month later, he presented with severe right leg pain, fever 100.3°F, night sweats, orthopnea, and dyspnea on exertion (DOE). Exam showed 3/6 holosystolic murmur. The right calf was tender, with absence of dorsalis pedis pulse. Computed tomographic (CT) angiogram showed intraluminal filling defects within the right common femoral artery. Patient underwent MV replacement and right femoral endarterectomy with a vein patch angioplasty. Patient was continued on ceftriaxone and did well postoperatively.

Discussion: C valvarum is a newly proposed species and, like *Cardiobacterium hominis,* is a rare cause of endocarditis. Since 2004, a total of 9 cases of *C valvarum* IE have been described, including this case. Like other cases, the onset in our case was insidious, with low-grade fever and extensive valve tissue destruction. Four cases had bicuspid aortic valve (AV), one had tricuspid AV, one case had moderate MV prolapse and mitral insufficiency, and one case had bioprosthetic AV. Our case had a completely normal MV with no history of recent dental procedure, and no further focus was known. Two of the 9 cases were complicated by neurological events: subarachnoid hemorrhage secondary to a mycotic aneurysm and ischemic stroke. Our patient had extensive retinal artery and common femoral artery distal embolization. All patients were treated with β-lactam antibiotics. In summary, this is the 9th case of IE due to *C valvarum*, the 3rd case affecting a native valve, the 2nd case affecting a low jet flow valve, and it is the 1st case affecting completely normal native valve with extensive septic distal embolization. Further advances and widespread use of molecular techniques will likely reveal more cases. Physicians should be aware that *C valvarum* is a potential agent of IE.

Spontaneous Rectal Perforation Presenting as Necrotizing Fasciitis of the Lower Limb

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Introduction: Necrotising fasciitis (NF) is a life-threatening soft tissue infection associated with high mortality and morbidity. We report an unusual case of lateral lower limb NF following spontaneous rectal perforation.

Case: A 68-year-old man with a history of type 2 diabetes mellitus (DM), T3 N2 M0 colorectal carcinoma S/P rectal resection, colorectal anastomosis, and chemotherapy presented with a 2-week history of left-sided back pain radiating to his hip, for which he was started on steroids. He had a number of small-bowel obstructions and underwent enterolysis along with abdominal washout. He also had fever and chills, then became lethargic and confused. At presentation, he was toxic looking, afebrile, and hypotensive. Physical examination revealed left hip swelling, tenderness, and subcutaneous crepitus of the left lower limb. Initial labs revealed WBC of 30,700 with left-sided shift. His creatinine was up to 2.50. Lumbar spine magnetic resonance imaging (MRI) showed no evidence of diskitis. CT scan of the abdomen and pelvis showed rectal perforation with large amount of gas extending from the rectum laterally to the left, following muscle planes and bundles down into the left upper leg. Patient underwent sigmoid resection with end colostomy, decompression fasciotomy of the left thigh, and irrigation and debridement of a deep thigh abscess that required further wound debridements. He was started on broad-spectrum intravenous (IV) antibiotics and hyperbaric oxygen treatment. Wound cultures grew *E. coli* along with Pseudomonas and Bacteroides. The patient improved significantly.

Discussion: NF is a rare complication associated with colorectal malignancy. The majority of cases reported involve spontaneous perforation due to colorectal malignancy, with infection limited to the perineum, such as Fournier's gangrene, with the exception of 2 cases that presented as direct tumor invasion into the abdominal wall, and psoas abscess. There was 1 case of NF of the lower limb following traumatic rectal perforation in a patient with history of rectal cancer 5 years prior to the presentation. Our case appears unique, as we found no case reports of a bowel perforation causing NF of the lateral lower limb following spontaneous rectal perforation in a patient with history of treated colorectal cancer with no evidence of cancer recurrence, direct trauma, abdominal signs at presentation, or preceding changes in bowel habit. With regard to its etiology, we postulate systemic immunosuppression secondary to the cumulative effects of steroids therapy and DM in our patient. Treatment involves the use of high-dose antibiotic therapy, systemic support, and prompt and radical surgical debridement of the infected tissues. High index of suspicion and prompt surgical intervention are the cornerstone of treatment for improving the disease outcome.

Patient with Cystic Fibrosis-related Diabetes Presenting with Diabetic Myonecrosis

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Case: This case involves a 32-year-old white man with cystic fibrosis (CF) and 2 delta F508 mutations, status post lung transplant in 2008 and uncontrolled cystic fibrosis related diabetes mellitus (CFRD). He presented with worsening pain in the left thigh and calf of 3-week duration, of a magnitude preempting the leg from bearing weight. While examination of the right lower extremity was nontender and showed a normal range of motion, the patient was unable to flex the left lower extremity beyond 20 degrees. The posterior thigh and the calf were mildly tender to palpation. Erythema, swelling, and deformity were absent. Pulses were positive bilaterally. MRI showed extensive edema with inflammatory changes involving several muscles in the left thigh and calf on T1-weighted images suggestive of diabetic myonecrosis. Treatment included complete bed rest, analgesics, antiplatelet agent, aspirin 81 mg/day, and adequate glycemic control. The patient's condition improved and he was discharged 3 days later.

Discussion: Diabetic myonecrosis is an uncommon complication of poorly controlled diabetes mellitus. Numerous case reports/case series have been reported, but to our knowledge this is the 2nd published case of a CFRD patient presenting with diabetic myonecrosis. The only other report we found was a very recent abstract of a case presented by Dopp et al, "Sugar Pains: Novel Diabetic Myonecrosis in a Cystic Fibrosis Patient." CFRD is a common comorbidity in patients with CF, with prevalence in adult patients as high as 50%, increasing with age. Typical clinical presentation of diabetic myonecrosis consists of sudden onset of pain in the affected muscle, in association with swelling with thigh muscles most commonly affected, followed by calf muscles. The imaging modality of choice for soft tissue evaluation is MRI, which shows findings of increased signal on T2 imaging in patients presenting with edema. Diabetic myonecrosis is normally self-limiting, and

good glycemic control with supportive care is the mainstay of treatment. A high index of suspicion for diabetic myonecrosis should accompany a patient with CFRD presenting with lower extremity pain.

Unusual Presentation of a Rare Cancer: Histiocytic Sarcoma in the Brain 16 Years After Treatment for Acute Lymphoblastic Leukemia

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Case: A 44-year-old man presented to the emergency department (ED) with unsteadiness, loss of balance, and left-sided weakness for 2 weeks. A CT scan and MRI of the brain showed 2 intra-axial enhancing lesions: one in the corpus callosum of 3.5 cm and the other adjacent to the right lateral ventricle of 2.6 cm, both associated with vasogenic edema. The patient's history was significant for T lymphoblastic leukemia (T-ALL) with cerebrospinal fluid (CSF) involvement 16 years prior for which he received craniospinal irradiation and intrathecal chemotherapy for approximately 26 months with no additional significant health problems. A biopsy of the right parietal brain tumor was done. The final pathological diagnosis was atypical histiocytic infiltrate consistent with histiocytic sarcoma (HS). The patient was treated with 2 doses of intravenous methotrexate, but his condition continued to decline. He then was treated with 2600 cGy of whole brain radiotherapy, with an additional 2000 cGy boost to each lesion. He received temozolomide 150 mg/m2 for 5 consecutive days during the whole brain radiotherapy. As there was no improvement clinically, he declined further treatment. He was enrolled in hospice and died 4 months later, 27 weeks after initial presentation.

Discussion: Histiocytic sarcoma is a very rare hematopoietic neoplasm that has been reported in association with other hematological malignancies. Presentation of HS in the central nervous system (CNS) is even less common. Diagnosis of HS requires the presence of histiocytic markers and the systematic exclusion of markers of other cell lineages. Primary HS CNS tumors are aggressive and generally have poor outcomes. There are no standard treatment guidelines due to lack of clinical trials and a limited number of case reports.

Flaccid Paralysis of Lower Extremities in a Young Man with Uncontrolled Hyperthyroidism

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Introduction: Thyrotoxic periodic paralysis (TPP) is a syndrome of episodic muscle weakness accompanied by severe hypokalemia in patients with uncontrolled hyperthyroidism. It occurs more commonly in Asian males with hyperthyroidism in their 3rd or 4th decades. Early recognition is crucial for providing life-saving therapy.

Case: A 31-year-old Hmong man with a history of hyperthyroidism presented with an acute onset of bilateral leg weakness for 1 day. Over the previous 3 to 4 months, he lost 75 pounds and had frequent night sweats, diarrhea, and heat intolerance. He was prescribed, but had not been taking, methimazole since the diagnosis with hyperthyroidism 4 months prior. For 2 weeks he had intermittent painful bilateral leg cramps for which he took ibuprofen. He also reported going through a recent divorce and had a high carbohydrate meal for dinner 1 day prior to admission. On exam, he was alert and oriented. He had no lid lag, proptosis, or periorbital edema. His thyroid exam was unremarkable. His neurological exam was notable for fine bilateral hand tremor and marked weakness in his lower extremities (1/5) with decreased reflexes despite normal sensation. His labs were significant for a potassium of 1.2 mg/dl, magnesium 1.5 mg/dl, phosphorus 1.1 mg/dl, thyrotropin (TSH) 0.02 uIU/ml, free thyroxine (T4) of 3.6 ug/dl, and free triiodothyronine (T3) of 8.9 ug/dl. He was admitted to the intensive care unit (ICU), and his electrolytes were aggressively supplemented. Following their normalization, his leg weakness improved. Subsequent thyroid ultrasound showed a diffusely heterogeneous and hypervascular thyroid, and thyroid-stimulating immunoglobulins were severely elevated. These were consistent with Grave's disease. A diagnosis of thyrotoxic periodic paralysis was made, and he was given methimazole along with propranolol. He was subsequently discharged home on day 3 of admission.

Discussion: TPP typically is triggered by a large carbohydrate meal, stress, or vigorous exercise. The underlying cause appears to be the increased activation of the Na/K-ATPase pump by excessive thyroid hormone, leading to an influx of potassium into the intracellular space. Thyroid hormone also enhances beta adrenergic receptors on muscle cells to stimulate Na/K- ATPase pump. TPP is diagnosed by the presentation of flaccid paralysis, hypokalemia, suppressed TSH, and elevated T4 and T3 levels. It is important to distinguish TPP from FHPP (familial hypokalemic periodic paralysis) because TPP is responsive to treatment with oral/IV propranolol. Screening with TSH therefore can be very helpful for patients presenting with hypokalemia and paralysis. Since hypokalemia is due to an intracellular shift of K ions rather than from actual loss, the hypokalemic state is only transient and often can resolve without interventions. However, life-threatening arrhythmia as well as respiratory failure from muscle weakness has been reported due to severe hypokalemia. In addition, 1 study showed that giving IV potassium shortened the recovery time by about half. There were studies that showed efficacy of using a large dose of oral or IV propranolol in treatment of TPP. If potassium is given, there often is a risk of rebound hyperkalemia, which has not been observed in the treatment with propranolol alone. Propranolol also has been found to decrease future attacks of TPP; however, the most effective prevention for recurrence lies in the treatment of the underlying hyperthyroidism.

Coronary-Pulmonary Fistula: Case Report and Brief Review of Existing Literature

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Case: An 86-year-old woman with history of hypertension, diabetes, hyperlipidemia, and coronary artery disease, admitted with

new-onset congestive heart failure and pneumonia, underwent cardiac catheterization after suffering a non-ST elevation myocardial infarction. Coronary angiogram revealed severe coronary artery disease and coronary pulmonary fistulas involving proximal right coronary artery and a branch from left main coronary artery. Coronary artery fistulas are abnormal communication between one or more coronary arteries and great vessels or a cardiac chamber. We reviewed 15 cases of coronary-pulmonary fistulas published in PUBMED and studied the clinical features of coronary artery fistulas.

Scientific Evidence Underlying National Comprehensive Cancer Network Guidelines for Supportive Care

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Introduction: The National Comprehensive Cancer Network's (NCCN) guidelines for supportive care of cancer patients have not been systematically investigated. Our objective was to describe the distribution of categories of evidence and consensus (EC) among the 10 available supportive care guidelines with regards to screening, treatment, and follow-up.

Methods: We obtained the latest versions (January 18, 2011) of relevant supportive care guidelines from the NCCN website (www.nccn.org). The definitions for various categories of EC used by NCCN panel members were as follows: Category 1 (high level evidence such as randomized controlled trials with uniform consensus), Category 2A (lower level of evidence with uniform consensus), Category 2B (lower level of evidence without a uniform consensus but with no major disagreement), and Category 3 (any level of evidence but with major disagreement).

Results: 680 guidelines were available (140 for screening, 394 for treatment, 146 for follow-up). The proportions of category I, IIA, and IIB were 5%, 92%, and 3% respectively. Guidelines with the most category I recommendations were cancer-related infection (14%) and cancer-related fatigue (12%), antiemesis (7%), venous thromboembolism (4%), and distress management (2%). Nine percent of all therapeutic recommendations were category I and were found in prevention and treatment of cancer-related infections (63%), myeloid growth factors (11%), venous thromboembolism (8%), antiemesis (6%), cancer-related fatigue (6%), and distress management (6%). Category I guidelines were not available for palliative care, senior adult oncology, cancer and chemotherapy-induced anemia, and adult cancer pain. Category I guidelines also were not available for screening or follow-up.

Conclusion: Almost all of the NCCN supportive care guidelines are based on lower level of evidence but with uniform expert consensus. Huge opportunity exists for research to make recommended guidelines more evidence-based.

Attitudes and Behavior of Nursing Staff Towards In-patient Rounding by Hospitalists

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Introduction: Hospital medicine by design necessitates interaction of providers with nursing staff, specialists, and other clinical and nonclinical staff on a daily basis to care for patients with complex medical conditions.

Methods: Attitudes and satisfaction of nursing staff towards hospitalist rounding and communication were assessed before and 3 months after implementing a "patient-centered inpatient rounding" model.

Results: Three months after implementation, we noticed significant improvement in staff attitudes and behaviors. Compared with 3% satisfaction before implementing the model, 42% of staff were "completely satisfied" by our rounding; 44% reported improved communication with hospitalist staff vs 6.5% before implementation; 57% indicated they felt valued as a health care team member and their job satisfaction improved to 63%; and 53% reported a positive impact on their workflow.

Discussion: Patient-centered inpatient rounding is a great way to take patient care to the patient's bedside. It improves communication between physicians and nurses, a cornerstone of cost-effective and safe patient care.

Senior Care in the ED: A Qualitative Study

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Introduction: Senior citizens account for 11.7 million US emergency department visits annually; however, EDs are not equipped to adequately and safely care for seniors. Potential hazards in the ED and atypical presentation of illnesses make assessments and care more challenging. We sought to learn the difficulties and unmet needs of seniors in the ED to inform improved care at community hospitals.

Methods: Qualitative exploration using semi-structured key informant interviews (n=39) and "shadowing" observation sessions (n=32). Analysis of written text was performed using an editing style format by 2 authors who did not participate in data collection.

Setting: One central city and 1 suburban community hospital ED in Southeastern Wisconsin.

Subjects: Fourteen physicians, 8 physician assistants, 14 registered nurses, 2 emergency medical technicians, and incidentally encountered patients.

Results: Frustrations, challenges, and opportunities expressed by interviewees (227 listed items) were separated into 3 broad themes: complexity of the geriatric ED patient (98 items), including difficulty obtaining the history and its complexity and impaired patient communication; issues of patient flow and transitions (70 items), including perceived need for more and specialized staff, inadequate triage and barriers to disposition, system inefficiencies, and lack of continuity and access to care; and need for a senior-friendly environment (59 items) including physical space and amenities, and safety issues.

Observations (115 listed items) revealed positive (22) and negative (23) staff behaviors involving courtesy and safety, system innovations (4) and inefficiencies (28), unpleasant environmental features (29), and positive attributes of patients and families (9).

Conclusions: Our synthesis of staff interviews and observations suggest numerous opportunities to improve care of seniors in EDs. Quality improvement programs should focus on system efficiencies, use of nonclinical staff, environmental modifications, and improved communication during transitions.

Advancing Bedside Procedure Education with a Simulator-Based Workshop

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Introduction: In 2007 the American Medical Association (AMA) repeated its 1986 survey of numbers and types of procedures performed by general internists, which clearly demonstrated a decreasing trend in general internists' procedural practice. The American Board of Internal Medicine (ABIM) no longer requires proficiency in the majority of bedside procedures. Contrary to these regulatory changes, many ICUs are run by hospitalists and general internists. In the ICU setting, clinicians must be capable of performing many bedside procedures; so improving internal medicine training in this area is essential.

Methods: Fifty-two first-year internal medicine residents went through a 1-day, simulator-based procedure workshop. Bedside procedures included arterial line placement, central venous line (CVL) placement, lumbar puncture (LP), arthrocentesis, and advanced cardiac life support (ACLS) leadership training. Residents completed a survey of their confidence performing these procedures on a 10-point scale: 1 being least confident, 10 being most confident. Given the small sample size (N=52), we were unable to assume the probability distributions of variables. Hence, significance was calculated using Wilcoxon signed-ranked test.

Results: Our survey showed statistically significant increases in confidence in all procedures: arterial line placement (before: median 5, standard deviation (SD) = 2.39; after: median 7, SD = 1.82; percent increase in median = 40%; P <0.001), CVL (before: median 3, SD = 2.30; after: median 7, SD = 1.90; percent increase in median = 133%; P<0.001), LP (before: median 5, SD = 2.35; after: median 7.5, SD = 1.87; percent increase in median = 50%; P<0.001), arthrocentesis (before: median 5, SD = 2.38; after: median 8, SD = 1.73; percent increase in median = 60%; P<0.001), and ACLS (before: median 4, SD = 2.09; after: median 6, SD = 1.90, percent increase in median = 50%, P<0.001).

Conclusion: Education in bedside procedures is becoming increasingly difficult in the modern health care system. The traditional teaching style of "see one, do one, and teach one" is becoming obsolete in today's higher acuity clinical environment with increasing time demands on trainees. Our simulator-based procedure training successfully increased residents' confidence in performing bedside procedures. Future studies will need to focus on demonstration of improved patient care outcomes.

A Case of Endobronchial Granular Cell Tumor: A Rare Entity

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Introduction: Granular cell tumors (GCT) are benign neural tumors first described in 1926. Mostly located in the head and neck region, skin, and subcutaneous tissues, their presence in the endobronchial region is uncommon, with less than 100 cases reported.

Case: A 54-year-old woman was seen in consultation for chronic obstructive pulmonary disease exacerbation. Chest radiograph showed mild apical fibro nodular scarring. Despite appropriate treatment, the patient continued to have shortness of breath, cough, and wheezing along with increasing oxygen requirements. A high resolution CT scan showed a wedge-shaped opacity in the medial left upper lobe. Bronchoscopy was performed revealing an endobronchial whitish growth at the subcarina. Biopsy was obtained. Microscopic examination showed bland appearing eosinophillic cells within the endobronchial submucosa. Cells had intact nuclear to cytoplasmic ratio and immunohistochemical stains were positive for CD56, S-100 and vimentin. A diagnosis of endobronchial GCT was made.

Discussion: Granular cell tumors of the lung are rare. They comprise only 0.2% of all intrapulmonary neoplasms. Two percent to 6% of GCTs occur in the lung, and of these, 90% are endobronchial. It has been established now that they arise from Schwann cells. Patients with benign endobronchial tumors may present with cough, dyspnea, wheezing, hemoptysis, and post obstructive pneumonia. Chest radiographs may be completely normal. Depending on the size of the endobronchial mass, there may be signs of distal pneumonia, atelectasis, mucoid impaction, bronchiectasis, and air trapping. In some instances, malignant GCTs also have been report ed. Endobronchial ablation using argon plasma coagulation is the current treatment of choice with special emphasis on bronchoscopy for follow-up due to the risk of recurrence.

Thrombocytopenia as the Initial Presentation Angioimmunoblastic T-Cell Lymphoma: A Case Report

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Introduction: Angio immunoblastic T-cell lymphoma (AITL) is a peripheral T-cell lymphoma that typically presents with generalized lymphadenopathy and systemic B symptoms. We describe a patient with AITL who had an unusual presentation with only thrombocytopenia on a routine complete blood cell count (CBC).

Case: An 85-year-old woman presented with complaints of knee pain and generalized weakness for a week. Platelet count was 10,000, which led to her admission. Physical exam was unremarkable. No lymphadenopathy appreciated. Platelets and hemocrit continued to fall, and she subsequently received intravenous immunoglobulin, dexamethasone, platelets, and blood transfusions. CT abdomen showed extensive retroperitoneal, pelvic, and mesenteric lymphadenopathy. Bone marrow biopsy showed normocytic

anemia, severe thrombocytopenia, and mild immature myeloid shift. A right axillary lymph node biopsy showed AITL.

Discussion: AITL is a type of peripheral T-cell non-Hodgkin lymphoma that commonly presents with systemic B symptoms and generalized lymphadenopathy. One study found that 99% of patients with AITL had peripheral lymph node enlargement on initial presentation and 91% had involvement of at least 2 or more lymph node groups, which was absent or at best very obscure in our patient. Seven percent of patients had idiopathic thrombocytopenic purpura. Bone marrow was infiltrated in 60% of the cases in the study. In other studies, thrombocytopenia was present in 30% and 18.5% of the cases. In another study that examined bone marrow involvement in AITL, only 1 out of the 6 patients with AITL who had uninvolved bone marrow had platelet count below 150,000 x 109/L.

Conclusion: Although thrombocytopenia is rarely the initial presentation, AITL must be kept in mind in the setting of unexplained thrombocytopenia even if the typical features of a lymphoma are absent.

Medullary Renal Cell Carcinoma in a Patient with Sickle Cell Trait

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Case: A 57-year-old African-American woman presented with a past medical history significant for morbid obesity, hypertension, and sickle cell trait. She was diagnosed with large right-sided renal mass as a result of workup of recurrent urinary tract infections. Subsequent MRI of the abdomen confirmed this finding, and further demonstrated invasion of the inferior vena cava (IVC) and adjacent lymph nodes. No mass was seen on imaging studies 1 year prior. Patient underwent nephrectomy, and pathology revealed renal medullary carcinoma. Subsequent workup showed multiple pulmonary lesions consistent with metastatic disease. Patient was initiated on bortezomib.

Discussion: Medullary renal carcinomas are rare, rapidly progressive cancers of the kidney, and primarily affect young black patients with sickle-cell disease or trait. Survival is very poor, even with aggressive treatment, including surgical resection and various chemotherapeutic regimens. Currently, no effective therapy has been reported for this disease. Chemotherapy is based largely on very limited published data. Despite its close association with sickle cell trait and cytogenetic abnormalities, no specific genetic abnormalities were identified. Due to its rapid development, this cancer often is metastasized at the time of diagnosis. Early diagnosis and treatment will be the key to improve survival. Therefore, identification of the disease-specific genetic abnormality will be extremely helpful, and if a patient with sickle cell trait or disease presents with urinary symptoms, an imaging test is strongly indicated and should be considered early on, as renal medullary carcinoma is one of the differential diagnoses.

Atypical Presentation of Extra Adrenal Malignant Pheochromocytoma

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Introduction: It is believed 85% of pheochromocytomas are adrenal origin and 15% are extra adrenal paragangliomas. Metastasic pheochromocytomas are more common in extra adrenal abdominal pheochromocytomas in about 36% to 50%.

Case: A 51-year-old woman with past medical history of hypertension and migraines presented to the ED with 2-week history of generalized weakness, dull abdominal pain, nausea, and vomiting. Patient was hypercalcemic and was diagnosed with primary hyperparathyrodism. Due to hypertension, patient urine metanephrines and catecholamines were performed. She was discharged in stable condition after treatment for primary hyperparathyroidism and was readmitted within 2 weeks with worsening abdominal pain. Results of the previous tests were concerning for significant catecholamine release. Patient had a CT of abdomen, which showed no abnormalities of adrenal glands but a necrotic mass within the pancreas as well as multiple metastasis within the liver. At that time, she started to develop palpitations and significant diaphoresis. She was started on alpha blockage with no significant improvement of symptoms. First biopsy of liver lesion was not indicative of pheochromocytoma. Due to worsening symptoms, a second biopsy of liver lesion was performed, confirming metastatic malignant pheochromocytoma. Patient was scheduled for embolization of liver metastasis, but decided not to follow up with treatment as well as chemotherapy.

Discussion: Case depicts an atypical presentation of a malignant extra adrenal pheochromocytoma. Even if a patient does not present with typical symptoms of palpitations, diaphoresis, or episodic hypertension, pheochromocytoma should be kept on the differential in a patient with hypertension. Absence of adrenal mass does not exclude pheochromocytoma; if there is a clinical suspicion screening should be performed.

A Case of Extraskeletal Calcification-Calciphylaxis

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Introduction: Calciphylaxis is a rare, often fatal disorder characterized by systemic medial calcification of the arterioles that leads to ischemia and subcutaneous necrosis. It is seen almost exclusively in patients with end-stage renal disease (ESRD) and hyperparathyroidism, affecting 1% to 4% of the population with ESRD.

Case: A 48-year-old woman with history of ESRD due to focal sclerosing glomerulonephritis on hemodialysis and history of failed kidney transplant presented with a very painful skin rash over the lower abdomen and chest. There were no vesicles or ulcerations, but lesions were progressively darkening and enlarging in size over 3 weeks. There was no fever, joint pain, or sore throat. On physical examination, pulse rate 106/min, temperature 37.8°C, respiratory rate 18/min, blood pressure 90/60mmHg. She had marked areas of necrotic papulomacular lesions over lower abdomen, bilateral breast fold areas, and right upper thigh. There was bilateral pitting edema, but peripheral pulses were palpable symmetrically. The rest of physical examination was unremarkable. Laboratory

workup showed blood urea nitrogen 31mg/dl, creatinine 9.8mg/dl, parathyroid hormone (PTH) 63 pg/ml, calcium 7.5mg/dl, phosphorous 8.4mg/dl, hematocrit 29.6%, WBC 6800/mm3 and international normalized ratio (INR) was 1.0. Autoimmune work up for vasculitis was negative. Skin biopsy revealed intimal calcification in the small- and medium-sized blood vessels with necrosis of the overlying skin consistent with calciphylaxis. She was treated with phosphate binders, short interval dialyses, and sodium thiosulfate. The patient developed ulcerative lesions 3 months after discharge and is receiving outpatient wound care and pain control.

Discussion: Calciphylaxis is characterized by areas of painful ischemic necrosis that usually develop on areas with greatest adiposity including abdomen, buttock, and thigh. These ischemic changes lead to livedo reticularis and violaceous plaque-like subcutaneous nodules that progress to necrotic ulcers that often become super infected. There are no specific diagnostic laboratory tests for calciphylaxis. Skin biopsy with strong clinical suspicion is helpful in confirming diagnosis. Treatment is mainly supportive. There are no controlled prospective studies that compare different treatment strategies. Both medical and surgical interventions can be tried. Correcting PTH using cinacalcet or parathyroidectomy in refractory cases and normalizing serum calcium and phosphate abnormalities using noncalcium-containing phosphate binders is recommended. In patients with debilitating necrotic lesions, treatment with sodium thiosulfate has shown significant reduction in pain and skin lesions.

Record-Breaking Vancomycin Level Causes Kidney Catastrophe

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Introduction: Vancomycin-induced nephrotoxicity is a well-known condition affecting 5% to 7% of treated patients. Our case represents the highest measured serum vancomycin level ever recorded in the medical literature to cause acute renal injury.

Case: A 52-year-old man with past medical history of newly diagnosed type 2 diabetes mellitus presented with left hand cellulitis and abscess. The patient denied taking any medications prior. He was started on IV vancomycin and piperacillin-tazobactam for broad spectrum coverage. He then underwent incision and drainage of the abscess with cultures of the wound positive for methicillin-resistant staphylococcus aureus. On day 7, he was discharged home on vancomycin 1.75 grams intravenously every 8 hours. One week later, his routine vancomycin trough level was 145.1 mcg/mL (therapeutic 10 - 40 mcg/mL). He was readmitted, vancomycin was discontinued, and repeat levels rose to 177.7 mcg/mL. His only complaint was a 3-day history of weakness and fatigue. Physical exam revealed a well-healing left hand wound and was otherwise unremarkable. Further workup uncovered his serum creatinine had climbed to 5.60 mg/dL from his baseline of 0.9 mg/dL 9 days prior. Urinalysis showed 1-5 white blood cells and no eosinophils. His fractional excretion of sodium was 6.3%, indicating intrinsic renal injury. Bilateral renal gallium scan demonstrated no increased uptake of contrast. Renal biopsy was not done. The etiology of the patient's injury likely was acute tubular necrosis due to the direct renal toxicity from vancomycin. After 4 days his symptoms resolved and he was discharged home. Follow-up labs demonstrated gradual improvement in renal function, but 19 weeks later the serum creatinine was 1.65 mg/dL.

Discussion: Vancomycin-induced nephrotoxicity is known to cause acute tubular necrosis or acute tubular interstitial nephritis. Treatment is simply discontinuation of vancomycin with close monitoring. To date, this is the highest known serum vancomycin level ever recorded in humans. Our case further exemplifies the importance of clinically managing vancomycin through careful dosing and drug level monitoring.

A Unique Presentation of *Clostridium difficile* Colitis

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Introduction: The classic presentation of *Clostridium difficile* colitis includes symptoms of watery diarrhea in the context of recent antibiotics while hospitalized. We present a case of fulminant pseudomembranous *C difficile* colitis in a patient who did not fit this classic paradigm.

Case: An 82-year-old man was admitted to our institution with progressively worsening bilateral lower quadrant abdominal pain 1 month in duration. Midway through this course he was evaluated in the ED and found to have CT evidence of inflammatory changes about the lower left colon concerning for diverticulitis. He was prescribed oral ciprofloxacin and metronidazole therapy, along with close outpatient follow-up. However, his symptoms of severe "waves of pain" worsened, prompting hospital admission. Review of systems was negative for fevers, chills, weight loss, nausea, vomiting, diarrhea, constipation, or gastrointestinal (GI) blood loss. He had no sick contacts, recent travel, or mitigating factors. Pertinent past medical history included severe diverticulitis 10 years prior that led to a partial sigmoid resection with anastomotic repair subsequent to a ruptured diverticulum. Two years later he had required balloon dilation at the anastomosis secondary to a localized narrowing.

On exam, patient was afebrile and hemodynamically stable. He appeared uncomfortable but had a nonsurgical abdomen. Bowel sounds were present with moderate tenderness to palpation of the bilateral lower quadrants. Laboratory analysis included normal hemogram, electrolytes, and creatinine but with C-reactive protein (CRP) elevation to 4.5 (normal 0.0-0.8). Repeat CT scan revealed similar inflammatory changes as prior but dilation of the colon proximal to the inflammation also was noted. A gastroenterology consult was obtained with recommended colonoscopy to further define the inflammation. Interestingly, a stool sample obtained prior to colonoscopy tested positive for *C difficile* toxin. Endoscopic evaluation revealed fulminant, pseudomembranous colitis proximal to a tight stricture. Unfortunately, despite aggressive medical therapy, our patient developed toxic megacolon with subsequent rupture a few days later. He had an emergent total colectomy followed by a prolonged ICU stay but eventually passed away.

Discussion: C difficile infection is on the rise.

Heightened awareness of its presence and its potential to cause significant morbidity and mortality is needed. This case is unique in that our patient's lack of diarrhea was secondary to his colonic stricture, which was presumably worsened by surrounding inflammation.

Blast From the Past

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Case: A 54-year-old man living in Wisconsin, with no medical problems started experiencing numbness over his abdomen and back. Over the next 3 months, he developed leg weakness and difficulty walking. He was evaluated at a local ED where he had a normal head CT, chest x-ray, CBC, urine analysis, TSH, creatine kinase (CK), and basic metabolic panel. Lumbar spine x-ray revealed mild degenerative joint disease. He was referred subsequently to a free clinic due to lack of insurance.

The next month he was evaluated in our ED due to persistent symptoms and was found to have a stiff-legged gait but otherwise unremarkable neurological exam. Erythrocyte sedimentation rate (ESR) and B12 were normal. Patient was asked to follow up with neurology.

At his neurology clinic visit a month later he was noted to have 3/5 strength and hyperreflexia in his legs along with symmetric loss to pinprick sensation caudal to T4 and positive Romberg's test. He also had developed issues with bladder incontinence. MRI spine revealed destructive mass lesion at C7-T2 with epidural involvement and cord compression suggestive of TB, fungal infection, or neoplasm. Fine needle aspirate was nondiagnostic. Open biopsy specimen showed granulomatous inflammation with Blastomyces dermatidis organisms. Patient received induction liposomal amphotericin B, which ultimately led to renal failure. He was switched to oral voriconazole, which is to be continued for several months. He underwent physical therapy and was showing gradual improvement in strength when seen at 3-month follow-up in clinic.

Discussion: Vertebral blastomycosis is a rare, potentially fatal fungal infection of the spine with myriad presentations. It often leads to delayed diagnosis, such as in our patient, with resulting neurological deficits and deformities. There are no pathognomonic findings on imaging studies. For patients who live in endemic areas who present with epidural masses/abscesses, the differential should include blastomycosis. Definitive diagnosis includes culture of this dimorphic fungus or direct visualization of the broad-based, budding yeast on histopathology. Amphotericin B is the first line treatment for life-threatening or CNS infections. Therapy can be switched to an oral azole once the disease is under control. Surgical management is reserved for those who do not respond to medication or those with progressive/severe neurologic deficits, spinal deformity, or instability.

Overlap Syndrome in the Presence of Renal Cell Carcinoma

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Introduction: Connective tissue disorders have been associated with malignancies. We describe a patient with an overlap syndrome whose rapid disease progression coincided with the discovery of a renal tumor.

Case: A 75-year-old woman presented with a 3-month history of progressive difficulty grasping objects, unsteadiness, dyspnea, xerostomia, xerophthalmia, and a 35-pound weight loss. She also described a several-year history of gastroesophageal reflux and Raynaud's phenomenon. Physical exam revealed facial telangiectasias, bibasilar inspiratory rales, sclerodactyly, and absent pinprick and vibratory sensation in her toes. Several metacarpophalangeal joints, proximal interphalangeal joints, and both ankles were swollen and tender.

Laboratory tests showed ESR 79, estimated glomerular filtration rate (eGFR) 39.9, ANA HEp-2 1:160, RF 80, SSA > 8.0, positive antineutrophil cytoplasmic antibody (c-ANCA), and proteinase 3 (PR3) > 8.0. Urinalysis revealed 3+ hematuria. Nerve conduction studies and electromyography (EMG) revealed a length-dependent, predominantly axonal, mixed sensorimotor neuropathy. CT of the chest and abdomen revealed a patulous esophagus, pulmonary fibrosis, and a left renal mass. A left heminephrectomy was performed; tissue biopsies confirmed renal cell carcinoma, plus polyangiitis and granulomatosis. The patient's presentation is consistent with an overlap syndrome of limited scleroderma, Sjögren's syndrome, and Wegener's granulomatosis. Treatment with methylprednisolone and rituximab improved her sclerodactyly, polyarthritis, dyspnea, and renal function (eGFR 61.0) and stabilized her neuropathy.

Discussion: Patients with rheumatic disease are at increased risk for malignancy. Conversely, connective tissue disorders may manifest as rheumatological paraneoplastic syndromes, appearing at cancer diagnosis or earlier. Primary and secondary presentations are indistinguishable. Renal cell carcinoma has been reported independently to occur simultaneously with scleroderma and Wegener's granulomatosis, suggesting a common pathogenesis. Partial remission of symptoms has been achieved in some patients following treatment for a co-existing renal tumor.

Conclusion: Diagnosis of an autoimmune disorder in the presence of a malignancy should prompt the clinician to consider a secondary etiology. Eradication of the tumor may reduce the amount of immunosuppressive therapy required to treat the rheumatological disease.

Pyoderma Gangrenosum as the First Manifestation of Essential Thrombocythemia

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Introduction: Pyoderma gangrenosum (PG) is a rare disorder that physicians should consider in patients presenting with nonhealing ulcers. PG has been associated with inflammatory bowel disease, arthritides, and hematological conditions. We report the rare case of PG in a patient with essential thrombocythemia (ET).

Case: A 78-year-old man was admitted for IV antibiotic therapy for a nonhealing ulcer. On admission, he had elevated WBC of 24,000/ul and platelet count of 900,000/ul, which initially was thought to be reactive. After

48 hours of IV antibiotic therapy there was no clinical improvement. Initial and repeat cultures from the wound were negative for all organisms. Skin biopsy revealed intense neutrophilic dermatoses consistent with PG. Bone marrow biopsy was consistent with essential thrombocythemia showing increased megakaryocytes. He was treated successfully with hydroxyurea and prednisone.

Discussion: PG was first described in 1916 by Brocq. Studies have reported a low incidence ranging between 3 million and 10 million per year. It occurs in patients 20 to 50 years of age with a slightly female predominance. The pathogenesis is not clearly understood. Although it is idiopathic in 50% of the cases, it can be associated with other systemic illnesses. Multiple theories have been postulated including abnormal neutrophil trafficking, dysregulation of innate immunity, pathergy, and cytokine release. Rarely familial forms have been described.

PG is associated more commonly with inflammatory bowel disease and less commonly with arthritis, malignancies, and paraproteinemias. It starts as a painful nodule most frequently occuring on lower extremities. There are 5 subtypes, with bullous being the most common form associated with hematologic malignancies.

PG is a diagnosis of exclusion. Skin biopsy shows intense neutrophil dermatoses. The mainstay of treatment is corticosteroids. Cyclosporine or other immunosuppressive agents can be used. Biologic therapy with anti-tumor necrosis factor-alpha (TNF-alpha) have been used for refractory PG. Emerging research suggests granulocyte apheresis and phosphodiesterase-4 inhibitor may have a role in treatment.

"Blessing for the Bleeder": Bevacizumab in Hereditary Hemorrhagic Telangiectasia—A Novel Therapeutic Approach

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Introduction: Hereditary hemorrhagic telangiectasia (HHT) is a vascular disorder characterized by cutaneous and mucocutaneous telangiectases resulting in severe and recurrent epistaxis and gastrointestinal hemorrhages. Role of bevacizumab in HHT has been reported to show improvement in epistaxis, telangiectasias, and hemoglobin stabilization. However the optimal dose and schedule of administration in HHT is unknown.

Case: A 56-year-old woman diagnosed with HHT at age 35 was on oral iron supplementation and maintained normal hemoglobin until June 2007 when her hemoglobin declined to <10 gm/dl and she was started on parenteral iron therapy. Because of persistent melena she was started on ethinyl estradiol. She developed dyspnea when her hemoglobin was <8.5 gm/dl, requiring 2 to 4 units packed red blood cell (PRBC) transfusions every month to maintain hemoglobin >8.5 gm/dl. In 09/2011, bevacizumab was started at 10mg/kg at 2 weekly intervals. Melena resolved within a week, hemoglobin rose to 14.2 g% within 4 weeks; serum ferritin increased (from 28 ng/ml to 246 ng/ml) within 6 weeks, with no further parenteral iron supplementation and marked decrease in episodes of epistaxis. She received total of 9 doses of bevacizumab at 10mg/kg body weight (3 doses each at increasing intervals) and 2 doses at 7.5 mg/kg body weight (every 4 weeks, still ongoing). Her hemoglobin continues to remain stable with negligible epistaxis, without the need for blood/iron infusions.

Discussion: Because of the molecular mechanisms involved in both angiogenesis and HHT, a vascular endothelial growth factor inhibitor such as bevacizumab may be an effective treatment for HHT. Prior studies used bevacizumab in doses ranging from 10 mg/kg to 5 mg/kg body weight every 2 weeks. We attempted to find a schedule minimizing side effects without compromising therapeutic benefits. Our observations suggest that bevacizumab at dose of 7.5 mg/kg every 4 weeks is efficacious in controlling symptoms in HHT.

Cervical Osteomyelitis After Repeated Esophageal Dilation for Dysphagia Associated with Chemoradiation-induced Esophageal Strictures

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Introduction: Dysphagia secondary to esophageal strictures is a common complaint of patients with head and neck cancers following treatment with chemoradiotherapy. We report a rare case of cervical osteomyelitis after multiple endoscopic dilations for chemoradiation-induced esophageal strictures.

Case: A 69-year-old man with stage IVa squamous cell carcinoma of the larynx was treated with chemoradiotherapy with prophylactic placement of a percutaneous endoscopic gastrostomy (PEG). He developed dysphagia 6 months after chemoradiation for which he underwent esophagogastroduodenoscopy via his PEG tube and was found to have high-grade proximal esophageal stenosis. After 6 endoscopic dilations to 20 mm over a 4-month course, his dysphagia gradually resolved and the PEG tube was removed.

He presented to the ED 6 weeks after his last dilation, complaining of progressive neck pain for 1 month. On examination he appeared healthy overall, except for a temperature of 103°F and marked tenderness on paravertebral cervical spine muscles. Cervical spine MRI studies demonstrated C6 and C7 pathological fractures, osteomyelitis at the C6-7 level, and an esophageal-spinal fistula. His blood culture was positive for peptostreptococcus micros. Given the absence of neurological deficits, he was treated conservatively with intravenous ertapenem for 10 weeks, followed by 6 weeks of augmentin, and cervical spine stabilization. He received nothing by mouth and a PEG tube was re-placed for nutritional support. Sequential MRI studies of the cervical spine showed progressive resolution. Over the course of 4 months, he remained neurologically stable.

Discussion: Esophageal strictures are a common sequela after chemoradiation therapy for head and neck cancers and can lead to significant dysphagia. Cervical osteomyelitis is a rare complication of multiple esophageal dilations in these patients. Its major clinical manifestation is neck pain without neurological deficits. A high index of suspicion is, therefore, necessary in all patients having neck pain post esophageal dilation for malignant esophageal strictures.

Erythromycin in Acute Upper Gastrointestinal Bleeding: A Meta-Analysis

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Introduction: Emergent upper endoscopy is the standard of care in patients with upper gastrointestinal bleeding (UGIB). Adequate visualization of the GI tract is important for diagnosis and therapy. Several studies have evaluated the role of erythromycin before endoscopy with mixed results. We performed a meta-analysis of randomized controlled trials (RCTs) to assess the efficacy of erythromycin for acute UGIB prior to endoscopy.

Methods: MEDLINE, Cochrane Central Register of Controlled Trials and Database of Systematic Reviews, PubMed, and recent abstracts from major conference proceedings were searched (through June 2012). RCTs evaluating the role of erythromycin in acute UGIB in adult patients were included. Two independent reviewers extracted data using standard forms. Data regarding the following outcomes were extracted: visualization of the mucosa, need for repeat endoscopy, blood transfusion, and length of stay. Summary statistics were computed using Comprehensive Meta-analysis software. Publication bias was assessed by funnel plots. Heterogeneity was assessed.

Results: Seven studies met the inclusion criteria (n=657). Patients with both variceal and nonvariceal bleeding were included. Mean age ranged from 56 to 64.5 years. Dose of erythromycin administered varied from 125mg to 3mg/kg. Endoscopy was performed 20 to 120 minutes after administration of erythromycin. Erythromycin group showed improvement in mucosal visualization (relative risk [RR] 1.6; 95% CI 1.14-2.35, *P*=0.008), number needed to treat (NNT) was 4 (95% CI, 2-11), decreased need for repeat endoscopy (RR 0.52, 95% CI 0.31-0.89, *P*=0.02, I2 =18, NNT 11). The need for blood transfusion was lower (weighted mean difference) -0.52; 95% CI -0.957 to 0.08), *P*=0.02) and length of hospital stay was shorter (mean difference: 1.56, 95% CI 0.6-2.5) in erythromycin group.

Conclusion: Erythromycin prior to endoscopy in adult patients with upper GI bleed improves visualization of the mucosa and decreases the need for repeat endoscopy, hospital stay, and the need for blood transfusion.

Cytomegalovirus Colitis During Mycophenolate Mofetil Therapy for Anti-synthetase Syndrome

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Introduction: Mycophenolate is an immunosuppressive medication that inhibits purine synthesis and is often used in solid organ transplant patients. There is hardly more than 1 case report in the literature where there is a suggestion that mycophenolate on its own has the immunomodulatory power to cause cytomegalovirus (CMV) reactivation.

Case: A 49-year-old Caucasian woman who was receiving mycophenolate mofetil for anti-synthetase syndrome presented with a 2-week history of watery diarrhea, nausea, and vomiting. This was associated with right upper quadrant abdominal pain, low grade fevers, and malaise. Preliminary stool studies, cultures, and *C difficile* work-up were negative. Liver chemistries were slightly deranged in a noncholestatic pattern. Viral hepatitis panel was normal. Chest radiograph was consistent with patchy bilateral infiltrates suggestive of pneumonitis. CMV serology was positive. Colonoscopy was done for tissue diagnosis, light microscopy revealed CMV inclusions, and immunostains were positive confirming diagnosis. Mycophenolate therapy was discontinued and the patient was started on valgancyclovir for 3 weeks. Her symptoms resolved and imaging and laboratory markers improved.

Discussion: Colitis is a frequent manifestation of acute CMV infection. While there is evidence that mycophenolate may have increased risk of CMV disease in solid organ transplant patients, there are very few reported cases of CMV disease in patients receiving mycophenolate immunosupressive therapy for other causes.

Triple Antiviral Therapy in Hepatitis C-Induced Cryoglobulinemic Vasculitis and Lymphoproliferative Disorder

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Introduction: Mixed cryoglobulinemia (MC) and B-cell lymphoma are known complications in patients with hepatitis C due to antigenic stimulation by hepatits C E2. There is emerging evidence suggesting that combination therapy with ribavirin and interferon alfa is beneficial in patients with hepatitis C-induced cryoglobulinemia. The effect of protease inhibitors on cryoglobulinemia has not been studied yet. We present a case of mixed cryoglobulinemia secondary to HCV genotype 1 that presented with clonal B-cell proliferation and was successfully treated with triple antiviral therapy using protease inhibitors.

Case: A 58-year-old-man with history of intravenous drug abuse was hospitalized for maculopapular rash and severe Raynaud's phenomenon. Physical examination revealed massive splenomegaly and severe digital cyanosis. Laboratory tests were significant for pancytopenia, normal aspartate aminotransferase (AST) and alanine aminotransferase (ALT), positive rheumatoid factor and cryoglobulins, and low complement levels. Serology was positive for hepatitis C and negative for lyme, parvovirus, and human immunodeficiency virus (HIV). RNA amplification studies isolated genotype 1b. Imaging studies revealed a normal liver size and echo texture, massive splenomegaly, normal portal pressure, and retroperitoneal lymphadenopathy. Flow cytometry revealed a polyclonal B-cell proliferation. The patient was treated with peginterferon, telaprevir, and ribavirin (triple antiviral therapy) for HCV. There was marked clinical improvement with symptom resolution, nondetectable viral load and significant decrease in the cryocrit levels 4 weeks after treatment.

Discussion: Pathophysiology behind hepatitis C virus infection and the development of lymphoma is still under debate. However it is likely that mechanisms involved in mixed cryoglobulinemia and B-cell lymphoma share

similar features. Standard treatment for MC vasculitis has included pegylated interferon and ribavirin, reserving rituximab for severe cases. Introduction of new NS3/4A serine protease inhibitor like telaprevir and boceprevir has markedly improved sustained virological response. Combination of new NS3 serine protease inhibitors with peginterferon and ribavarin has not been studied yet.

Association of Nursing Home Regulatory Compliance and Emergency Department and Inpatient Admissions for Fall-related Injuries

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Objective: To evaluate the relationship between nursing home regulatory compliance and staffing with the occurrence of falls requiring ED or hospital inpatient care.

Methods: A county-level analysis of Wisconsin nursing home, ED, and inpatient data from the Wisconsin Hospital Association, Center for Medicare Services, and Wisconsin Department of Health Services was performed. There were 59,186 Wisconsin nursing home residents 65 years of age and older in 2007-2008; hospital inpatient and ED discharge records documented 715 admissions from skilled nursing facilities (ie, nursing homes). These admissions were reported in 56 of the 71 counties with nursing homes. A multivariate analysis of these 56 counties was performed using negative binomial regression to analyze the association between nursing home staffing, demographics, federal violations, and ED/inpatient admissions for fall-related injuries.

Results: Residents from counties with nursing homes having a greater number of federal violations had a significantly greater risk of ED/inpatient admissions for fall-related injuries, particularly with violations in the "Quality of Life" category. Counties with a fewer number of nursing homes per county and in large fringe metropolitan counties also had a significantly greater risk of ED/inpatient admissions for fall-related injuries.

Conclusion: Increased compliance with federal nursing home standards may decrease ED/inpatient admissions from nursing homes for fall-related injuries.

Pure Red Cell Aplasia and Anti-erythropoietin Antibodies—Not Only in Chronic Kidney Disease Patients

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Introduction: Acquired pure red cell aplasia (PRCA) is a rare condition causing severe anemia and characterized by a low reticulocyte count, absence of red blood cell precursors, and normal leukocyte and platelet morphology. PRCA, often idiopathic, has been linked to several medical conditions, such as thymomas, hematologic malignancies, autoimmune disorders, and a variety of drugs and viral infections. Review of the literature does show reported cases linking PRCA to the use of recombinant human erythropoietin (EPO). We present the case of PRCA secondary to anti-EPO antibodies.

Case: A 64-year-old man with cirrhosis secondary to hepatitis C and pancytopenia was admitted for anemia with hemoglobin of 5.5 g/dL. Six months prior he was started on treatment for hepatitis C with telaprevir, ribavirin, and peginterferon. He had baseline hemoglobin of 11.5 g/dL. Four weeks later, he started procrit injections (epoetin alpha, 40,000 units weekly) due to decrease hemoglobin to 7.0 g/dL. He responded to treatment and dosing was continued. He completed 12 weeks of treatment with telaprevir. Ribavirin and peginterferon were discontinued due to new onset of decompensated cirrhosis. Despite stopping the hepatitis C treatment and continuing epoetin injections, his hemoglobin decreased to 5.5 g/dL. On the day of his admission, his reticulocyte count was undetectable raising concern for PRCA. He was given blood transfusions, and EPO injections were discontinued. A bone marrow biopsy showed "markedly hypocellular bone marrow with red cell aplasia." Further workup was negative for parvovirus, CMV, and Epstein-Barr virus (EBV). Chest CT did not show a thymoma or lymphadenopathy. Anti-EPO antibody titers were positive.

Discussion: The majority of documented cases of PRCA occurred in patients with chronic kidney disease (CKD). Our patient illustrates that this phenomenon is not limited to this population. Most cases of anti-EPO antibodies have occurred with use of Eprex, an epoetin alpha product that is no longer manufactured. PRCA associated with anti-Procrit antibodies has been reported in only 6 cases. Data guiding management is limited. Treatment consists of blood transfusions, stopping EPO injections, and immunosuppressive therapy. Steroids alone or in combination with cyclophosphamide, and intravenous immunoglobulin have been used most widely. PRCA resolves spontaneously in 20% to 30% of cases associated with anti-epoetin antibodies. Rechallenge to EPO injections is contraindicated.

IIB or Not IIB? That is the Question

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Case: A 61-year-old man presenting with ST elevation infarct developed respiratory distress, hypotension, and thrombocytopenia to 26 post procedure. Eptifibatide and heparin were stopped and he received supportive measures including mechanical ventilation and pressure support. Initial work-up on chest x-ray and bronchoscopy revealed diffuse alveolar hemorrhage (DAH). Thrombocytopenia was negative for disseminated intravascular coagulation (DIC) and heparin-induced thrombocytopenia (HIT), but positive for eptifibatide antibodies. Platelets initially improved to 65, and 2 units of platelets were transfused with increase to 103, but again fell to the fifties. Repeat DIC panel gave a DIC score of 5 with low fibrinogen and elevated D dimer with shistocytes on smear. Ultimately the patient developed multi-organ failure and received comfort care.

Discussion: Glycoprotein IIB-IIIA inhibitor-induced thrombocytopenia is a rare, serious complication, occurring in roughly 0.3% to 0.7% of patients. Onset of eptifibatide-induced thrombocytopenia (EIT) tends to occur within minutes to hours of administration (usually within 24 hours) and can be severe, with platelet counts dropping below 30,000. Other causes of acute thrombocytopenia should be excluded including pseudothrombocytopenia, DIC, and HIT. Treatment includes discontinuation of the offending agent, platelet and red blood cell transfusions in the case of significant bleeding, and other supportive measures. Platelet count should

improve over the next 3 to 6 days. DAH is also a complication of eptifibatide use first reported in 2004, with a growing number of case reports highlighting this emerging risk. Recent retrospective analysis has found DAH rates to be from 0.2% to 0.3%. Symptoms can include hypoxia, anemia, hemoptysis (though one-third do not have this symptom), and new chest infiltrates. Treatment includes discontinuation of IIB-IIIA inhibitors and other anticoagulation and supportive treatment to maintain O2 saturations. This is a unique case in that our patient developed not only EIT with DAH, but subsequently developed DIC within hours leading to persistent thrombocytopenia and multi-organ failure. Thus, even in the setting of possible EIT, one must monitor platelet counts after stopping the medication and, if not improving, consider alternative or co-commitment pathology.

The Case of Cancer Incognito

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Case: A 59-year-old man with a history of hypertension, hyperlipidemia, and recent onset of partial seizures presented with a 2-day history of fluent aphasia and right hemiparesis. After admission to another hospital, he suffered a complex partial seizure followed by simple partial status epilepticus with a focus in the left temporoparietal lobe. He was transferred to our facility for further evaluation after being started on antiepileptic drugs (AEDs). Brain MRI and CT angiography were negative for cerebral infarct and aneurysm, but his MRI displayed abnormal fluid-attenuated inversion recovery (FLAIR) signal involving the left temporal lobe and peri-insular cortex, of concern for herpes simplex virus (HSV) encephalitis. He underwent lumbar puncture and was started empirically on acyclovir. CSF analysis revealed an elevated protein of 145 mg/dL, normal glucose of 65 mg/dL, and no leukocytes. HSV nucleic acid amplification test (NAAT) was negative, but CSF HSV IgG and IgM from CSF came back elevated. He was continued on acyclovir and had no further seizures. His fluent aphasia improved markedly over the next 5 days though he continued to have word-finding difficulty and some intermittent weakness on his right side with numbness and tingling. He was discharged home, and 1 month later had a repeat brain MRI that revealed a new necrotic lesion in the same location in the left temporal lobe. Magnetic resonance spectroscopy (MRS) was performed to better characterize the lesion and was found to be most consistent with glioblastoma multiforme (GBM). Resection confirmed GBM, and the patient has since begun chemoradiation therapy.

Discussion: GBM presenting as acute encephalitis syndrome (AES) is rare; it is the cause of encephalopathy in 1.5% of patients in a few case series. Brain MRI reveals geographic ring enhancing lesions of highly dense neoplastic cells with a hypodense core on T1 images representing necrosis. T2 and FLAIR reveal a surrounding zone of vasogenic edema. Our patient's clinical picture, MRI, and response to antivirals were suggestive of HSV encephalitis despite a negative PCR, which can occur early on in HSV encephalitis. Follow-up MRI in HSV encephalitis is suggested to monitor for late sequelae including hemorrhage and necrosis. The new necrotic lesion on our patient's follow-up MRI was concerning for post HSV sequelae, but MRS was performed to better characterize the lesion. MRS in GBM demonstrates increased choline to creatinine peak ratio, increased lactate peak and decreased N-acetylaspartate (NAA) peak, which our patient had. This case stresses the importance of including tumors such as GBM in a differential diagnosis of AES.

Paraproteinemia-associated Polyarteritis Nodosa

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Introduction: Polyarteritis nodosa (PAN) is a systemic necrotizing vasculitis of medium-sized vessels with clinical manifestations resulting from inflammation and ischemia of affected organs. PAN has been described in association with viral infections and various lymphoproliferative disorders. Few case reports exist describing PAN associated with multiple myeloma.

Case: A 44-year-old woman presented with worsening neck and back pain of 7 months duration associated with right lower extremity pain, paresthesia, and weakness with ankle dorsiflexion that started 3 months prior to admission. She also complained of severe fatigue and a recent 10-pound weight loss. On admission the patient was afebrile, hypertensive, and tachycardic. Exam revealed weakness with right ankle dorsiflexion and diminished sensation to light touch on the dorsum of the foot. Laboratory studies showed a creatinine of 1.75 mg/dl, normocytic anemia, positive antinuclear antibody (ANA) (1:80 titer), and elevated ESR and CRP. Urinalysis also showed 3+ protein and blood with a protein to creatinine ratio of 1.34. Serum protein electrophoresis revealed monoclonal paraproteinemia. The patient underwent kidney biopsy showing medium-sized vessel vasculitis consistent with PAN. Bone marrow biopsy and skeletal survey were completed and the patient was subsequently diagnosed with stage II IgG lambda multiple myeloma.

Discussion: While the association between vasculitis and cancer has been well described in the literature, there are only a small number of case reports describing paraneoplastic vasculitis in association with multiple myeloma. Hematologic malignancies, most frequently lymphomas, are the most commonly described malignancies associated with PAN. Clinical findings associated with PAN are nonspecific and, in general, no different than those seen in patients without underlying malignancy. The most common clinical features include fatigue, weight loss, and fever. Diagnosis requires vigilance and the integration of patient history, clinical findings, and biopsy data.

Respiratory Failure in Cryptogenic Organizing Pneumonia

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Introduction: Cryptogenic organizing pneumonia often presents with persistent coughing of 1 to 2 months duration, dyspnea on exertion, and weight loss in the setting of failed treatment for community acquired pneumonia. In many cases, this disease is managed on an outpatient basis after a lung biopsy confirms the findings of intraluminal

inflammation of alveoli including alveolar ducts. Treatment largely consists of steroids, which are slowly weaned over months.

Case: A 30-year-old man with a history of cognitive delay and CKD was brought by his mother to his primary care physician for a new-onset cough 5 days prior to hospitalization. His mother reported that aside from the new cough, he was well and continued to participate in daycare 3 days per week. He was placed on a 5-day course of azithromycin for atypical pneumonia but did not improve. They returned for reevaluation of his cough as well as a 1-day history of increased agitation. Initial workup was suggestive of pneumonia on clinical exam and chest radiograph, along with worsening kidney function. While in the ED, he developed increasing respiratory insufficiency and required intubation. He was started on broad spectrum antibiotic therapy and underwent diagnostic bronchoscopy on the first day of admission. Upon admission, he had leukocytosis that continued to rise despite therapy. After 7 days of IV antibiotic therapy and a large workup that remained negative, a lung biopsy showed evidence of organizing pneumonia.

Discussion: This case of biopsy-proven cryptogenic organizing pneumonia is unique because it presented in a 30-year-old man, and it was associated with respiratory failure requiring prolonged intubation. His initial chest radiograph showed bilateral pleural effusions with alveolar infiltration that could suggest a multifactorial cause as the reason for the respiratory failure. His leukocytosis continued to rise despite antibiotic therapy. Bronchoscopy with bronchoalveolar lavage (BAL) was performed on initial presentation to ICU and 5 days later, but both sets of cultures remained negative leading us to consider cryptogenic organizing pneumonia. Steroid treatment was the only therapy to improve his clinical status and ultimately allowed him to be extubated.

Still a Challenging Diagnosis

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Case: A 35-year-old man with a past medical history significant for juvenile idiopathic arthritis presented with 2 days of sharp, substernal chest pain preceded by 3 days of pharyngitis, fevers, and diffuse myalgias. Tachycardia, tachypnea, proximal muscle weakness, and white tonsillar exudate were present on physical examination. Initial diagnostic studies were significant for a leukocytosis of 13,000/uL, slightly elevated aminotransferase levels, an elevated troponin level, and PR segment depression in the inferior leads on electrocardiogram (ECG). A TTE was unremarkable. An initial diagnosis of myopericarditis was made, and treatment with colchicine and aspirin was initiated. Cardiac MRI showed changes consistent with myocarditis. Tests for HIV, parvovirus B19, coxsackie A and B viruses, cytomegalovirus, and hepatitis A and B were all negative. Multiple urine, respiratory, and blood cultures were also negative. The patient continued to spike high fevers each night, even after resolution of the chest and pleuritic pain, and his leukocytosis persisted. A ferritin level was checked and found to be significantly elevated at 3440 ng/mL. Based on the Yamaguchi criteria, the patient was diagnosed with adult-onset Still's disease.

Discussion: Adult-onset Still's disease (ASD) is an inflammatory disorder characterized by high daily fevers, arthralgia, and an evanescent rash. It is a rare condition, occurring in less than 1 per 100,000 people with a bimodal age distribution peaking between ages 15-25 and 36-46. Although an infectious origin is suspected, the etiology remains unproven. There is no definitive test or laboratory value to diagnose ASD. The Yamaguchi criteria are used to establish the diagnosis. The 4 major criteria are persistent high fever, leukocytosis, arthritis or arthralgia, and a skin rash that is usually present during the febrile episodes. The minor criteria include a sore throat, organomegaly, elevated liver function tests, lymphadenopathy, and normal ANA and rheumatoid factor. Five of these features must be present, including two of the major criteria. The serum ferritin level is also markedly elevated in the majority of these patients. Several treatment options are available, including nonsteroidal anti-inflammatory drugs, glucocorticoids, disease-modifying antirheumatic drugs, and biologic immunomodulatory agents. The prognosis in ASD is generally favorable.

Raynaud's to Renanl Crisis: An Atypical Scleroderma Presentation

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Introduction: Scleroderma renal crisis is a well-known severe complication of systemic sclerosis. However the renal crisis is only uncommonly the presenting feature of scleroderma without prior disease manifestations and requires a high degree of clinical suspicion to diagnose.

Case: A 25-year-old Hispanic woman with a history of Raynaud's phenomenon was hospitalized after her outpatient nephrologist noted her creatinine steadily rising over a week in conjunction with elevated blood pressures and new thrombocytopenia. An admission 1 month prior for hypertension and tachycardia resulted in an exclusionary diagnosis of constipation-induced hypertension. On present admission, examination was negative except for elevated blood pressures and trace pedal edema. Thrombotic thrombocytopenia was excluded, as were pheochromocytoma and renal artery stenosis. The patient's renal function continued to worsen, and a kidney biopsy was performed showing thrombotic microangiopathy. Hemodialysis was initiated. The patients' blood pressures remained elevated despite multiple medications, however no angiotensin-converting enzyme (ACE) inhibitor was initially begun. An autoimmune workup revealed a positive ANA and, despite no synovitis or skin abnormalities, a rheumatology consultation was obtained. The consulting service suggested the early presentation of systemic sclerosis based on the overall clinical picture. A subsequent esophagram revealed a widely patent gastroesophageal junction consistent with the patulous gastroesophageal (GE) junction often seen in patients with scleroderma. The patient was begun on an ACE inhibitor with improvement in her blood pressure, and eventually was discharged with continued hemodialysis and close nephrology and rheumatology follow-up.

Discussion: Though commonly diagnosed by rheumatologists, scleroderma can present atypically with minimal clinical evidence and requires a high degree of clinical suspicion to diagnose. A usual presentation of scleroderma

would be in a 30- to 50-year-old woman with Raynaud's, skin tightening, and intestinal symptoms. True Raynaud's phenomenon is not normal and can represent the early pathological immune infiltration and microvascular damage of scleroderma.

Tricuspid Regurgitation: Valvular Dysfunction on the Rise

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Case: A 75-year-old man with a history of coronary artery disease, congestive heart failure and second-degree atrioventricular heart block status-post pacemaker presented from an outside hospital for progressive weight gain and increasing abdominal girth over a year. Patient denied shortness of breath, alcohol or drug use, or recent travels. On labs, AST, ALT, and alkaline phosphate were mildly elevated with a normal bilirubin, INR, and albumin. He also had acute kidney injury and thrombocytopenia, but the remainder of the CBC and complete metabolic panel were normal. Abdominal ultrasound revealed findings consistent with cirrhosis (portal hypertension, a moderate ascites, and bidirectional flow within the portal vein). On admission to our hospital, viral serologies for hepatitis were negative. His pacemaker was interrogated and revealed new atrial fibrillation. A repeat echocardiogram showed a left ventricular ejection fraction (EF) of 45% to 50%, normal right ventricular function, severe biatrial dilation and pinning of the posterior leaflet of the tricuspid valve by the pacemaker lead with wide-open tricuspid regurgitation. Patient had a normal pulmonary artery systolic pressure. Patient was aggressively diuresed, amiodarone was initiated, and patient was cardioverted with restoration of sinus rhythm. His ascites, peripheral edema, acute kidney injury, and thrombocytopenia improved. On discharge he was scheduled for a repeat echocardiogram to reassess his tricuspid regurgitation.

Discussion: Pacemakers and implantable cardioverter-defibrillators (ICDs) are important medical devices used in the treatment of a variety of cardiac diseases. With the aging population and an increase in life expectancy, utilization of these devices is expected to continue to rise. As such, it is important that general internists appreciate not only the indications, but also the complications that can occur secondary to these devices. Tricuspid regurgitation is one such known but underappreciated complication. Limited data on the frequency of tricuspid regurgitation related to endocardial lead implantation is conflicting, but the importance and clinical impact is not. Severe tricuspid regurgitation is known to be associated increased mortality. Early diagnosis of and intervention is critical for addressing an iatrogenic cause of valvular dysfunction.

Methanol Toxicity and a Normal Osmolar Gap

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Introduction: In patients presenting with volatile alcohol toxicity, early diagnosis and treatment is critical to prevent organ damage and death. The goal standard for diagnosing methanol and ethylene glycol (EG) toxicity is gas chromatography. Results can take up to days and many hospitals are not equipped to provide such test. Clinicians must rely on the clinical presentation and other laboratory tests such osmolar gap (OG) to make a diagnosis. An OG of >10 indicates the presence of other osmoles in the blood such as methanol or EG. We present a case of methanol toxicity and a normal osmolar gap.

Case: A 48-year-old Caucasian man was admitted to a community hospital 20 minutes after ingesting > 500 tablets of extra-strength acetaminophen. N-acetylcysteine infusion was initiated. He was mechanically ventilated due to impending respiratory failure. Initial laboratory revealed acetaminophen level of 86 mg/L, high anion gap metabolic acidosis (AGMA), negative urine analysis and serum drug screen. The patient was transferred to our facility (tertiary center) for further management. Upon arrival, acetaminophen level was >800 mg/L and lactic acid was 10.5 mmol/L. Serum osmolality was 296 mOmol/Kg with a normal osmolal gap (OG). Later, he developed acute hepatic and renal failure. Despite appropriate management, he had persistent metabolic acidosis, thus a volatile gas screen was ordered. The results were available within 3 hours and were positive for methanol intoxication. The patient was started on renal replacement therapy and fomepizole infusion. The remaining of the hospital course was significant for development of cerebral edema. Hypothermia protocol was initiated. He then had an upper GI bleed that was likely secondary to caustic ingestion.

Discussion: An elevated OG is highly sensitive for volatile alcohol intoxication, but a normal OG does not necessarily rule it out. Once methanol is converted to its toxic metabolite—formic acid, this compound is no longer osmotically active. In the case of our patien, the OG may have been normal because it was checked several hours after the ingestion. Methanol may have been converted to formate, which causes AGMA. In addition, some patients may have an OG in the negative range at baseline (children have an OG of -2 +/- 6), making an OG <10 abnormal in such cases.

Lupus-Related Pulmonary Hemorrhage

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Introduction: Systemic lupus erythematosus (SLE) is an autoimmune disorder that can affect any organ system. Pulmonary hemorrhage (PH) is a rare (<2%-5.4%) but catastrophic complication (mortality 26%-92%) of SLE.

Case: A 29-year-old African-American woman with SLE managed with prednisone and mycophenolate presented with hemoptysis. Her initial exam revealed tachypnea and diffuse right-sided rales. Labs showed a normal white cell count, hemoglobin at baseline of 10.1 g/dL, platelets of 127,000, normal basic metabolic panel, elevated CRP of 1.0 mg/dL, low C3 of 74 mg/dL, and normal C4. She was intubated after several episodes of hemoptysis and increasing oxygen requirements. Chest radiograph revealed patchy infiltrates throughout the right lung, which rapidly progressed to diffuse bilateral alveolar infiltrates. Broad spectrum antibiotics were initiated and bronchoscopy revealed bloody secretions from her bilateral bronchi. High-dose IV methylprednisolone was initi-

ated, and she was continued on oral mycophenolate. After 3 days of IV steroids without improvement, plasmapheresis was initiated, resulting in significant improvement and extubation after the first of 5 sessions. At discharge, she had complete resolution of pulmonary hemorrhage and stable blood counts.

Discussion: Due to varied clinical presentation and nonspecific radiological findings, the diagnosis of PH may be challenging. No clear predictors of patients at increased risk of developing PH exist. Bronchoscopy with BAL is reliable in diagnosing PH and identifying possible infection. This is critical as treatment of PH requires high-dose immunosuppression. Broad spectrum antibiotics are recommended while awaiting culture results. After PH diagnosis, high dose IV steroids and cyclophosphamide should be initiated. Due to previous treatment failure with cyclophosphamide, our patient was treated with high dose IV steroids and mycophenolate. However, plasmapheresis is effective in patients who fail initial therapy, as seen in our patient.

Doubly Uncommon

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Introduction: Fusobacterium nucleatum is an anaerobic gram-negative bacillus best known for its role in causing periodontal disease. This is a rare case of a patient who presented atypically with infective endocarditis, found to be secondary to *F nucleatum.*

Case: A 71-year-old woman presented with a 1-week history of right index finger pain. Physical exam was significant for fever, cyanosis of the right distal phalanx, and a new III/VI systolic murmur. Blood cultures were drawn, and she was started on empiric antibiotics for concern of endocarditis. TTE did not identify any masses or vegetations, but transesophageal echocardiography (TEE) revealed a small, serpiginous echodensity in continuity with the posterior leaflet. Over 48 hours later, one blood culture returned positive for *F nucleatum*, and the patient was treated with ertapenem for endocarditis. At subsequent follow-up, she had improvement in her right index finger pain and resolution of her murmur.

Discussion: Although documented cases of *F nucleatum*-causing endocarditis are quite rare, many of the features of this patient's case are consistent with prior known cases. Thromboembolic phenomena, the presenting feature in this patient, have been frequently associated with *F nucleatum*. Additionally, this patient had no underlying valvular disease, which was also the case in a high proportion of previously documented cases of *F nucleatum* endocarditis. Although *F nucleatum* bacteremia can be fatal, its presentation often is insidious, as it was in this patient. Diagnosis of IE relies heavily on the use of blood cultures and echocardiography. In this patient, a new onset murmur was the most useful tool in establishing the diagnosis, serving as a reminder that while blood cultures and echocardiography are important, overutilization of them should not serve as a substitute for a thorough history and physical examination.

Thrombolytics and Hypothermia Protocol in Early Gestation Pregnancy with Pulseless Electrical Activity Arrest

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Introduction: The hypothermia protocol was developed for patients who underwent ventricular fibrillation arrests in the field, but it is being utilized more widely.

Case: A 34-year-old woman with 13-week pregnancy was found down by her husband. Cardiopulmonary resuscitation (CPR) was started 10 minutes later with emergency medical services (EMS). She regained pulses after 7 minutes of compressions. Upon arrival, she was nonreactive and subsequently underwent CPR twice more. Bedside echocardiogram noted right ventricular strain and CT scan showed massive bilateral pulmonary embolism with thrombus extending to the segmental arteries. She was treated with thrombolytics, and hypothermia protocol was initiated. Rewarming was completed without acute events, with pressor support discontinued and extubation the day after. She did return to the medical intensive care unit (MICU) for respiratory distress secondary to blood clot found in the airway, which was removed without issue. She was discharged with normal neurologic exam. Follow-up as outpatient showed normalization of her right and left ventricular function. Unfortunately, the fetus shows evidence of fetal hydrops but persistent cardiac rhythm, and the family plans to complete to term.

Discussion: Cardiopulmonary arrest occurs in 1:30,000 pregnancies. There have been several case reports of successful resuscitation in pregnant women, with varying viability of the fetus. The International Liaison Committee on Resuscitation and the American Heart Association advocate delivery within 5 minutes of loss of maternal circulation for best chance of survival. However, in the field this is often impractical. This particular case illustrates the importance of timely diagnosis and intervention in that the administration of thrombolytics and hypothermia likely had significant impact on the return of the mother's neurologic status.

Mixed Picture – A Probable Case of NSAID-induced Hepatotoxicity

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Introduction: Sulindac is the nonsteroidal anti-inflammatory drug (NSAID) most frequently associated with hepatotoxicity at a rate about 5 to 10 times that of other NSAIDs. The pattern of injury is usually mixed, representing both hepatocellular and cholestatic injury with an idiosyncratic mechanism of action.

Case: A 53-year-old man with a past history of hepatitis B infection and recent colitis presented with nausea, abdominal pain, and fatigue of 1 day's duration. He described the pain as dull in quality, diffuse in location, and exacerbated by eating, but not accompanied by vomiting, diarrhea, bloody or black stools. His medications included sulindac, cyclobenzaprine, doxazosin, omeprazole, and tramadol. His initial vital signs were normal, and his physical exam was significant for diffuse abdominal tenderness on palpation with voluntary guarding most pronounced in the right upper quadrant. His initial laboratory studies were significant for a leukocytosis with total bilirubin 1.4 mg/dl, alkaline phosphatase 347 U/l, AST 199 U/l, ALT 198 U/l, and γ-Glutamyltransferase 1589 U/l. His sulindac was discontinued due to the

possibility of NSAID hepatotoxicity. A conservative approach of bowel rest, pain control, and hydration was taken while awaiting further laboratory tests, including infectious and metabolic causes of mixed hepatotoxicity. The patient improved clinically over the next 4 days without further imaging or intervention, and several weeks later his hepatic function studies had nearly normalized.

Discussion: This case reinforces the importance of medication reconciliation during history taking, critical thinking, and the value of conservative medical management in patients with abdominal pain. NSAID-induced hepatotoxicity is relatively common and well-documented in the literature as the cause for about 10% of overall drug-induced liver injury. It is associated with moderate morbidity, but low mortality rates as it rarely leads to fulminant hepatic failure. Most patients don't even require hospital admission; therefore, early addition of this diagnosis to the differential in a patient on NSAIDs with acute abdominal pain can reduce unnecessary imaging, laboratory workup, and potentially days of hospital stay.

First Do No Harm: Corticosteroids and Recurrent Pericarditis

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Introduction: Recurrent pericarditis is a particularly troublesome complication of acute pericarditis and is seen in up to 30% of patients. Corticosteroid therapy is an independent risk factor for development of recurrent pericarditis. We present a case of recurrent pericarditis due to inappropriate use of corticosteroids to treat presumed viral bronchitis.

Case: A 43-year-old man without any past medical history presented to the urgent care clinic with cough, subjective fever, and wheezing. He was diagnosed with acute bronchitis and given tapering dose of prednisone and doxycycline. He came to the ED 1 week later with c/o substernal chest pain, fever, tachypnea, tachycardia, and pulsus paradoxus of 40 mmHg. CT showed significant left pleural effusion and large circumferential pericardial effusion. A diagnosis of symptomatic pleuropericarditis with effusions was made. Echocardiogram confirmed large pericardial effusion. Pleural fluid studies were consistent with a transudate. Repeat echocardiogram showed improvement in pericardial effusion and patient was discharged home on ibuprofen and colchicine. He presented to ED 1 week later with worsening shortness of breath due to reaccumulation of pericardial effusion. A pigtail drain was placed in his pleural space with removal of over 1 liter of fluid. At this point, corticosteroids were introduced to treat his recurrent pericardial effusion. Autoimmune testing was equivocal. He was discharged on colchicine, ibuprofen, and prednisone.

Discussion: Recurrent pericarditis is a troublesome complication of acute pericarditis and occurs in 15% to 50% of cases. While corticosteroids traditionally have been used to treat acute pericarditis, it is now believed that treatment with corticosteroids during the index attack is an independent risk factor for development of recurrent disease. Corticosteroids can be used to treat refractory, recurrent, autoimmune, and uremic pericarditis.

Gemcitabine: A New Cause of Veno-Occlusive Disease

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Introduction: Veno-occlusive disease (VOD) is a rare complication of high-dose chemotherapy with significant mortality, most commonly seen in patients undergoing allogeneic stem cell transplantation. Gemcitabine is a common chemotherapy agent used in the treatment of various cancers, like non-small-cell lung cancer, pancreatic cancer, metastatic breast cancer, and in salvage therapy for lymphoma. Common side effects include myelosuppression, metabolic, pulmonary, and cardiac complications. This case illustrates 2 rare complications of gemcitabine: thrombotic thrombocytic purpura (TTP) and VOD.

Case: A 65-year-old woman with history of peripheral T-cell lymphoma was admitted with weakness and falls. Patient was noted to have progression of disease despite treatment with other chemotherapy regimens and was started on gemcitabine and dexamethasone. On day 3 after administration, patient developed elevated liver enzymes, doubled total bilirubin, and elevated direct bilirubin, and chemotherapy was held. She soon developed worsening renal function and thrombocytopenia with schistocytes, indicative of TTP. Unfortunately patient's medical condition continued to worsen and bilirubin continued to trend up. Liver biopsy showed VOD. Patient received comfort care and died 2 days later.

Discussion: VOD is believed to be related to endothelial injury in liver venules; initially presenting with weight gain, ascites, tender hepatomegaly, and elevated bilirubin levels; and associated with renal failure. This case represents non-bone marrow transplant patient who developed rare side-effects of VOD and TTP in the setting of gemcitabine. This case demonstrates an established chronological relationship with gemcitabine and biopsy-proven VOD along with femcitabine-related TTP diagnosed simultaneously. It is important to recognize VOD in the context of gemcitabine exposure, especially in patients with symptoms suggestive of VOD, even if they are not stem cell transplant recipients, as they must be managed aggressively given severe mortality associated with the disease.

Critical Illness Polyneuromyopathy

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Introduction: Development of neuromuscular weakness is a clinical finding often seen in patients admitted to the ICU. In these patients, the diagnoses of either critical illness myopathy (CIM) or critical illness polyneuropathy (CIP) must be considered. In certain cases, both of these diagnoses may be present.

Case: A 46-year-old woman presented with a 2-week history of dyspnea, cough, and fever. Her past medical history was remarkable for non-Hodgkin's lymphoma diagnosed 13 years ago and treated with radiation, chemotherapy, and bone marrow transplant. She subsequently developed renal failure and underwent renal transplant 3 years ago, for which she was currently on immunosuppressive therapy. In addition, she had a history of interstitial lung disease and had developed nontuberculous mycobacterial disease

6 months prior to admission. Initial evaluation demonstrated a systemic inflammatory response syndrome without a clear infectious source. Treatment in the ICU initially consisted of broad-spectrum antibiotics for presumed hospital-acquired pneumonia as well as stress dose steroids and IV fluid resuscitation, resulting in improvement in the her clinical status. Subsequent negative bacterial cultures and positive respiratory syncytial virus (RSV) NAAT led to discontinuation of antibiotics. Despite identification of the patient's infectious disease and improvement in other clinical parameters, her respiratory status worsened, leading to intubation with mechanical ventilation. Broad-spectrum antibiotics and IV methylprednisolone were initiated again with little to no improvement in her respiratory status and failure to wean mechanical ventilation over the next 9 days. She subsequently developed generalized flaccid weakness as well as absent reflexes. Nerve conduction studies (NCS) and EMG findings, along with the aforementioned clinical features, were consistent with a diagnosis of critical illness polyneuromyopathy. Continued attempts to wean mechanical ventilation failed, and the patient's clinical status continued to deteriorate. On hospital day 25, she had cardiac arrest and died.

Discussion: The diagnosis of critical illness polyneuromyopathy is made when a patient has signs, symptoms, and test results consistent with both CIM and CIP. CIM, which is often associated with IV glucocorticoids, presents with flaccid paralysis of all 4 extremities with preservation of sensation. In CIP, which is associated with severe sepsis, the patient has loss of sensory function in addition to muscle weakness and absent reflexes. EMG and NCS are used to confirm each diagnosis respectively. Muscle biopsy showing myosin loss in the setting of electrophysiologic evidence of axonal motor and sensory polyneuropathy is helpful in confirming the diagnosis. Recent studies indicate that an acquired sodium channelopathy may be the underlying cause for critical illness polyneuromyopathy. Management is aimed at the diagnosis responsible for the critical illness. Resolution of symptoms, if it occurs, takes weeks to months.

Dermatomyositis with Absent Skin Findings

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Introduction: Dermatomyositis is an idiopathic inflammatory myopathy characterized by distinctive dermatological findings such as shawl sign, Gottron's papules, and heliotropic rash. Antisynthetase syndrome is a condition that presents with interstitial lung disease, arthritis, fever, Raynaud's syndrome, and myositis with anti-Jo1 antibodies. Diagnosis is established by elevated muscle enzymes, electromyography, and muscle biopsy.

Case: We report the case of a 38-year-old woman who presented with complaints of worsening cough, muscle pain, and weakness that began 1 week prior to admission. She had had previous multiple admissions for similar symptoms with uncertain diagnosis. Examination showed decreased strength in the proximal muscles, as well as diffuse muscle tenderness. Examination was negative for skin rash, Raynaud's phenomenon, or mechanic's hands. Initial chest CT showed severe scarring in bilateral lung bases. Serology was positive for ANA antibodies and anti-Jo1 antibodies, suggesting the diagnosis of inflammatory myopathy associated with interstitial lung disease. BAL was negative for infectious pathology. Muscle biopsy performed on day 4 of admission illustrated a clear inflammatory response, with variable fiber size, myophagocytosis, and perivascular muscle atrophy. The latter finding is considered to be pathognomonic for dermatomyositis. She was started on both prednisone and tacrolimus. Her condition improved significantly with this regimen, in addition to physical and respiratory therapy. She was discharged to acute rehabilitation therapy and scheduled for outpatient malignancy screening.

Discussion: Dermatomyositis without any of the characteristic skin manifestations is an uncommon finding. Patients with antisynthetase syndrome can present with myriad symptoms; however, these symptoms are not all required or frequently seen, posing a challenge for the clinician to diagnose. This diagnosis is crucial, however, as approximately 15% of patients with dermatomyositis have an associated malignancy. Treatment and prognosis of patients with antisynthetase syndrome varies greatly depending on the type, severity, and progression of the lung disease. For patients such as ours with severe interstitial lung disease, systemic glucocorticoids with the addition of a second immunosuppressive agent are the treatment of choice.

Certolizumab-induced Cardiotoxicity in the Treatment of Ulcerative Colitis

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Case: A 28-year-old woman with a 13-year history of ulcerative colitis (UC) with significant clinical symptoms despite multiple conventional medical regimens was placed on infliximab therapy for 3 years with initial good response. Later, due to development of serum sickness, infliximab was replaced by adalimumab for 4 months without response, then certolizumab was used. However, her symptoms remained poorly controlled with persistent active pancolitis, elevated ESR (average 6.35 mg/dL), and CRP (average 42.6mm/hr). Over the following 6 months, she underwent 4 hospitalizations, including hospitalization for gram-negative bacillary sepsis and *C difficile* colitis. Finally, colectomy was performed. Fifteen month after initiation of certolizumab, during a hospitalization, she developed intermittent dizziness, palpitations, and left-sided chest pain unrelated to exertion. She had no orthopenea or dyspnea with exertion. Echocardiogram showed borderline enlargement of the left ventricle with severe systolic dysfunction (EF 30%-35%). She had no prior cardiac history and other causes of cardiotoxicity were excluded. Certolizumab was stopped due to the concern it may be the cause of cardiotoxicity. Seventeen months after stopping certolizumab, repeat echocardiogram showed a normal-sized left ventricle and only mild systolic dysfunction (EF 45%-50%).

Discussion: One of the most significant developments in the treatment of moderate to severe inflammatory bowel disease has been the class of biologics that are therapeutic antibodies against TNF-alpha. Certolizumab is a humanized pegylated anti–TNF-alpha antibody Fab fragment with clear efficacy in the

treatment of Crohn's disease with closure of draining fistulas, reduction of chronic glucocorticoid medication, and lasting remission. Recently, certolizumab also has been used in the treatment of UC. In addition to common side effects associated with immunomodulatory agents, cardiotoxicity has been reported with certolizumab. Although this complication is rare, it can be fatal. Therefore, monitoring cardiac function is critical when using any anti-TNF agent.

The Effects of Allergy Medications on the Evaluation and Diagnosis of Eosinophilic Esophagitis

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Introduction: Eosinophilic esophagitis (EoE) is an increasingly recognized cause of dysphagia and food impactions in adults. EoE is a chronic immune, antigen-mediated, esophageal disease characterized histologically by eosinophil predominant inflammation. EoE patients have atopy/allergy predisposition and frequently are treated with allergy medications prior to EoE diagnosis. We sought to evaluate the effect allergy medications have on diagnosis of patients with EoE.

Methods: A retrospective cohort of 51 patients diagnosed with EoE was enlisted over a 3-year period from dysphagia clinic. Use of allergy medication prior to EoE diagnosis was recorded. Each patient's endoscopic severity was graded on a 10-point scale. A pathologist blinded to the results recorded max number of eosinophils and histologic severity. Patients taking allergy medications (inhaled and nasal steroids, antihistamines, leukotriene antagonists) were compared to those not taking medications.

Results: Of the 51 patients in the study, 20 (39%) were on at least 1 allergy medication at the time of their diagnosis. There was a trend toward patients on allergy medications having a lower max eosinophil count (24.5 vs 31.5) on biopsy, although this did not reach statistical significance. There were more patients with <15 eosinophils on biopsy in the medication group compared to the non-medication group (35% vs 16%). There was a trend towards decreased endoscopic severity in the medication group, but this difference did not meet statistical significance (3.2 vs 2.95). Subgroup analysis of patients on steroids also did not show significant differences in eosinophil count or endoscopic severity.

Acute Mitral Regurgitation: Another Great Masquerader?

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Introduction: Asymmetric or unilateral pulmonary edema is a rare cause of focal abnormalities on chest imaging, and it is frequently mistaken for more common conditions such as infection or malignancy. Acute mitral regurgitation is an important etiology of pulmonary edema and should be considered in any patient presenting with respiratory symptoms and abnormal lung imaging.

Case: An 87-year-old woman presented with dyspnea and hypoxia. Her chest CT revealed extensive consolidation and ground glass opacities predominantly in the right lung. She was treated with antibiotics for a presumed atypical infection without significant improvement. TTE showed mitral valve prolapse but no regurgitation. However, TEE demonstrated an extremely eccentric (explaining the lack of TTE findings), severe mitral regurgitation with a flail anterior leaflet due to idiopathic chordae rupture. The regurgitant jet generated more significant flow reversal in the right pulmonary veins than it did in the left, which could explain the unilateral chest findings. Myocardial infarction as an etiology was excluded. Other less common conditions associated with ruptured chordae, such as IE, blunt chest trauma, acute rheumatic fever, extensive mitral annular calcification, hypertrophic cardiomyopathy, and myxomatous disease, were unlikely. Due to advanced age and comorbidities, our patient chose medical management with afterload reduction rather than surgical valve repair.

Discussion: This case highlights the importance of recognizing the variation in clinical manifestations of acute mitral regurgitation. Acute mitral regurgitation is commonly misdiagnosed on presentation because the history and imaging findings may mimic an acute pulmonary process such as infection, acute pneumonitis, or acute respiratory distress syndrome. Physicians may need to include acute valvular regurgitation in the differential diagnosis of any patient presenting with pulmonary manifestations, even with focal findings on chest imaging.

Hungry Bone Syndrome: How Much Calcium Is Enough?

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Introduction: After surgical correction of tertiary hyperparathyroidism with subtotal parathyroidectomy, aggressive bone remineralization and functional hypoparathyroidism can cause severe prolonged hypocalcemia known as "Hungry Bone Syndrome." As the following case illustrates, the duration of hypocalcemia is difficult to predict in this setting. Safe titration of calcium supplementation requires early identification of appropriate treatment targets.

Case: A 28-year-old woman with history of chronic dialysis-dependent ESRD presented with 4 days of weakness, dizziness, and paresthesias. She had undergone a subtotal parathyroidectomy 20 day prior due to severe tertiary hyperparathyroidism. Peak PTH prior to surgery was 3752 pg/ml; postoperatively it fell to 15-17 pg/ml. On admission she was noted to have tetany with serum calcium level of 5.2 mg/dL (ionized calcium 3.15 mg/dL). PTH on admission was 98 pg/ml. She was diagnosed with Hungry Bone syndrome and treated with a continuous infusion of IV calcium gluconate, oral calcium carbonate, and calcitriol. After 3 weeks, she was discharged on oral calcium and calcitriol; however, 48 hours later, she was readmitted with hypocalcemic tetany requiring reinitiation of continuous calcium infusion. After 3 more weeks of treatment with IV calcium infusion, she was discharged home successfully on oral therapy without recurrence of symptomatic hypocalcemia.

Discussion: Standard goals of therapy in Hungry Bone syndrome are to relieve symptoms and maintain low-normal serum calcium concentrations, typically 7.5-8.5 mg/dL. Rapidly progressive or symptomatic hypocalcemia after parathyroidectomy should be treated with 1-2g IV calcium gluconate followed by continuous infusion

of 0.5-1.5mg/kg/hr elemental calcium and 2-4g/day of elemental calcium orally. Serum phosphorus and magnesium should be monitored and replenished aggressively. Vitamin D deficiency should be corrected. Calcitriol is necessary in ESRD because of impaired 1-alpha hydroxylase activity. To prevent cardiac and neurologic complications, intensive monitoring and treatment must continue until symptoms are controlled and calcium levels are stable.

Dyspnea on Exertion and Cardiac Sarcoid

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Introduction: The lifetime risk of developing sarcoidosis ranges from 0.85% to 2.4%. Approximately 5% of patients with sardoidosis develop clinically relevant myocardial involvement.

Case: A 59-year-old white man presented to his primary care provider (PCP) to discuss a 6-month history of worsening DOE. The patient's only medical history included hypertension (HTN). ETT was negative. He reported running 5 miles per day previously, but now had difficulty climbing 1 flight of stairs. TTE showed depressed left ventricular ejection fraction (LVEF) 40%, severely reduced RV systolic function with dilation and apical wink, severely dilated right atrium, and a small pericardial effusion. The PCP told the patient to present to the ED for pulmonary embolism (PE) evaluation. In the ED, he complained of worsening DOE and new left-sided chest pain radiating down his left arm and lasting a few seconds. An ECG noted normal sinus rhythm, 1AVB, RBBB, and anterior ST-elevation with inverted T waves. He had no acute complaints and his vital signs were within normal limits. A CT angiogram (CTA) chest ruled out PE. Basic labs were drawn in addition to a troponin, which was positive at 0.27ng/ml. The patient was admitted to the cardiology ward for further workup. He was stable overnight and his troponin peaked at 0.30ng/ml. The next morning, coronary catheterization showed nonocclusive coronary artery disease and cardiac MRI was consistent with cardiac sarcoid. The CT angiogram chest showed mediastinal and bilateral hilar lymphadenopathy consistent with sarcoidosis. An ACE level was positive. The patient was discharged on steroids.

Discussion: This case illustrates the varied presentations of sarcoidosis and the importance of a thorough evaluation of new onset heart failure.

Autoimmune Lymphoproliferative Syndrome: A Case Report

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Introduction: Discriminating between self and foreign antigens is an integral component of immunity. One mechanism by which lymphocytes accomplish this is through FAS-mediated apoptosis. Ineffective apoptosis results in a rare genetic condition known as autoimmune lymphoproliferative syndrome (ALPS).

Case: J is a 26-year-old man whose clinical picture is consistent with this rare disorder. He first came to medical attention at age 5, when he presented multiple times with epistaxis, petechiae, and mucosal bleeding secondary to thrombocytopenia. He was found to have an autoimmune hemolytic anemia. These episodes responded to high-dose steroids. By age 14 he had had 3 episodes of shingles and an episode of severe onychomycosis. Subsequent T-cell and immunoglobulin analysis showed low absolute lymphocytes and IgA deficiency.

He remained well from age 16 to 23, when he was hospitalized with a subdural hematoma 3 days following a snowboarding accident. He was found to have a hemoglobin of 3 and a massive spleen. He was treated with splenectomy, rituximab, and a steroid taper with good response. In 2011 he presented with diffuse lymphadenopathy, leukocytosis, and fevers. Malignancy workup was negative. He had numerous hospitalizations in 2011-2012 for bleeding from immune thrombocytopenia and Coombs-positive hemolytic anemia. He became resistant to high-dose steroids, rituximab, and mycophenolate and required greater than 90 units of red blood cells. Bone marrow biopsies showed erythroid hyperplasia and a complete absence of megakaryocytes.

J meets the 2 required diagnostic criteria and 2 of the secondary accessory criteria for ALPS based on the 2009 National Institutes of Health international workshop, giving him a diagnosis of probable ALPS. FAS mutation testing done by NIH was negative, placing him in the category of probable ALPS-U. Since diagnosis was made, he has been treated with antithymocyte immunoglobulin and cyclosporine and is again in a clinical remission. His history and negative FAS mutation studies raise the question to the existence of alternative mediators of apoptosis and self-recognition.

The Budd-Chiari Syndrome: An Important Consideration in New-Onset Ascites

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Introduction: New-onset ascites can be a diagnostic challenge, especially in previously healthy patients with no risk factors for liver disease. As this case demonstrates, the Budd-Chiari syndrome should be considered in any patient with new ascites and portal HTN as early recognition has important implications for treatment and prognosis.

Case: A 29 year-old woman presented to her PCP with 2 months of increasing abdominal distention and fatigue. She was concerned about possible pregnancy but home tests were negative. Physical exam was notable for marked abdominal distention, significant lower extremity edema, and spider angiomata with massive ascites confirmed by ultrasound. Upon admission, laboratory evaluation revealed total bilirubin of 3.1, mild transaminitis, an INR of 1.7 and a hemoglobin of 16.8. Ascitic fluid analysis showed serum-ascites albumin gradient of 3.25 consistent with portal HTN. Additional history obtained was negative for alcohol use, hepatitis risk factors, or family history of liver disease; serologic testing was unrevealing. CTA revealed splenomegaly, nodular liver suggestive of cirrhosis, and diffuse heterogeneous hepatic enhancement with non-visualized hepatic veins. Doppler ultrasound showed hepatic congestion with absence of hepatic venous flow, leading to a diagnosis of Budd-Chiari syndrome. Genetic testing confirmed the presence of the JAK2 (V617F) mutation and heterozygosity for Factor V Leiden. Subsequent bone marrow biopsy

revealed markedly hypercellular marrow (80%-90%) with panhyperplasia indicative of a myeloproliferative process and consistent with polycythemia vera. Treatment was initiated with anticoagulation, diuretics, and phlebotomy, with referral for consideration of liver transplantation given her advanced liver disease.

Discussion: Budd-Chiari syndrome results from any process that causes disruption of blood flow from the liver, but most commonly refers to thrombosis in the hepatic veins or inferior vena cava. It is a rare but important cause of ascites and liver disease. Myeloproliferative disorders are associated with up to 50% of Budd-Chiari syndrome cases, such as in this patient with previously undiagnosed JAK2-mutation polycythemia vera and Factor V Leiden heterozygosity. Treatment of underlying disorders is essential, highlighting the value of performing a comprehensive diagnostic evaluation for patients presenting with new-onset ascites and cirrhosis.

Emphysematous Pyelonephritis in the Setting of Poorly Controlled Diabetes Mellitus

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Introduction: Emphysematous pyelonephritis (EP) is a life-threatening necrotizing kidney infection characterized by intrarenal or perinephric gas seen primarily in diabetics.

Case: A 56-year-old man with non-insulin-dependent diabetes mellitus presented with a 2-week history of fever, chills, and right flank pain. Exam revealed an ill-appearing man in moderate distress with BP 109/49 mmHg, temperature 37°C, HR 85/min, respiratory rate of 25/min, and SaO2 99% on FiO2 of 0.28. Abdominal examination revealed right-sided costovertebral angle tenderness. Laboratory studies showed WBC 35.8 × 109/l, a serum glucose level of >750 mg/dl, pH 7.24, HCO3 of 12 mmol/l, pCO2 of 41 mmHg, potassium of 7.7 mmol/l, anion gap of 24, a creatinine level of 9.90 mg/dl and serum ketones were mildly elevated. Urine cultured *Eshcherichia coli.* CT showed gas in the right kidney, extending into the retroperitoneum, consistent with EP. Initial treatment consisted of large-volume fluid resuscitation, insulin infusion and broad-spectrum antibiotics. An emergency nephrectomy was performed. A significant amount of purulent fluid was noted in the retroperitoneum and the kidney was partly necrotic. Postoperatively the patient required short-term dialysis but then improved and was off ventilator and vasopressors 36 hours from surgery.

Discussion: EP is an acute infection of the renal parenchyma that is most often observed in patients with poorly controlled diabetes mellitus (~95%) and is usually caused by *E coli* (70%). Depending on the severity of the infection, medical management plus either percutaneous drainage or nephrectomy is recommended. Risk factors associated with increased mortality include acute renal failure, thrombocytopenia, altered level of consciousness, and shock. CT is the diagnostic method of choice but a plain radiograph detects renal gas in the majority of cases. Even with early diagnosis and aggressive management, mortality remains high (~14%).

Myocardial Infarction, Deep Vein Thrombosis, Pulmonary Embolism, and In-stent Restenosis in a Patient with Heparin-induced Thrombocytopenia

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Introduction: Most commonly in heparin-induced thrombotic events, deep vein thrombosis (DVT) and PE comprise 25% of life-threatening events. Less commonly, arterial thrombotic events occur which can cause stroke, myocardial infarction, and limb ischemia.

Case: A 61-year-old man was hospitalized and placed on heparin for DVT prophylaxis. Ten days later, he had a ST-segment elevation myocardial infarction (STEMI) to his PRCA requiring a BMS. Two days later, he developed right lower extremity swelling. Doppler study showed extensive clot extending from the popliteal vein to the common femoral vein and patient was started on a heparin infusion (platelets 194,000). The next evening, he became bradycardic, tachypnic, and hypoxic. CTA chest revealed extensive acute bilateral pulmonary embolus (platelets 41,000). The thrombocytopenia with advent of clotting led to the suspicion of heparin-induced thrombocytonpenia (HIT). Therefore, heparin infusion was stopped, HIT antibody sent (which was later positive), and tissue plasminogen activator (tPA) was given followed by argatroban. Patient was intubated and hypoxia briefly improved after tPA administration. Later that night, hypoxia and hypotension worsened, requiring multiple vasopressors. Patient was sent to the cardiac catheterization lab for hemodynamic support; PRCA was 100% reoccluded. An aspiration thrombectomy was performed. Intraprocedurally, the patient went into complete heart block, which required placement of an intravenous pacer. Based on the angiographic appearance, the right ventricle and inferior base were not contracting. Therefore, an intra-aortic balloon pump (IABP) and a right ventricular assist device (RVAD) were placed. The right ventricle recovered enough to allow removal of the RVAD and IABP 3 days after its placement. Head CT 8 days after initiation of argatroban revealed an intraventricular hemorrhage. Argatroban was discontinued due to the intracranial hemorrhage and IVC filter was placed. The patient exhibited gradual improvement and was discharged home.

Discussion: This case demonstrates the morbidity of HIT, and reminds clinicians to have a high suspicion when thrombosis develops with thrombocytopenia.

A Case of Severe Anemia with Low Reticulocyte Count and Hemolysis

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Introduction: Anemia can result from blood loss, destruction of cells, or impaired production of cells. The first 2 causes often are accompanied by reticulocytosis, whereas the third is characterized by reduced reticulocyte count. We present the case of an anemic patient with a low reticulocyte count and evidence of hemolysis due to a unifying cause.

Case: A 48-year-old African American woman with a history of tricuspid valve repair presented with 1 month of generalized fatigue. Laboratory evaluation showed a hemoglobin 5.5 g/dL, mean corpuscular volume 109

fL, platelet count 80K, and normal WBC. Her reticulocyte count was 0.5%, and she had undetectable haptoglobin with LDH of 5439 U/L and total bilirubin of 1.8 mg/dL. B12 was 553 pg/mL (normal), and folate was also normal. Peripheral smear showed occasional fragments, ovalocytes, and teardrop cells. This constellation of findings raised concern for bone marrow dysfunction. Bone marrow biopsy revealed hypercellularity and megaloblastic red cells. Further lab testing showed significantly elevated homocysteine and methylmalonate (MMA) levels. She was treated with intramuscular cyanocobalamin and responded with a reticulocytosis and resolution of her macrocytosis and thrombocytopenia. She was found to have intrinsic factor blocking antibodies and was diagnosed with pernicious anemia.

Discussion: Pernicious anemia is a common malabsorptive cause of cobalamin deficiency. Cobalamin deficiency disrupts folate metabolism, affecting DNA synthesis and, consequently, cell division. Peripheral smear shows macrocytic ovalocytes and hypersegmented neutrophils, which are evidence of impaired hematopoiesis. Due to destruction of immature erythrocytes in the marrow, laboratory analysis may show elevated iron levels and evidence of hemolysis.

Cobalamin deficiency is distinguished from other types of megaloblastic anemia by measurements of the serum cobalamin, homocysteine, and MMA levels. Cobalamin levels above 300 pg/mL usually exclude deficiency, while levels below 200 pg/mL suggest deficiency. When levels are indeterminant, elevated homocysteine and MMA levels confirm deficiency, and high MMA level distinguishes B12 deficiency from folate deficiency. In this patient, cobalamin level was normal, but further testing was pursued given megaloblastic changes on biopsy. Treatment of pernicious anemia (diagnosed with anti-intrinsic factor antibodies) is lifelong B12 replacement.

Dress Syndrome in a Patient Undergoing Treatment for Prostate Cancer

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Introduction: Differentiation of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) from severe sepsis is essential due to the mortality associated with both syndromes. Yet definitions of DRESS remain in flux. We present a case of a patient with DRESS by the RegiSCAR scoring system currently undergoing treatment for prostate cancer to illustrate the difficulty in recognizing the syndrome, especially when a drug not usually associated with DRESS is the culprit.

Case: A 74-year-old man with prostate cancer was transferred for severe sepsis without identifiable source and worsening pancytopenia. The patient had received 2 leuprolide injections, with the second 2 months prior to presentation, and undergone a week of radiation 1 month prior. Three weeks later, he developed a confluent, blistering, pruritic rash over his entire body, including palms and soles. He subsequently developed nausea and vomiting, productive cough, fever, rigors, dizziness, dyspnea on exertion, fatigue, and tongue soreness. He was admitted and treated for sepsis and acute kidney injury. Overnight, he spiked fevers to 39.4°C with tachycardia and hypotension requiring pressor support. Following transfer, CBC showed pancytopenia with 24% eosinophils, CT suggested colitis, and skin biopsy demonstrated spongiotic dermatitis. Epstein-Barr virus was positive. Bone marrow biopsy showed hypercellular marrow with trilineage hematopoiesis. The patient required multiple transfusions for thrombocytopenia and anemia, and improved only with high-dose steroids. The patient had been taking allopurinol, a well-known cause of DRESS, for 4 years without incident, so suspicion turned to leuprolide, with case reports supporting this.

Discussion: DRESS is a life-threatening syndrome thought to be mediated by CD8+ T-cells and often including reactivation of a herpes virus. It can present with fever, rash, lymphadenopathy, eosinophilia, atypical lymphocytes, and involvement of the liver, kidney, heart, or other organ. With these symptoms, once infection has been ruled out, DRESS should be considered as a potential diagnosis.

Heparin-induced Thrombocytopenia and Thromboembolism in Lung Transplantation

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Introduction: Heparin-induced Thrombocytopenia (HIT) results in thrombotic complications in up to 50% of patients. We are not aware of previously reported cases of HIT-associated venous thromboembolism (VTE) in lung transplant recipients and present 3 patients who developed life-threatening VTE associated with HIT following successful lung transplant.

Cases: A 38-year-old man with idiopathic pulmonary fibrosis (IPF) who received a bilateral lung transplant was given routine postoperative DVT prophylaxis. He suffered cardiac arrest on postoperative day 12 and immediately received CPR but was asystolic for 32 minutes. Emergent pulmonary embolectomy was performed while receiving cardiopulmonary bypass. It became apparent that he had developed bilateral lower extremity DVT and a massive saddle pulmonary embolus (PE), and it was noted that the platelet count had fallen significantly over 2 days. Antiheparin antibody was positive, non-eparin anticoagulation was given, and an IVC filter placed. He completely recovered without sequelae.

A 51-year-old man underwent bilateral lung transplant for sarcoidosis. On postoperative day 14, he developed extensive PE in the left segmental pulmonary arteries and an upper extremity DVT that prompted the initiation of heparin therapy. He had a history of prior exposure to heparin, and a fall in platelet count prompted testing for antiheparin antibodies, which was positive.

A 64-year-old man with IPF underwent single lung transplant. He developed neutropenic fever and was found to have pulmonary aspergillosis at 1 year post-transplant and was admitted to the ICU. He developed bilateral lower extremity DVT and was started on IV heparin. An internal jugular vein thrombosis was detected 5 days later, and antiheparin antibody testing was positive.

Discussion: VTE can be a life-threatening postoperative complication in lung transplant recipients, and VTE/PE associated with HIT may occur. HIT should be considered in lung transplant recipients who develop VTE, especially if associated with a drop in platelet count.

Soft Tissue Presentation of Thyroid Cancer

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Introduction: Thyroid cancer is one of the most common, and often curable, malignancies. Atypical manifestations of thyroid cancer delay diagnosis and treatment, affecting prognosis. We present a case of metastatic follicular thyroid cancer, presenting as a nodule on the back.

Case: A 70-year-old woman presented with an asymptomatic "lump" on her back. CT chest showed a 9.3x4.7x5.4 cm lesion, extending from the right T8-T9 neural foramen to the posterolateral chest wall and involving the right ninth rib and T9 vertebra, consistent with a schwannoma, or neurofibroma. She was monitored by neurosurgery and later developed right paraspinal pain. Repeat MRI showed tumor growth causing new central canal stenosis. Biopsy was consistent with follicular thyroid cancer. Patient subsequently underwent thoracic laminectomy, corpectomy, and tumor removal with fusion of T6-T11 vertebral bodies. Pathology showed a solid pattern of growth in most of the tumor with rare colloid-filled follicles. TSH was normal with markedly elevated thyroglobulin and negative thyroglobulin antibody levels. Ultrasound revealed multiple thyroid nodules. She had a total thyroidectomy with pathology showing only a 10x7x7 mm focus of follicular carcinoma with capsular and vascular invasion limited to the thyroid. She underwent thyroid hormone withdrawal and radioactive iodine therapy. Post-treatment scan revealed iodine avid metastatic lesions in the spine, chest wall, and ileum. Patient was monitored with plans for radiation therapy should her disease progress.

Discussion: Thyroid cancer can have atypical manifestations, with a 4% incidence of distant metastases in differentiated thyroid cancer at initial presentation. This is least common with papillary thyroid carcinoma (10%) and most common with Hurthle cell variants (33%). The overall long-term survival in patients presenting with distant metastases is 50%. Thyroid cancer is a common disorder, and we should have a low threshold to consider this disease in our differential of abnormal soft tissue lesions in the appropriate clinical context.

An Unusual Presentation of Merkel Cell Carcinoma

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Introduction: Merkel cell carcinoma (MCC) is a rare malignant neuroendocrine tumor of the skin. We describe a highly unusual initial presentation of MCC leading to acute fulminant liver failure and death in an elderly patient.

Case: An 87-year-old man with a history of prostate cancer treated only with the biologic agent bicalutamide for relief of lower urinary tract symptoms and no history of bony metastasis was admitted to the hospital after presenting with acute worsening of chronic low back pain, subjective lower extremity weakness, and dyspnea on exertion for the past several weeks. He notably had lost 10 pounds in the preceding 2 months, and had tender hepatosplenomegaly on examination. Labs were significant for new mild anemia, thrombocytopenia (96K), elevated liver transaminases, and marked hypoalbuminemia. Ultrasound of the right upper quadrant showed abnormal hepatic echotexture, concerning for an infiltrative disorder. Infectious workup was negative. Over the next several days, the patient's anemia and thrombocytopenia worsened, and peripheral blood smears showed leukoerythroblastosis, suggestive of a myelophthistic process in the bone marrow. A bone marrow biopsy demonstrated marrow involvement by metastatic carcinoma. The patient's liver and kidney function rapidly declined, and he began to bleed from his bone marrow biopsy site and upper GI tract. Intravenous steroids were given for symptom palliation. Due to his rapid clinical deterioration and previously stated wishes, his family transitioned him to palliative measures only, and he died 6 days after admission. Immunohistochemical evaluation of the bone marrow biopsy demonstrated that the malignant cells coexpressed cytokeratin 20, neuron specific enolase, and synaptophysin without cytokeratin 7, CD117, or TTF-1, consistent with MCC. The primary site of disease was not identified.

Discussion: MCC usually presents as an asymptomatic, rapidly expanding pink or red tumor on the sun-exposed skin of elderly Caucasians and demonstrates a high propensity for recurrence and metastasis. While still considered rare, its incidence is increasing rapidly. Recent studies have implicated a newly identified Merkel cell polyomavirus in most MCC cases. The clinical presentation of fulminant hepatic failure and pathologic findings of marked bone marrow involvement without an identifiable primary site make this case an unusual presentation for MCC.

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