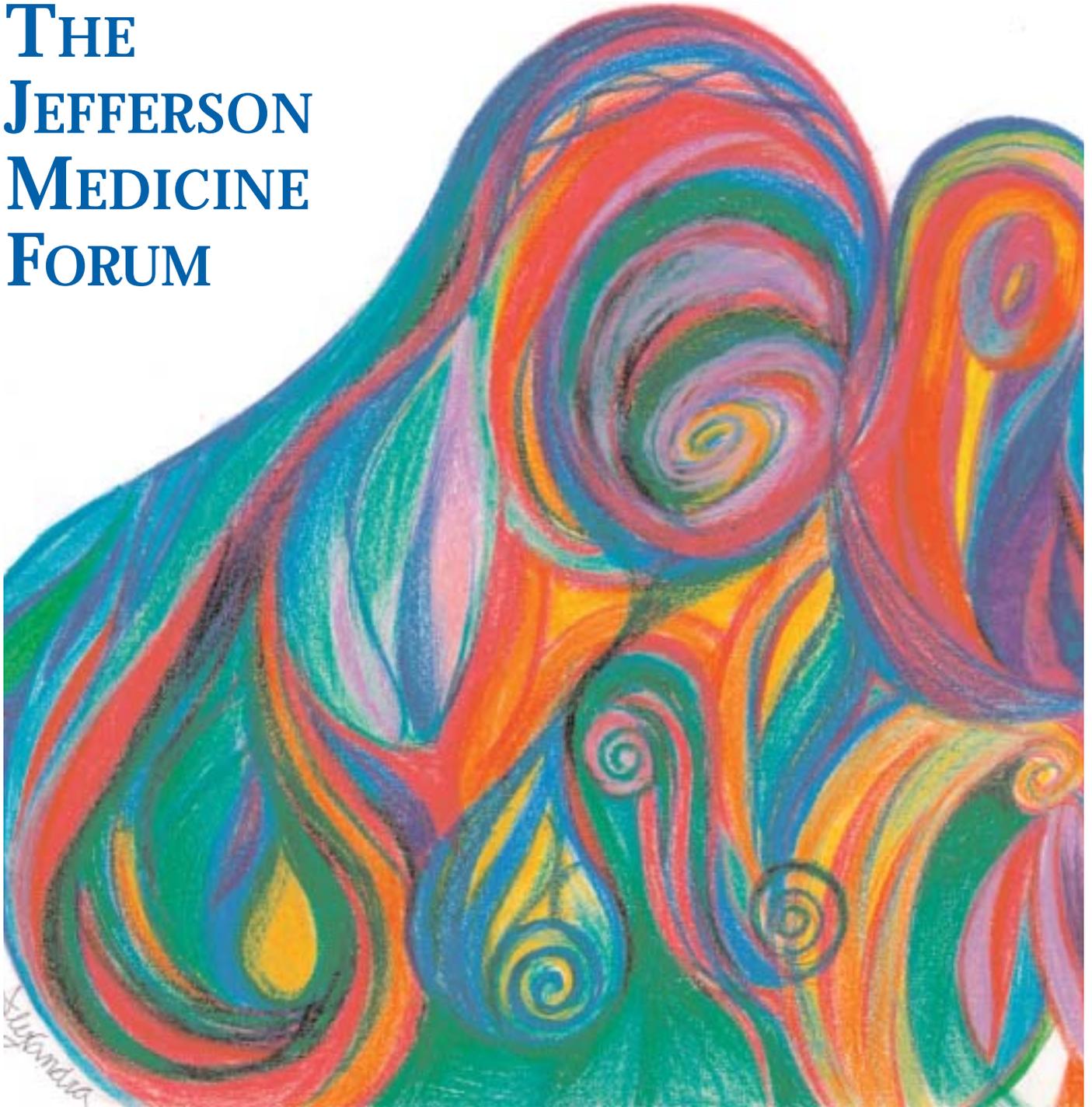


THE JEFFERSON MEDICINE FORUM



*The Journal of Thomas Jefferson University Hospital
Department of Internal Medicine*

Vol. 5 Winter 2003

**Advanced Medicine.
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Foxglove, *Digitalis purpurea*
Photographed by Nicole Weinberg, MD

About the Cover Artist

Alexandra is currently a senior at Lower Merion High School, where she is an art major. Her love of art and creation was cultivated at a young age through the influence of her father, who is also an artist. She has strong ties to Jefferson where her uncle, John Masonis, graduated from medical school and her mother, Susan Masonis, is currently finishing her residency. Presently, Alexandra is applying to colleges and plans to pursue a career in the arts.

From the Residency Program Director

The goal of a Residency Program in Internal Medicine is to strive to train the next generation of practitioners and academicians in Medicine who will become physicians-scholars, scientists, teachers, and humanists.

We are excited that many of our residents are pursuing research opportunities in the laboratory or clinic. Such participation is a requirement for training at Jefferson. In addition, this journal serves as an outlet for scholarly work of a variety of types. We are pleased to support another issue of the *Jefferson Forum* to continue to highlight this work. This represents the fifth installment of *Jefferson Forum*, which first debuted in 1999. The journal is supported entirely through private contributions and unrestricted educational grants. Subscriptions to the members of the Department of Medicine are provided at no cost. The editors have maintained

complete editorial independence to assemble and peer review the submissions for this installment.

The editors deserve our praise for a job well done. Please recognize that the creation of this journal is accomplished by a small team who still have to contend with the daily rigors of residency including night call, teaching their inpatient teams, long days, and preparing for boards. I thank them for extending Jefferson's tradition of excellence in education and enhancing the experience of our residents.

Gregory C. Kane, MD
Associate Professor of Medicine
Residency Program Director
Department of Medicine

Editors Aparna Mukherjee, MD, Nicole Weinberg, MD, Nicholas Ruggiero, MD

My co-editors and I welcome you to the 5th edition of the Jefferson Medicine Forum. This annual publication is a compilation of scholarly works produced by Jefferson's Internal Medicine residents. We are especially proud of this year's edition, which includes a wide variety of case presentations, individual research pursuits, reviews of interesting medical topics, and provocative images reflecting important disease processes. We applaud the efforts of our contributing authors for their commitment to scholarly pursuit during their residency training and their hard work in producing the articles which fill these pages. We proudly present them to you now. Happy reading!

Aparna Mukherjee, MD

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A Man With A Soft Tissue Lesion Of The Hand

Susan Masonis MD, PGY-3 Internal Medicine

A fifty year old male presents with a lesion on his right hand. Approximately 2 months prior to presentation, the patient, who is a dentist and avid boater, first noted the lesion after hitting his hand when working in his boat's engine room. Initially he had a 1 cm erythematous macular lesion on the dorsum of his right hand at the 5th metacarpal. He believed the lesion was present prior to the time he struck his hand, and the injury brought it to his attention.

A week later, the erythematous region became raised and a central pustule formed. The lesion was tender to palpation and a small satellite lesion was also noted (See Figure A, Color Plates page 19). The initial lesion eventually ulcerated and drained serosanguinous fluid. The patient took a 7-day course of cephalexin without significant improvement.

The patient was seen by a dermatologist after the course of antibiotics. The dermatologist prescribed a 3rd-generation cephalosporin and cultured the discharge. After a 7-day course of this second antibiotic, there was no improvement in the lesion and the patient sought advice from a plastic surgeon. The surgeon unroofed the lesion and sent tissue and fluid for both routine bacterial and mycobacterial culture. Four weeks later the patient returned to the surgeon and received a corticosteroid injection to reduce the inflammation. At that time he was told that there was no growth on the cultures.

The patient's past medical history includes hypertension, atopic dermatitis, asthma and hyperlipidemia. As previously stated, he works as a dentist and reports always wearing gloves during procedures. Outside of work, he owns a boat and spends most of his free time sailing in the Chesapeake Bay.

Six weeks after the surgeon performed the culture, the laboratory reported a mycobacterial species had been isolated and the patient was referred to an infectious diseases specialist. The final culture grew *Mycobacterium marinum*. The patient has improved on current oral antibiotic therapy with clarithromycin and rifampin.

Non-tuberculous mycobacteria in soft tissue lesions

Non-tuberculous mycobacterium infections can present with an assortment of cutaneous findings. During the past two decades, there has been an increase in the incidence of non-tuberculous mycobacterial infections, due in large part to an increase in the number of surgical procedures and number of immunocompromised individuals.

The most common mycobacteria involved in cutaneous infections include *M. marinum*, *M. ulcerans*, *M. fortuitum*, *M. chelonae* and *M. abscessus*. These infections may present as nodules, abscesses, ulcerations or cellulitis. *M. abscessus* and *M. fortuitum* infections are often associated with surgical procedures; the former is also associated with post injection abscesses. *M. chelonae* is most often reported in individuals using systemic corticosteroids. *M. ulcerans*, previously noted predominately in regions near temperate rainforests, has recently been associated with several post-surgical infections.

Mycobacterium marinum is an organism found in both saltwater and freshwater. Several vectors of transmission have been reported, including fish, shrimp, snails and water fleas. Most human infections are acquired from direct contact with water. The term "fish tank granuloma" refers to *M. marinum* cutaneous infection, arising from aquarium maintenance. Infection is usually established following skin abrasions or other minor trauma. After a two to six week incubation period, a nodule or papule typically appears. The lesions are usually solitary, with 20-40% developing a sporotichoid distribution (additional proximal lesions along the lymphatic channel).

Infections with this organism are usually limited to skin, because optimal growth of *M. marinum* is between 30 and 33 degrees Celsius. However, *M. marinum* can spread to deeper structures and cause tenosynovitis, arthritis, and osteomyelitis. Such deep extension has a higher incidence of treatment failure. Disseminated infections with *M. Marinum* are rare.

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Successful diagnosis and treatment of cutaneous infection due to non-tuberculous mycobacteria require a high index of suspicion and proper cultures. A clinician should consider mycobacteria in any patient presenting with a non-healing or draining nodule, chronic panniculitis or cellulitis, and particularly if the patient has a recent history of trauma, immunosuppression, or surgery. An adequate tissue sample, defined as a 6 mm punch biopsy, should be sent for analysis.

Routine bacterial cultures often provide false negative results, because standard incubation temperature is 37 degrees Celsius. The physician must alert the laboratory if non-tuberculous mycobacterium is suspected. Standard mycobacterial media can then be utilized, usually at lower incubation temperatures. *M. Marinum* typically begins to grow within 10 to 28 days, but cultures should be held for at least six weeks.

Optimal treatment for *M. marinum* cutaneous infection has not been established. The Archives of Internal Medicine recently published a review of 63 cases of *M. marinum* cutaneous infections occurring between 1996 and 1998. Prior to this report, only case studies were available. The most frequently used antibiotics in this

review included clarithromycin, doxycycline, minocycline, rifampin, and ethambutol. The authors noted that all strains of *M. Marinum* in these patients had similar antimicrobial susceptibility patterns. Acquired antimicrobial resistance did not occur during therapy. Therapy duration ranged from 1-25 months with a median of 3.5 months. The duration was significantly longer for deeper structure infections. There was a 93% cure rate for individuals with soft tissue infection only. One-half of those individuals who were successfully treated received monotherapy and the other half received dual antimicrobial therapy. No conclusive recommendations were made for treatment of this infection. However, clarithromycin with rifampin was the most common combination prescribed, and minocycline or doxycycline were most frequently employed as monotherapy.

References

1. Aubry, A., Chosidow, O., Sixty-three Cases of *Mycobacterium marinum* Infection. Archives of Internal Medicine. 2002;162:1746-1752.
2. Weitzel, S., Eichorn, P., Pandya, A., Nontuberculous Mycobacterial Infections of the Skin. Dermatologic Clinics. April, 2000; 18:2.

A Man With an Elevated Hemoglobin

Paula Sorokanich MD, PGY-3 Internal Medicine

A 50-year-old male with history of severe gout and degenerative joint disease presented to his PCP for a physical. On routine blood work he was found to have an elevated hemoglobin/hematocrit. This was confirmed on repeat analysis and work-up was pursued.

His past medical and surgical history includes hypertension, severe gout, degenerative joint disease of the knees and shoulders, hypokalemia, and right ulnar nerve manipulation at the elbow. He denied IV drug or tobacco use, although he occasionally smokes cannabis, and has a history of moderate alcohol use for which he was in rehabilitation in 1998. His parents are both alive with diabetes and hypertension, and he has three healthy siblings. There is no family history of blood disorders. He denied any recent travel and has always lived in Delaware or Maryland except when stationed in Germany when he was in the military. He lives alone and previously worked as an item processor.

On review of systems, he denied fevers, sweats, or chills. He had noted an approximate 15lb weight gain over the past year, which he attributed to dietary indiscretions. He denied any change in vision, or hearing and had not experienced any lightheadedness or dizziness. He denied chest pain, shortness of breath, but occasionally notes palpitations with increased activity. He also denied skin changes, flushing, or pruritus.

His medications include:

Allopurinol 300mg po qd
Folic acid 1mg po qd
Magnesium oxide 420mg po qd
Multivitamin 1 tab po qd
Naprosyn 500mg po bid prn
Potassium chloride 8meq po qd
Thiamine 100mg po qd
ASA 325mg po qd

Physical examination revealed a ruddy-faced male, in no acute distress, with stable vital signs. Significant findings included hepatomegaly at 16cm and a spleen tip palpable 3-4 fingerbreadths below the costal margin. His left third digit PIP had mild erythema and swelling, per his typical gouty attacks, and he had a few excoriations on his chest. The remainder of the exam was unremarkable.

Multiple Laboratory Studies

Lab study	Patient value	Reference range
WBC	15.0	4.0-11.0 B/L
Neutrophils %	69.4	40-73%
Monocytes %	5.7	3-13%
Lymphocytes %	22.2	20-44%
Eosinophils %	1.4	0-6%
Basophils %	1.3	0-3%
HgB 20.0	12.5-15.0 g/dL	
Hct	60.0	36.0-46.0 g/dL
Platelets	253	140-400 B/L
Iron 243	40-155 mcg/dL	
TIBC 379	250-400 mcg/dL	
% Iron Saturation	64	20-55%
Ferritin	436.9	12-300ng/mL
Erythropoietin	4.4	4.0-15.4 mU/mL
B12	559	100-250 pg/mL
B12 binding capacity	1986	1000-2000 pg/mL
Folate	3.4	>2ng/mL
LAP 132	11-95	
Uric acid	9.2	3.4-7.0 mg/dL
AST 45	2-50 u/L	
ALT 40	2-60 u/L	
ABG on room air	7.44/ 30/ 109/ 96	

Ultrasound studies showed normal kidneys, splenomegaly, and fatty change of the liver. No space-occupying lesions or ductal dilatation was noted. The blood flow and waveforms of the hepatic vein, portal vein, and IVC were unremarkable. Chest x-ray was negative. Based on the patient's hemotological abnormalities on labs, a bone marrow biopsy of the left iliac crest was performed. Mild hypercellularity was seen, with increased megakaryocytes, normoblastic erythropoiesis, and myeloid precursors in all stages, without a block in maturation. Reticulin stain demonstrated foci of early fibrosis, while Prussian blue staining identified increased iron stores with rare ringed sideroblasts (See Figures B and C, Color Plates page 19). After careful review, findings appeared consistent with polycythemia vera. It was felt that the patient was likely early in the course of disease, given the larger than expected iron stores consistent with the amount of erythropoiesis.

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The patient was phlebotomized 3.5 units initially, and then again another 3 units to keep his hematocrit less than 45%. He tolerated these procedures without difficulty and was scheduled for repeat blood work and future phlebotomies.

Discussion

The myeloproliferative disorders include polycythemia vera, essential thrombocytosis, and myelofibrosis with myeloid metaplasia. Chronic myelogenous leukemia is often considered separately because of its known chromosomal association: the Philadelphia chromosome. Polycythemia vera (PV) demonstrates a clonal proliferation of hematopoietic stem cells and is characterized by an increased red blood cell mass. The erythroid cells proliferate independently of erythropoietin (EPO). Overproduction of all three cell lines can be seen.

PV is more common in males than females with a ratio of 1.2:1. Epidemiological studies completed in Rochester, Minnesota show an incidence of 2.3/100,000. Median age at diagnosis is approximately 60 years.¹

Presenting signs and symptoms of PV are often nonspecific and include headache, tinnitus, fatigue, epigastric discomfort, hepatomegaly, splenomegaly (75%), and facial plethora. Pruritus, especially after a hot bath or shower, is typical. The exact etiology of this is uncertain but is likely linked to histamine release or prostaglandins. Erythromelalgia, burning sensations in one's hands or feet with concomitant pallor, cyanosis, or erythema, in presence of palpable pulses, is also seen. This is felt to be a microvascular complication of the disease.² Episodes of thrombosis, like Budd Chiari syndrome, as well as bleeding and peptic ulcer disease can be evident. A prothrombotic latent phase of approximately two years involving arteries and veins has been described.⁵ Increased uric acid levels are often noted as well.¹

Typically, an increased hemoglobin/hematocrit is noted. The hemoglobin is usually greater than 16.5 g/dL and 18.5 g/dL in women and men, respectively. A spurious polycythemia can be noted when a patient is volume depleted. This is often seen in patients on diuretic therapy and reverts to normal with volume repletion. Once an elevated hemoglobin is noted, decisions must be made to determine whether it is a primary or secondary

polycythemia. Secondary polycythemia can be due to hypoxia from cardiac or pulmonary disease, as well as from high altitude. Smoking is another etiology of erythrocytosis. Renal disease should be excluded as an EPO secreting tumor may be present.² If there is a decreased MCV and iron studies, indicative of iron deficiency anemia in the presence of a high normal hemoglobin, some have advocated iron supplementation to see if an erythrocytosis is unmasked. This would place the patient at an increased risk of thrombosis and it is more prudent to assume that the patient has a true erythrocytosis.⁴

In the 1960s-1970s, the Polycythemia Vera Study Group set forth diagnostic criteria. These criteria were made to select patients for clinical trials. It included three major and four minor criteria. The main criteria included increased red cell mass (males >36mL/kg, females >32mL/kg), normal hemoglobin oxygen saturation (>92%), and splenomegaly. A leukocytosis >12,000cell/uL, thrombocytosis >400,000cell/uL, elevated leukocyte alkaline phosphatase >100, and an increased vitamin B12 or B12 binding capacity were minor criteria.³ As leukocytosis may be secondary to other etiologies, an ANC >10,000 has been used of late. Recently, there has been a trend away from using these criteria due to the number of false positive and negative results. Rather than diagnostic criteria many clinicians are using an algorithmic approach.

Once an elevated hemoglobin has been noted and the diagnosis of PV is suspected, a full work-up should ensue. In the past, an increased red blood cell mass was needed for diagnosis. This test is not widely available and is expensive. If the patient is early in the disease process or has concomitant microcytic anemia, it may be falsely negative, and if using hemoglobin measurements greater than 2 standard deviations greater than the mean, the test is typically positive. Therefore, in most cases, this test is not ordered and a serum EPO level is measured.² If it is high, etiologies of secondary polycythemia should be further investigated. If it is normal or low, PV is possible. In PV, it is typically low but may be low normal. Many then proceed to a bone marrow biopsy. Bone marrow biopsy in PV demonstrates hypercellularity, increased megakaryocytes, decreased iron stores, and

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mild reticulin fibrosis. If the diagnosis is still uncertain, further cytogenetic tests may be completed. For example, a decreased expression of the TPO receptor by megakaryocytes supports the diagnosis.¹ An endogenous erythroid colony assay, not widely available, could be done. This study determines if erythroid colonies proliferate in the absence of EPO.²

The main treatment for PV continues to be phlebotomy. The goal is to keep the hematocrit below 45% in males and 42% in females. This is to avoid thrombotic complications. Patients should be instructed to avoid iron supplementation. In patients who are felt to be at especially high risk for thrombosis, based on platelet count, past medical and family history, chemotherapy may be an option. Hydroxyurea, busulfan, alpha-interferon, 32P, and anagrelide have been used. The concern is adverse effects of the drugs including leukemia.¹ Alkylating agents especially are associated with an increased risk of neoplasm. Phlebotomy alone is associated with an increased risk of thrombosis and fibrosis.⁵ A survey in 2002 by the American Society of Hematology demonstrated that 69% of physicians used phlebotomy as first line of treatment. Nearly 28% used the combination of phlebotomy and hydroxyurea, and only 10% employed the use of hydroxyurea alone.³ Erythromelalgia seems to respond to low dose aspirin. The pruritus often responds to aspirin, antihistamines, and in some instances selective serotonin reuptake inhibitors.¹ Low dose aspirin (30-75 mg/day) may also be beneficial in preventing thrombosis and is not associated with the increased risk of bleeding seen at higher dosages.⁵ Allopurinol is used in those with symptomatic hyperuricemia.¹

Previously, untreated PV had a life expectancy of 6 to 18 months after diagnosis but with current treatment approaches it is felt to be greater than 15 years. The main complications are those of thrombosis and progression of the disease to myeloid metaplasia with myelofibrosis (MMM) or acute myeloid leukemia. The most frequent causes of death linked to thrombosis include myocardial infarction, ischemic cerebrovascular events, and thromboembolism. The risk of thrombosis increases with age. There is debate over the percentage of patients who progress to MMM.⁴ It is currently felt that about 10 years after diagnosis, approximately 10% of patients will have MMM.¹ This number increases with length of survival.⁴ In the same time frame, there is approximately a 5% transformation rate to acute leukemia.¹ Research to explore other therapeutic options for PV is ongoing.

References

1. Tefferi, A. Polycythemia Vera: A Comprehensive Review and Clinical Recommendations. *Mayo Clinic Proceedings* 2003; 78(2): 174-194.
2. Tefferi, A. Diagnosing Polycythemia Vera: A Paradigm Shift. *Mayo Clinic Proceedings* 1999; 74(2): 159-162.
3. Streiff et al. The diagnosis and management of polycythemia vera in the era since the Polycythemia Vera Study Group: a survey of American Society of Hematology members' practice patterns. *Blood* 2002; 99(4): 1144-1149.
4. Pearson et al. A Polycythemia Vera Update: Diagnosis, Pathobiology, and Treatment. *American Society of Hematology Education Program Book*. Hematology 2000.
5. Gruppo Italiano Studio Policitemia. Polycythemia Vera: The natural history of 1213 patients followed for 20 years. *Annals of Internal Medicine* 1995; 123(9): 656-664.

A Man With Diarrhea And Achalasia

Dan Valancius MD, PGY-3 Internal Medicine

A 78 y/o male with an extensive history of CAD s/p multiple MIs and CABG surgery, presents with two and one half weeks of diarrhea. About 9 weeks prior, he had been diagnosed with achalasia, and was treated with a botulinum toxin injection, with resolution of his symptoms of dysphagia. He was also hospitalized a month ago after experiencing chest pain, and subsequently ruled in for a small non-ST elevation MI. He underwent coronary catheterization at that time, and was found to have severe multivessel disease unamenable to PTCA or bypass surgery. Now, he presents with progressively frequent "brown watery" diarrhea for the past couple of weeks, reporting up to 20 episodes a day, occurring also at night and causing episodes of fecal incontinence. He denies blood in his stools, or recent antibiotic use. Diarrhea is associated with abdominal cramping, and is not relieved with Lomotil taken every 8 hours. During this period, the patient also notes several episodes of non-bloody, non-bilious emesis, the last occurring one day ago, with an inability to tolerate po intake and a 10 lb weight loss over the two weeks. He denies recurrent dysphagia, fevers or chills, recent travel, heat intolerance, or palpitations. He had a routine screening colonoscopy 6 years ago that was reportedly 'normal'.

Past medical history includes multivessel coronary artery disease status post 3 vessel bypass surgery in 1998, chronic renal insufficiency with a baseline Cr of 1.7, and newly diagnosed achalasia.

His present medications include lisinopril, diltiazem, metoprolol, isosorbide mononitrate, aspirin, atorvastatin, clopidogrel, pantoprazole, and sublingual nitroglycerine as needed. He has no known drug allergies or food intolerances.

Family history is significant for a father who died of an unspecified ileitis, and a paternal uncle with Crohn's disease. The patient smoked 5-6 cigars a day for 45 years. He lives with his wife at home and often babysits his healthy 5 y/o grandson.

Vital signs include a temperature of 97.9 degrees, respirations 12 per minute, 99% saturation on room air, supine BP 90/50 and HR 68, and standing BP 80/50

and HR 68. Physical examination reveals a thin male in no acute distress. Dry mucus membranes are noted, with flat neck veins, a normal cardiac exam, and lungs clear to auscultation. He has normoactive bowel sounds, a non-tender, non-distended abdomen without organomegaly. On rectal exam, he was found to have heme negative brown stool in the vault with good rectal tone. There was no evidence of peripheral edema and he was neurologically intact.

Laboratory tests obtained on admission are shown in tables 1 and 2.

Table 1. Admission Hematology Labs

White cells (per mm ³)	11,300
Differential count (%)	
Neutrophils	54
Lymphocytes	17
Monocytes	6
Eosinophils	22 (0-6)
Basophils	1
Hemoglobin (g/dL)	14
Hematocrit (%)	40.8
Platelet (B/L)	193
ESR (mm/hr)	17 (0-15)
PTT (sec)	29
INR	1.13
PT (sec)	14.4

Table 2. Admission Blood Chemistry

Sodium (mmol/L)	133
Potassium (mmol/L)	4.6
Chloride (mmol/L)	101
Bicarbonate (mmol/L)	22
BUN (mg/dL)	60
Creatinine (mg/dL)	3.5
Total protein (g/dL)	5.8(6.0-8.5)
Albumin (g/dL)	4.5
Total bilirubin (mg/dL)	1.0
Direct bilirubin (mg/dL)	0.3
Alk Phos (IU/L)	104
AST (IU/L)	20
ALT (IU/L)	27

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*(Continued from previous page)*Table 3. **Stool Studies**

Sodium (mmol/L)	88 (135-146)
Potassium (mmol/L)	42.2(3.5-5.0)
Chloride (mmol/L)	77(98-109)
C.diff	Negative x3 sets
Fecal leukocytes	Negative x2
Stool ova and parasite	Negative x2
Stool giardia antigen	negative

Hospital Course

Given the patient's recent hospitalization, he was initially started on oral metronidazole for the possibility of *Clostridium difficile* colitis, and rehydrated. Creatinine corrected to baseline over the next several days. Stool studies were performed, with results detailed in table 3.

Metronidazole and loperamide resulted in significant improvement of diarrhea, with bowel movements decreased to 6 episodes daily. When metronidazole was discontinued after negative C diff specimens, the patient again clinically worsened. A diagnostic flexible sigmoidoscopy was performed, which was essentially normal. Upper endoscopy for evaluation of the small bowel was then done, which showed the esophagus was mildly dilated, consistent with the patient's history of achalasia. Nonerosive gastritis was also visualized. Multiple biopsies were taken of antrum and duodenum. Pathology several days later revealed eosinophilic infiltration consistent with a diagnosis of eosinophilic gastroenteritis. H pylori stains were negative.

The patient was subsequently started on oral prednisone, with rapid resolution of both his diarrhea and peripheral eosinophilia.

Discussion

Eosinophilic gastroenteritis is an uncommon disease characterized by eosinophilic infiltration of the gastrointestinal tract. Diagnosis of eosinophilic gastroenteritis requires the following criteria: (i) presence of gastrointestinal symptoms, (ii) eosinophilic infiltration of one or more areas of the GI tract on biopsy, (iii) organs outside the GI tract must be free of eosinophilic infiltration, and (iv) parasitic infestation must be absent.¹ A slight male predominance has been reported, with patients typically presenting in the third through fifth decades of life.¹ Though any segment of the gastrointestinal tract may be affected, the stomach or small bowel are most commonly involved.^{1,2}

Eosinophilic gastroenteritis is classified according to the layer of bowel wall affected.³ Patients with mucosal layer disease present with protein-losing enteropathy, fecal blood loss, and malabsorption. Muscle layer disease may lead to obstruction, while subserosal involvement leads to eosinophilic ascites.³ However, clinical and pathologic features may overlap, with involvement of multiple layers of the gut wall.² In one series, abdominal pain was the most frequently recorded symptom (100%), followed by diarrhea (62.5%), vomiting (62.5%), and nausea (50%).³ Of note, as seen in our reported patient, isolated esophageal involvement may cause a variety of manometric abnormalities, including achalasia.⁴ About half of patients have a personal or family history of allergic disease, and half report a history of food intolerance or allergy.²

Peripheral eosinophilia is found in about 80% of patients, though the presence of peripheral eosinophilia is not a diagnostic criterion.^{1,2} Iron deficiency anemia can develop.¹ The serum albumin level may be low in 20-30% of cases, mostly with mucosal disease.¹ The erythrocyte sedimentation rate may be normal to moderately elevated.¹

Stool studies should be done to exclude parasitic infestation. Charcot-Leyden crystals may be seen on a stool wet mount examination.² Though stool may be positive for occult blood, this finding is variable.² The radiographic changes found in eosinophilic gastroenteritis are nonspecific, and in at least 40% of cases, are completely absent.⁵

Endoscopic findings also vary, including prominent mucosal folds, hyperemia, ulceration, or nodularity.⁶ The distribution of disease tends to be patchy, and for this reason, multiple biopsies (at least six) should be taken, if eosinophilic gastroenteritis is suspected.¹

Histologically, eosinophilic gastroenteritis is characterized by an inflammatory cell infiltrate comprised almost entirely of eosinophils.⁷ It should be noted, however, that eosinophilic infiltration is the most consistent histologic finding found on biopsy in gastroesophageal reflux as well.⁸ In cases where there is a question whether eosinophilic infiltration represents eosinophilic esophagitis or gastroesophageal reflux, the location may be a clue, with more proximal locations favoring eosinophilic esophagitis.² Table 4 outlines some of the important clinical and laboratory features of eosinophilic gastroenteritis.

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Table 4. Features Consistent with Eosinophilic Gastroenteritis

Mucosal layer disease
Pain, nausea, vomiting, diarrhea, weight loss
Iron deficiency anemia
Malabsorption
Protein-losing enteropathy
Muscle layer disease
Obstruction
Subserosal layer disease
Eosinophilic ascites
Peripheral eosinophilia 80%
Eosinophilic infiltration of GI tract on biopsy
Low serum albumin 20-30%
ESR normal to moderately increased
Negative stool studies for parasites
Stool positive for occult blood (variable)
Charcot-Leyden crystals on stool exam (unknown frequency)

Parasitic infections are characteristically associated with peripheral eosinophilia and should be ruled out. The hookworm *A. caninum* as well as the pinworm *Enterobius vermicularis* may cause eosinophilic colitis.² *Giardia lamblia* can be associated with jejunal infiltration with eosinophils, though peripheral eosinophilia is usually absent.² The consumption of raw fish may lead to infection with *Anisakis*.² Other parasites which may be considered include *T. stercoralis*, *Trichinella spiralis*, and *Schistosomiasis*.

Various drugs including azathioprine, gemfibrozil, carbamazepine or clofazimine may cause diarrhea and peripheral eosinophilia.² Vasculitic disorders may mimic eosinophilic gastroenteritis, including Churg-Strauss syndrome, typically seen in patients with a history of asthma, and polyarteritis nodosa, typified by peripheral eosinophilia in association with multisystem involvement including the kidney, lung, nervous system or skin.²

Other diagnostic considerations may include Crohn's disease, cancer, and hypereosinophilic syndrome. Histologic features should clearly separate Crohn's disease from eosinophilic gastroenteritis.² Gastric infiltration of eosinophils may be striking in gastric adenocarcinoma, though peripheral eosinophilia is unusual.² In hypereosinophilic syndrome, persistent peripheral eosinophilia is associated with infiltration of multiple organs including bone marrow, heart, lung liver, spleen kidneys, skin, and central nervous system.² Table 4 outlines other disorders which may mimic eosinophilic gastroenteritis

Table 4. Differential Diagnosis for Eosinophilic Gastroenteritis

Parasitic infections
Vasculitides
Inflammatory bowel disease
Hypereosinophilic syndrome
Drugs
Cancer (specifically gastric adenocarcinoma)

Steroids are the mainstay of therapy for eosinophilic gastroenteritis, and clinical response is usually dramatic.¹ In approximately 50% of cases, low dose prednisone therapy may be required to maintain remission.² Other therapies, including sodium cromoglycate, have been reported to be effective.² In patients who have traveled to, or live in areas that put them at high risk for parasitic infection, a trial of antimicrobial therapy such as mebendazole may be considered, prior to initiating steroids, since parasitic infection may be difficult to rule out.² Once recognizably diagnosed, eosinophilic gastroenteritis has a good prognosis without associated risk of cancer.¹

References

1. Talley NJ, Shorter RG, Phillips SF, et al. Eosinophilic Gastroenteritis: a clinicopathological study of patients with disease of the mucosae, muscle layer, and subserosal tissues. *Gut* 31:54, 1990.
2. Talley NJ. Chapter 100- Eosinophilic Gastroenteric. Feldman: Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 7th ed.
3. Lee CM, Changchien CS, et al. Eosinophilic Gastroenteritis: 10 Years Experience. *The American Journal of Gastroenterology* 88:70-74, 1993.
4. Dobbins JW, Sheahan DG, Behar J. Eosinophilic gastroenteritis with esophageal involvement. *Gastroenterology* 72:1312-1316 1977.
5. Stallmeyer MJ, Chew FS. Eosinophilic Gastroenteritis. *AJR American Journal of Roentgenology* 161L296,1993.
6. Kalantar SJ, Marks R, Lamber JR, et al. Dyspepsia due to Eosinophilic Gastroenteritis. *Digestive Disease Science* 42:2327, 1997.
7. Johnstone JM, Morson BC. Eosinophilic Gastroenteritis. *Histopathology* 2:335, 1978.
8. Brown LF, Goldman H, Antonioli DA. Intraepithelial eosinophils in endoscopic biopsies of adults with reflux esophagitis. *American Journal of Surgical Pathology* 8:899-905, 1984.

Prevention of Central Venous Catheter-related Infections

Raghuram Mallya MD, PGY-3 Internal Medicine

The central venous catheter is a valuable tool in inpatient medicine. However, with its use comes the risk of local and systemic infections. Kluger et al estimated that 250,000 cases of central line-associated blood stream infections occur annually. Mortality rates range from 12-25% per infection.¹ Therefore, it is essential that health care providers take all necessary precautionary measures to avoid infection. Guidelines have been published by the Centers for Disease Control and Prevention to provide an evidence-based medicine (EBM) approach for avoiding central venous catheter-related infections. Recommendations include proper skin cleansing, the use of maximal sterile barriers, selection of the subclavian site, avoiding routine replacement of central venous catheters, and using antiseptic/antibiotic impregnated catheters.

Aseptic technique is the first step in infection prevention. The patient's skin must be properly disinfected, prior to the insertion of any venous catheter. Typically, povidone iodine is used for skin antiseptics. However, Maki et al demonstrated a lower incidence of bacteremia with the use of 2% chlorhexidine gluconate, versus 10% povidone-iodine or 70% alcohol (0.5 versus 2.3 and 2.6 per 100 catheters, respectively).² Furthermore, Chaiyakunapruk et al performed a meta-analysis which showed a 50% overall reduction in catheter-related blood stream infections with the use of chlorhexidine.³

Once the skin has been properly disinfected, the practitioner must take additional measures to maintain sterile conditions. The use of sterile gloves and drapes alone are not enough. A study done in 1994 by Raad et al showed that using maximal sterile barrier precautions (a cap, gown, sterile gown, sterile gloves and a large sterile drape) substantially reduced catheter-related bloodstream infections, as opposed to standard precautions with only sterile gloves and small drapes.⁴

The site of the central venous catheter has also been linked to infection. Collignon et al found that the lowest rate of catheter colonization occurred with placement at the subclavian site, and the highest rate with catheters at the femoral site (15% vs 34%, respectively).⁵ Femoral catheters have also been associated with a higher risk for deep venous thrombosis (DVT). Therefore, from an EBM standpoint, the subclavian vein is the preferred site

of insertion for infection control purposes. Note that all factors must be taken into account when selecting a catheter site in a given patient, including operator skill, the potential for mechanical complication, patient comfort, anatomic variables, and bleeding diatheses.

Once the central venous catheter has been placed using proper aseptic technique, it should not be changed on a scheduled basis. Cobb et al conducted a randomized controlled trial where 160 patients underwent one of four methods of catheter exchange: replacement every three days by insertion at a new site (group 1); exchange over a guidewire every three days (group 2); replacement when clinically indicated by insertion at a new site (group 3); exchange over a guidewire when clinically indicated (group 4). The incidence rates of bloodstream infection per 1000 days of catheter use were 3 in group 1, 6 in group 2, 2 in group 3, and 3 in group 4. Therefore careful clinical inspection of that catheter site at least every other day is recommended versus prophylactic changes of catheter site.⁶ The exception to this is the Swan-Ganz catheter, which should be removed within 3-5 days and replaced at a new site if further monitoring is required. When changing a central venous catheter is clinically indicated, options include changing over a guidewire or insertion at a new site. For infection control purposes, placement at a clean site is preferred. However, this method is associated with a greater incidence of mechanical complications.

Lastly, the type of catheter used has been shown to affect the rate of infection. There is a higher incidence of infectious complications with multi-lumen catheters. Studies have also been done with antiseptic and antibiotic impregnated catheters. A meta-analysis by Veenstra et al showed a decrease in catheter colonization and catheter-related bloodstream infections with chlorhexidine/silver sulfadiazine-impregnated catheters, versus non-impregnated catheters.⁷ Reductions in bacteremia have also been noted with minocycline/rifampin-impregnated catheters.⁸ The chlorhexidine/silver sulfadiazine impregnated catheters were also more cost effective.⁹ Currently, the CDC recommends implementing a comprehensive strategy to lower the incidence of catheter related bloodstream

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infections (CRBSI), including education of practitioners, use of maximal barrier protection, and 2% chlorhexidine for skin antiseptics. If the CRBSI rate remains above the institutions goal despite these measures, then antibiotic/antiseptic impregnated catheters should be used in adult patients in whom the central venous catheter is expected to remain in place for >5 days.

Central venous catheter infections remain a prevalent problem in inpatient medicine. While risk of infection is always present with indwelling lines, measures can be taken to minimize this potentially fatal complication. Proper aseptic technique with thorough skin preparation and maximal barrier precautions, careful site selection, and diligent clinical inspection of a catheter site can drastically reduce infection risk and improve patient care.

Reference

1. Kluger, DM, Maki, DG. The relative risk of intravascular device related bloodstream infections in adults [abstract]. In: Abstracts of the 39th Interscience Conference on Antimicrobial Agents and Chemotherapy. San Francisco, CA: American Society for Microbiology 1999:514.
2. Maki, DG, Ringer, M, Alvaro, CJ. Prospective randomized trial of povidone-iodine, alcohol, and chlorhexidine for prevention of infection associated with central venous and arterial catheters. *Lancet* 1991; 338:339.
3. Chaiyakunapruk, N et al. Chlorhexidine compared with povidone-iodine solution for vascular catheter-site care: A meta-analysis. *Ann Intern Med* 2002; 136:792
4. Raad, II et al. Prevention of central venous catheter-related infections by using maximal sterile barrier precautions during insertion. *Infection Control Hospital Epidemiology* 1994; 15:231.

A Man with Dyspnea and Diffuse Abdominal Pain

Dominick Galluzzo MD, PGY-3 Internal Medicine

A 50 y/o male with a PMH significant for HIV/HCV co-infection, and chronic renal insufficiency, presented to the ED with a one week history of progressive dyspnea and diffuse abdominal discomfort. He reported resting shortness of breath without orthopnea, PND, or chest pain. His abdominal pain was diffuse, and he denied nausea, vomiting, increased abdominal girth or lower extremity edema.

He was diagnosed with HIV 3 months earlier, following an admission for septic arthritis. One month ago his CD4+ count was 125 and his viral load 200,000 copies, at which time he began antiretroviral therapy with Combivir (zidovudine/lamivudine) and Sustiva (efavirez) and prophylactic therapy with Bactrim. The patient reported strict compliance with his medical regimen.

On admission his vitals were as follows: temperature 98.9 F, pulse 107 bpm, blood pressure 112/63, respirations 28/min with an oxygen saturation of 96% on room air. The physical exam revealed a thin black male in moderate discomfort, exhibiting Kussmaul breathing with an otherwise clear lung exam. Abdominal exam revealed normal bowel sounds and mild diffuse tenderness, without rebound or guarding. There was no evidence of JVD, lower extremity edema, or S3.

Laboratory data revealed: sodium 136, potassium 5.6, chloride 112, bicarbonate 11, BUN 36, creatinine 2.6, glucose 113; WBC 6.4, hemoglobin 9.1, and platelets 193; AST 306, ALT 77, alkaline phosphatase 567, albumin 2.4. Arterial blood gas values were pH 7.33, pCO₂ 22, PO₂ 154. Finally, chest x-ray demonstrated clear lungs and EKG revealed normal sinus rhythm with T wave inversions in V1- V6.

Discussion Of The Acid-Base Disorder

- A “Normal Gap” Lactic Acidosis?

Initial review of the arterial blood gas and chemistry panel revealed a metabolic acidosis with an expected respiratory compensation (calculated PCO₂ by Winter's formula = 24+/-2). The calculated anion gap was 13, leading us to conclude that the primary disorder was a non-gap acidosis. However, prior lab studies were available for this patient, which revealed a baseline bicarbonate of 20 (presumably related to chronic renal

insufficiency) and anion gap of 5 (presumably related to hypoalbuminemia). The presence of a delta anion gap of 8 suggested a true anion gap acidosis. A serum lactate was subsequently measured, which was markedly elevated at 68.6.

Diagnosis And Clinical Outcome

The patient was admitted with the diagnosis of lactic acidosis, likely secondary to his nucleoside reverse transcriptase inhibitor (NRTI) therapy with Combivir. AST/ALT values peaked at 3621/721 respectively the morning after admission. By withholding antiretroviral therapy, the lactic acid level trended back to normal values and the patient's transaminases returned to his baseline. He continued to improve symptomatically within about 1 week and had returned to his baseline functional status.

Discussion on NRTIs and Lactic Acidosis

The development of lactic acidosis is a very rare, but often fatal, complication of therapy with nucleoside analogues. The estimated incidence of this disorder is only about 1-4 cases per 1000 person years; however it carries a sobering mortality rate of about 50%¹. Though an exact mechanism is yet to be clearly defined, it appears to be related to the inhibition of mitochondrial DNA polymerase and development of hepatic steatosis.

Perhaps of larger interest to clinicians is the ability to identify important risk factors for the development of lactic acidosis. Due to the rarity of this disorder, large-scale studies are difficult to design to evaluate this question. However, a series of case reports and cohort studies have been published. Treatment with any of the NRTIs has been associated with lactic acidosis; however the use of stavudine and lamivudine appears to confer the greatest risk^{2,3}. Another small cohort study suggests additional risk factors may include creatinine clearance of <70 mL/min and a nadir CD4+count of <200 cells/m³.⁴ Finally, pregnancy has also been targeted as a potential risk factor⁵⁻⁷.

In conclusion, the development of lactic acidosis during therapy with NRTIs is a rare but potentially lethal complication. Thus, clinicians should maintain a high level of clinical suspicion when HIV+ patients on such therapy complain of GI distress, dyspnea or general malaise, particularly in the setting of

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stavudine/lamivudine use, diminished creatinine clearance, pregnancy and CD4 counts less than 200. Furthermore the use of NRTIs should be immediately held, once the diagnosis of lactic acidosis is considered.

References

1. Ogedegbe, A et al. Hyperlactatemia syndromes associated with HIV therapy. *The Lancet Infect Dis* 2003; 3:29-37.
2. Boubaker, K et al. Hyperlactatemia and antiretroviral therapy: The Swiss Cohort Study. *Clin Infect Dis* 2001; 33:1931-7.
3. Moyle GJ, et al. Hyperlactatemia and lactic acidosis during antiretroviral therapy: relevance, reproducibility, and possible risk factors. *AIDS* 2002; 16:1341-9.

4. Bonnet, M et al. Risk factors for lactic acidosis in HIV-infected patients treated with nucleoside reverse-transcriptase inhibitors: a case-control study. *Clin Infect Dis* 2003; 36:1324-1328.
5. Sarner, L, Fakoya A. Acute onset lactic acidosis and pancreatitis in the third trimester of pregnancy in HIV-1 positive women taking antiretroviral medication. *Sex Transm Inf* 2002; 78:58-59.
6. Public Health Service task force recommendations for the use of antiretroviral drugs in pregnant HIV-1 infected women for maternal health and interventions to reduce perinatal HIV-1 transmission in the United States. *August 30,2002*: 6. NIH.

Don't Peek!

Answers to the Clinical Quiz at the end of this edition of Jefferson Forum

Submitted by Bryan Pukenas, MD

The procedure shown above is a thoracic duct embolization. The effusion can be seen at the apex of the left lung. Radiographic dye is injected into a surgically exposed lymphatic channel in the foot. After several minutes to hours, the dye migrates to the cisterna chyli and into the thoracic duct. At this point a needle is inserted into the thoracic duct and a glue-like material is injected, essentially thrombosing the entire duct. cases of chylothorax.

The diagnosis is chylothorax, which is characterized by pleural fluid with a turbid or milky white appearance, secondary to high lipid content (mostly triglycerides), that enters the pleural space via disruption of the thoracic duct. Patients report gradual onset of decreased exercise tolerance, dyspnea, fatigue, and a heavy feeling in the chest. Fever and chest pain often do not occur, because of the failure of chyle to produce an inflammatory response. Maligancy is responsible for 45 percent of total cases and 63 percent of nontraumatic cases. Lymphoma is the single most common cause of chylothorax, but Castleman's disease, sarcoïdosis, histoplasmosis, tuberculosis, lymphangiomyomatosis, multiple myeloma, and goiters are also associated with this pathology. Surgical procedures account for most traumatic

E – Radiograph

Submitted by Aparna Mukherjee, MD

Skin biopsy of a discrete lesion shows a foci of multiple giant multinucleated cells within the dermis layer. This finding is characteristic of herpes simplex, which systemically disseminated in this immunocompetent patient, causing multorgan failure. With intravenous antiviral therapy, the patient made a full recovery.

D – Slide

Submitted by Jun Liu, MD

Liver biopsy of the nodules shows microabscesses with fungal elements on GMS (silver) stain. Note the extracellular beaded fungal elements embedded in debris, surrounded by fibrosed liver parenchyma.

commonly in women, with an incidence of roughly 1 in 15,000. maligancy. This is a congenital abnormality seen more excised because of an increased risk of cholangitis and patient has minimal symptoms, the cyst needs to be surgically duct take-off from the choledochal cyst itself). Although the of the common hepatic and common bile ducts (note the cystic A 3 x 2 cm type Ia choledochal cyst is visualized at the junction

Submitted by Carl D. Mele, MD

C – Slide

Submitted by Carl D. Mele, MD

This is a pedunculated jejunal polyp. Because the patient is asymptomatic and the polyp is less than 15 mm in size, no therapeutic intervention is recommended at this time. Patients with FJS should be screened endoscopically with EGD, colonoscopy, and small bowel evaluation at least every two years after the age of 12.

A – Capsule Image

A Male with Chills and Arthralgias

Lo-Ku Chiang MD, PGY-3 Internal Medicine and Ambrish Ojha MD, PGY-5 Infectious Diseases

A 53-year old man presented to the ED with complaints of fevers and chills for 5 days. Two days prior, he started having generalized arthralgias and a painfully numb left index finger. Similar symptoms had also begun on his left great toe (See Figures D and E, Color Plates page 19). The patient denied recent trauma, although he was unsure if he had sustained an insect bite on the dorsal aspect of his left hand 8 hours prior to the onset of symptoms. Three sets of blood cultures obtained prior to admission were positive for methacillin-sensitive *Staphylococcus aureus*. The patient was treated with intravenous nafcillin and gentamicin. A transesophageal echocardiography was performed, which showed a friable and perforated left coronary cusp of the aortic valve, resulting in severe aortic insufficiency. The patient was scheduled for emergent aortic valve replacement. It was surmised that the initial site of infection was a badly ulcerated blister located on the patient's right great toe.

Discussion

There are numerous peripheral manifestations of bacterial endocarditis. The classic peripheral manifestations are found in up to half of the cases, but the prevalence has decreased in recent years. Janeway lesions are painless erythematous, hemorrhagic, or pustular lesions that are seen on the palms or soles and are often associated with acute bacterial endocarditis. Osler nodes, which are tender, subcutaneous nodules often located on the pulp of the digits typically seen with subacute bacterial endocarditis. Other vasculitic complications include major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, conjunctival petechiae and intracerebral hemorrhages. Immunologic phenomena include glomerulonephritis, a positive rheumatoid factor, Roth spots and superficial retinal hemorrhages. These clinical findings are part of the minor criteria in the Duke classification of diagnosing bacterial endocarditis.

Frequently, the presentation of endocarditis is not clear and a high level of clinical suspicion is essential in a patient with fever and systemic symptoms suggestive of infective endocarditis.

A Man with Fevers and Chest Pain

Jigar Patel MD, PGY-3 Internal Medicine

A 42 y/o Hispanic man without significant medical history presented to the ED with the complaint of increasing left-sided chest pain. The patient reported that symptoms began 4 days prior, when he developed a severe headache. That night, he noted increasing chills and sweats, with a fever measured at 103 degrees F. The following morning, he developed left-sided chest pain that he described as a pressure exacerbated by movement and breathing. For the next several days, he reported feeling worse with continuous chills and fever spikes up to 105 degrees F, along with increased severity and duration of his chest pain.

The patient mentioned that acetaminophen and over-the-counter analgesics did not relieve his symptoms. With his chest pain, he also noted associated shortness of breath with mild nausea. However, he denied abdominal pain or changes in his bowel habits, and he reported that his weight had been stable. He had never had these symptoms before.

The patient's past medical history was remarkable for a trauma-related leg fracture in 1995 that was repaired by open reduction and internal fixation. He also had oral surgery in 2000 for severe periodontitis and subsequently had to have a full mouth extraction.

He denied alcohol, tobacco or illicit drug use. He was married for 18 years with 2 healthy children. He denied any HIV risk factors. He also did not report any recent travel or exposure to known sick individuals. He worked at a surgical instrument manufacturing plant.

On admission, his vital signs were: blood pressure 99/62, pulse 133, respirations 22, temperature 99.6 degrees F and oxygenation saturation 96% on room air. He appeared to be acutely ill, although alert and cooperative to exam. His pupils were equal and reactive with normal extraocular movements. He had complete maxillary and mandibular dentures and dry mucus membranes. Cardiac exam revealed a normal S1 and S2, regular rate without appreciable murmurs. Notable findings on lung exam were bibasilar rales. His abdomen was benign, and he did not have evidence of rash or lesions.

An electrocardiogram revealed sinus tachycardia with a rate of 127. Chest x-ray showed bilateral interstitial opacities involving middle and lower lung fields suggestive of an atypical infectious process. There was no cardiomegaly, pulmonary edema or pleural effusions. Laboratory data indicated normal chemistries, a white blood cell count of 14.5 with 84% neutrophils, and 4% bands. Platelets were decreased at 47,000. Cardiac markers were all normal. The INR was 1.23 with a PTT of 36.

A presumptive diagnosis of community-acquired versus atypical pneumonia was made and the patient was rehydrated and started on iv moxifloxacin. The night of admission, the patient's clinical status quickly deteriorated with increasing oxygen requirements up to 5 liters via nasal cannula, with oxygen saturations in the low 90% range. Complete blood count drawn the next morning revealed a white blood cell count of 16.1 and platelets at 35,000. Physical exam the next day was noteworthy for a new systolic ejection murmur heard best at the apex with radiation to the axilla. A thorough skin exam revealed characteristic splinter hemorrhages and Janeway lesions on the palmer surface of hands and the soles of the feet (See Figures F and G, Color Plates page 19). A formal fundoscopic exam revealed Roth's spots in both eyes. A transthoracic echocardiogram was done, which showed a 1.6 cm x 1.4 cm mass attached to the lateral base of the posterior leaflet of the mitral valve. The mass was noted to be smooth with no projections. It was felt to be rather unusual and atypical for a vegetation. The ejection fraction was normal. Admission blood cultures came back positive for gram positive cocci in clusters. A DIC panel showed increased D-dimer, decreased fibrinogen and elevated INR.

The clinical picture was most consistent with acute bacterial endocarditis. The patient was started empirically on vancomycin and gentamycin.

He continued to do poorly with higher oxygen requirements to maintain saturations greater than 90%. A portable chest x-ray showed frank pulmonary edema. The patient was urgently transferred to the cardiac care unit with presumed mitral valve failure, secondary to the vegetation. His blood pressures were controlled with nipride and hydralazine and he was aggressively diuresed

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with iv furosemide. The antibiotic regimen was broadened to include Rifampin. Unfortunately, he did not improve clinically. Multiple blood cultures continued to show *Staphylococcus aureus*, despite several days of antibiotic therapy. The decision was made, in consultation with Cardiac Surgery, to take the patient to the operating room for emergent mitral valve replacement. Intraoperatively, a 2 cm x 2 cm friable vegetation was noted at the posterior leaflet of the mitral valve. There was also a large abscess cavity burrowing into the annulus destroying about 2/3 of the posterior annulus. Histopathology revealed *Staph aureus* colonies embedded within the vegetation (See Figures H-J, Color Plates page 19). Postoperatively, the patient did well for the next 48 hours, and was deemed stable for transfer out of the cardiothoracic critical care unit. Shortly thereafter, he again developed temperature spikes, with persistently positive blood cultures despite re-initiation of antibiotics. On post-op day 7, he had an acute episode of shortness of breath with evidence of pulmonary edema, requiring reintubation. It was determined that his prosthetic mitral valve had been reinfected and was failing. Despite all heroic efforts, the patient ultimately succumbed to sepsis.

Discussion

Infective endocarditis (IE) is defined as an infection which can produce vegetations on the endocardium, including valves, septae, or mural endocardium. IE is almost invariably fatal, if untreated. An estimated 10,000 to 15,000 new cases of IE are diagnosed in the USA each year, with male to female ratios ranging from 2:1 to as high as 9:1. IE can be broadly classified into native valve and prosthetic valve infection, with subdivisions within each category based on the microorganism (further classifications can also be made based on the nature of the infected valve; this will be expounded further in treatment options). Although native valve endocarditis can be caused by almost any kind of bacteria, the three most common include streptococci, staphylococci and enterococci. The HACEK organisms (*Haemophilus*, *Actinobacillus*, *Cardiobacterium*, *Eikenella*, and *Kingella*) are oral flora that cause a subacute presentation and are very difficult to grow on media, hence the term 'culture negative' endocarditis. In patients who have indwelling

catheters and/or are immunocompromised, fungal IE can occur with *Candidia* and *Aspergillus* species. Prosthetic valves predispose to endocarditis. In one study, IE of prosthetic valves accounted for 10-20 percent of cases. In addition to valves, intravascular sutures and pacemaker wires can also become foci of infection. Early onset prosthetic valve endocarditis (less than 60 days after surgery) is usually secondary to intraoperative contamination or perioperative bacteremia. Approximately half of all cases are caused by staphylococci, with *S. epidermidis* more frequent than *S.aureus*. Gram negative rods can account for up to 15 percent and fungi up to 10 percent of early cases. When late endocarditis occurs (onset > 60 days) the organism is usually a streptococcus species (about 40% of cases). Early prosthetic IE often runs a fulminant course, with valvular dysfunction and valve dehiscence. Although late prosthetic IE can progress similarly, more often the clinical course resembles non-prosthetic IE with streptococcus and is luckily not as catastrophic. There are several known risk factors for the development of IE, including injection drug use, prosthetic heart valves, and structural heart disease. Other factors have been postulated to increase the risk of IE. These form the theoretical basis for antimicrobial prophylaxis prior to planned invasive procedures in certain individuals. Several criteria have been developed for the diagnosis of IE. It should be noted that the diagnosis is ultimately based on the clinical picture and compulsory adherence to set criteria is usually not necessary. That being said, the Modified Duke Criteria is one of the most commonly used set of guidelines, using a schema of major and minor criteria. Major criteria include positive blood cultures for organisms that cause IE, evidence of endocardial involvement, suggestive echocardiogram findings, and new valvular regurgitation. Minor criteria are many and include: history of intravenous drug use or structural heart disease, fevers >100.4 degrees F, vascular stigmata such as Janeway lesions, or septic emboli, immunologic phenomena such as Osler's nodes or glomerulonephritis, and microbiological evidence. A definite diagnosis is made on either pathological OR clinical criteria. Clinical criteria usually requires 2 major criteria or 1 major and 3 minor or 5 minor criteria. Possible IE is defined as 1 major and 1 minor OR 3 minor.

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The treatment of IE is dependent on the valve, as well as the suspected organism. The following table summarizes the different regimens available to treat IE. (Although only one choice is presented, it should be noted that there are alternative antibiotics that can be used for each type of infection.)

Type of Infection	Antibiotic Choice	Length of Treatment
Native Valve IE from PCN sensitive Streptococcus	PCN G 12-18 million U/24hr OR Ceftriaxone 2gm IV q24h	4 weeks
Native Valve IE from PCN resistant Streptococcus	Vancomycin 30mg/kg per 24h IV in 2 divided doses	4 weeks
Standard Therapy for Endocarditis due to Enterococcus	Ampicillin 12g/24h IV WITH Gentamycin 1g/kg IV every 8h	4 – 6 weeks
Native Valve IE due to Methicillin Sensitive Staphylococcus	Nafcillin/Oxacillin 2gm IV every 4h WITH Gentamycin 1mg/kg IV every 8h	4 – 6 weeks
Prosthetic Valve IE with Methicillin Resistant Staphylococcus	Vancomycin 30mg/kg per 24h IV WITH Rifampin 300mg orally every 8h WITH Gentamycin 1mg/kg IV every 8h	Greater than 6 weeks
Prosthetic Valve IE with Methicillin Sensitive Staphylococcus	Nafcillin/Oxacillin 2g IV every 4h WITH Rifampin 300mg orally every 8h WITH Gentamycin 1mg/kg IV every 8h	Greater than 6 weeks
Therapy due to HACEK Microorganism	Ceftriaxone 2g IV every 24h	4 weeks

From Wilson, WR, Karchmer, AW, Dajani, AS, et al, JAMA 1995; 274:1706

References

1. Bansal, RC. Infective endocarditis. *Med Clin North Am* 1995; 79:1205.
2. Bayer AS, *Clin Infect Dis* 1993 Sep;17(3):313-20.
3. Fowler, VG, Durack, DT. Infective endocarditis. *Curr Opin Cardiol* 1994; 9:389.
4. Li, JS, Sexton, DJ, Mick, N, et al. Proposed modifications to the duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis* 2000; 30:633.
5. Molavi, A. Endocarditis: recognition, management, and prophylaxis. *Cardiovasc Clin* 1993; 23:139.
6. Petti, CA, Fowler, VG. Staphylococcus aureus bacteremia and endocarditis. *Cardiology Clinics* 2003; 21(2):219-33.
7. Watanakunakorn, C. Changing epidemiology and newer aspects of infective endocarditis. *Adv Intern Med* 1977; 22:21.
8. Wilson, WR, Karchmer, AW, Dajani, AS, et al. Antibiotic treatment of adults with infective endocarditis due to streptococci, enterococci, staphylococci, and HACEK microorganisms. American Heart Association. *JAMA* 1995; 274:1706.

Isolated Abducens Nerve Palsy Secondary To Varicella Zoster In A Patient With HIV

Ellen B. Lunenfeld MD, PGY-2 Internal Medicine; John A. Walker MD

Varicella Zoster, the recrudescence of the dormant varicella virus, occurs more often in older patients and in those who are immunocompromised. Herpes Zoster ophthalmicus (HZO) is the second most common manifestation of the disease, second only to thoracic and lumbar zoster.¹ HZO is estimated to account for 10% to 25% of cases.^{2,3} HZO can lead to a number of ocular complications, including proptosis, disciform keratitis, internal ophthalmoplegia, bilateral retinal detachments, Argyll-Robertson pupil, and progressive outer retinal neuropathy (PORN).^{1,4}

Cranial nerve palsies are a known complication of varicella zoster, most often involving the third cranial nerve, although they can include the third, fourth, fifth or sixth nerves, or any combination of these.⁴ Extraocular muscle paralysis, while well-documented, accounts for a small percentage of cases of ocular complications of herpes zoster ophthalmicus.³ Among these, isolated sixth nerve palsies are an infrequent manifestation and have not previously been reported in a patient with HIV. We report such a case.

Case report

A 45 year-old female with a 3-year history of untreated HIV infection was admitted to the hospital after she noted a painful vesicular rash on her face, accompanied by a high fever and decreased vision. Approximately two months prior to admission, she noted a painful rash in a dermatomal distribution on left side of her abdomen, extending from mid-axillary line to her back at approximately the level of her umbilicus. She was treated with oral acyclovir with resolution of the lesions. Approximately one month prior to admission she developed a similar rash on her face. The skin lesions were bilateral, in a mandibular distribution on her left side and on a maxillary distribution on her right side. She noted associated symptoms of malaise, high fever, and decreased vision. The patient was hospitalized for management with intravenous (IV) acyclovir. After 14 days of treatment, she was discharged with instructions to follow up at this institution's Retina- Vitreous service. There, she was diagnosed with progressive outer retinal neuropathy (PORN) and was begun on oral acyclovir. One week later, the patient's retinal disease was found to have worsened and she was admitted for more aggressive treatment.

On admission she was noted to have resolving skin lesions consistent with varicella zoster, along with bilateral involvement of her retina with progressive outer retinal neuropathy (PORN) and a right lateral rectus palsy. All other cranial nerves were intact. Her CD4 count and viral load were 21 cells/mL and 331,486 copies/mL, respectively. The patient was begun on a regimen of IV foscarnet, 1920 mg Q8 hr for a total of 14 days. On the 7th day of treatment she was begun on IV ganciclovir at 5 mg/kg. She was discharged on day 18 on continued ganciclovir treatment at 5 mg/kg/d. While her PORN had improved somewhat during the hospital admission, her right lateral rectus paralysis persisted.

Comment

Herpes zoster ophthalmicus is a common manifestation of varicella zoster disease with a distinct set of complications. It results when the latent virus, present in the trigeminal ganglia, is reactivated. Because of the numerous delicate structures in the vicinity of the infection, many clinically significant complications can occur.¹ Extraocular muscle paralysis can manifest with both primary varicella and zoster.^{2,5} Reports have varied with regard to prevalence of extraocular muscle paralysis among patients with HZO. Marsh et al. reviewed a series of 69 patients and found an incidence of 58 cases of extraocular muscle paralysis among 146 cases of herpes zoster ophthalmicus. In this group of patients, 42% experienced CN III involvement, 44% with CN VI involvement, and 30% with CN IV involvement. Isolated CN VI nerve paralysis accounted for 25% of cases.⁶ Ragozzino et al. noted 6 cases of motor deficits among 55 cases of herpes zoster ophthalmicus, none of which involved the extraocular muscles.³ Other reports have demonstrated an 11% to 29% incidence of extraocular muscle paralysis among patients with HZO.⁷ The order of prevalence is greatest for the third nerve and least for the trochlear nerve.⁶

There have been documented cases of abducens nerve paralysis in patients with herpes zoster ophthalmicus. Goldsmith documented a case of a lateral rectus muscle paralysis which resolved within 6 months.⁴ Nemet et al documented a case of an isolated lateral rectus muscle paralysis in a case of primary varicella.⁵ Archambault et

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al reported six cases of herpes zoster ophthalmoplegia, two of which were cases of sixth nerve paralysis, neither one of which occurred in isolation.⁷ Ramsell reported a case in which the second, third fourth, fifth and sixth nerves were all involved.⁸ A MEDLINE review of the literature from 1966 revealed no previously reported case of HZO-related CN VI palsy associated with HIV infection.

The exact cause of HZO-related cranial nerve palsy is unknown. There is limited documented pathology to allow definitive analysis of tissue damage.⁷ Perineural and perivascular inflammation occur as a consequence of herpes zoster ophthalmicus, and may account for some of the sequelae. Theories explaining possible causes of the involved neural tissue include direct damage caused by the virus, an allergic response to the viral infection, and an occlusive vasculitis triggered by the virus.⁶

Treatment of extraocular paralysis secondary to varicella zoster usually involves management with antivirals, such as acyclovir or famcyclovir. The natural history of the disease is slow and spontaneous resolution in the majority of patients, usually occurring between six weeks to eighteen months.⁴ There is no documentation to indicate whether patients with acquired immune deficiency syndrome have a longer recovery time, or if in fact their extraocular muscle paralysis is unlikely to resolve at all. Certainly cases of herpes zoster in HIV patients have been shown to be more severe and debilitating, presumably relating to the immunologic status of the patient.¹⁰ It is unknown, therefore, whether treatment should be directed differently towards these patients. Two months after discharge, our patient reported improved vision, but her right abducens nerve paralysis still had not resolved.

References

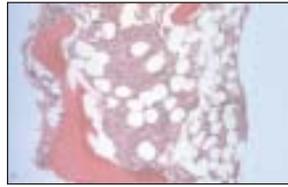
1. Pavan-Langston D. Herpes Zoster Ophthalmicus. *Neurology* 1995;45(12 Suppl.8):S50-1.
2. Cobo M. Reduction of the ocular complications of Herpes Zoster Ophthalmicus by oral acyclovir. *Am J Med* 1988;85(2A):90-3.
3. Ragozzino MW, Melton LJ, Kurland LT, Chu CP, Perry HO. Population-Based Study of Herpes Zoster and Its Sequelae. *Medicine* 1982;61(5):310-316.
4. Goldsmith MO. Herpes Zoster Ophthalmicus with sixth nerve palsy. *Can J Ophthalmol* 1996;3:279.
5. Nemet P, Ehrlich D, Lazar M. Benign Abducens Palsy in Varicella. *Am J Ophthalmol* 1974;78(5):859.
6. Marsch RJ, Dulley B, Kelly V. External ocular motor palsies in ophthalmic zoster: a review. *Br J Ophthalmol* 1977;61:677-682.
7. Archambault P, Wise JS, Rosen J, Polomeno RC, Auger N. Herpes Zoster Ophthalmoplegia: Report of Six Cases. *J Clin Neuro-Ophthalmol* 1988;8(3):185-191.
8. Ramsell TG. Complications of herpes zoster ophthalmicus. *Am J Ophthalmol* 1967;63(6):1796-8.
9. Vafai A, Berger M. Zoster in patients infected with HIV: a review. *Am J Med Sci* 2001;321(6):372-80.

Color Photos

Figure A

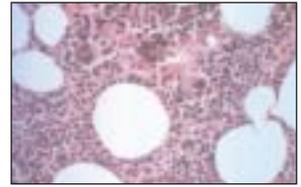


Figure B



A low power view of a bone marrow biopsy demonstrating focal hypercellularity.

Figure C



A high power view of a bone marrow biopsy demonstrating focal hypercellularity.

Figure D



Figure E



Figure F



Figure G



Figure J

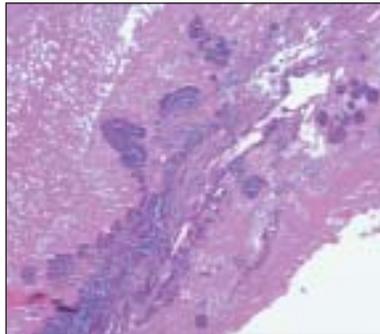


Figure H



Figure I



A Woman with Extreme Fatigue

Christopher DiMaio MD, Chief Medical Resident, Internal Medicine

A 23 year old female presented to her primary care provider's office complaining of extreme fatigue over the past few weeks.

The patient's past medical history is significant for stage 2B Hodgkin's lymphoma, diagnosed 2 years ago. The patient received 4 cycles of chemotherapy with ABVD, as well as multiple rounds of radiation therapy. Upon completion of treatment, her Hodgkin's was considered cured. The patient did develop hypothyroidism secondary to the radiation treatments, and requires permanent thyroid hormone replacement.

Four weeks prior to presentation, the patient noted the onset of her symptoms. She stated that she has been taking a lot of naps throughout the day, which is unusual for her. She denied fevers, chills, night sweats, changes in weight, or viral illnesses over this time.

At her primary care physician's office, the patient was found to have elevated LFT's. (Table 1)

Table 1. Outpatient Laboratory Values

	4 weeks prior to admission	1 week prior to admission
Total protein	6.2	-
Albumin	3.2	2.9
Total bilirubin	1.2	2.6
Direct bilirubin	-	-
AST	149	152
ALT	-	198
Alkaline phosphatase	182	158

The patient was referred to a gastroenterologist for evaluation and work-up. She began to develop visible jaundice, generalized pruritus, and dark urine, without fevers, abdominal pain, nausea, vomiting, or pale stools. She was subsequently hospitalized for further work-up.

On review of systems, the patient denies chest pain, shortness of breath, lymphadenopathy, diarrhea, constipation, myalgias, joint pains, or changes in her menstrual cycle. Her medications include levothyroxine and Depo-provera injections for birth control. She has used tobacco for the past 8 years, less than one-half pack of cigarettes per day, and consumes about 5 beers over 1 weekend per month. She denies any IVDA or

recreational drug use. The patient has one tattoo, dating about 8 years. She is sexually active in a monogamous relationship and her partner uses condoms.

Her vitals on presentation follow: blood pressure 126/78 mm Hg, heart rate 82, respirations 16, and temperature 98.6. The patient appears her stated age, and is in no apparent distress. Sclerae are anicteric, and conjunctivae pink. No oropharyngeal exudates or aphthous ulcers are seen, and there is no evidence of cervical, axillary, supraclavicular, or inguinal lymphadenopathy. Thyroid is not enlarged or tender. Cardiac exam is normal and her lungs are clear. Her abdomen is mildly obese, nontender and nondistended, with normoactive bowel sounds. There is no hepatosplenomegaly. No peripheral edema or joint abnormalities are appreciated, and she is neurologically intact.

Dermatologic exam is notable for generalized jaundice.

Admission laboratory data is listed in Table 2.

Table 2. Laboratory Values Upon Admission

Na	140	Hep B surface antigen	Negative
K	3.5	Hep B core antibody	Negative
Cl	109	Hep B surface antibody	Negative
CO2	27	Hep C antibody	Negative
BUN	10	AMA	Negative
Cr	.9	ANA	Negative
Wbc	5.0	Ceruloplasmin	6.0
Hgb	9.4*	Iron	122
MCV	109	TIBC	127
Plts	124	Iron saturation	96%
Total protein	5.6	Ferritin	1030
Albumin	2.5	Reticulocytes	15.1
Total bilirubin	10.9	Absolute reticulocyte count	110.9
Direct bilirubin	4.3	LDH	189
AST	95	B12	1242
ALT	30	Folate	13.4
Alkaline phosphatase	33	Haptoglobin	< 6.0
PT	21.0	TSH	3.69
INR	1.82		
PTT	43		
Hep A IgM/IgG	Negative		

*Hgb was 14.4 approximately 1 year ago.

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Isolated Abducens Nerve Palsy Secondary To Varicella Zoster In A Patient With HIV

Ellen B. Lunenfeld MD, PGY-2 Internal Medicine; John A. Walker MD

Varicella Zoster, the recrudescence of the dormant varicella virus, occurs more often in older patients and in those who are immunocompromised. Herpes Zoster ophthalmicus (HZO) is the second most common manifestation of the disease, second only to thoracic and lumbar zoster.¹ HZO is estimated to account for 10% to 25% of cases.^{2,3} HZO can lead to a number of ocular complications, including proptosis, disciform keratitis, internal ophthalmoplegia, bilateral retinal detachments, Argyll-Robertson pupil, and progressive outer retinal neuropathy (PORN).^{1,4}

Cranial nerve palsies are a known complication of varicella zoster, most often involving the third cranial nerve, although they can include the third, fourth, fifth or sixth nerves, or any combination of these.⁴ Extraocular muscle paralysis, while well-documented, accounts for a small percentage of cases of ocular complications of herpes zoster ophthalmicus.³ Among these, isolated sixth nerve palsies are an infrequent manifestation and have not previously been reported in a patient with HIV. We report such a case.

Case report

A 45 year-old female with a 3-year history of untreated HIV infection was admitted to the hospital after she noted a painful vesicular rash on her face, accompanied by a high fever and decreased vision. Approximately two months prior to admission, she noted a painful rash in a dermatomal distribution on left side of her abdomen, extending from mid-axillary line to her back at approximately the level of her umbilicus. She was treated with oral acyclovir with resolution of the lesions. Approximately one month prior to admission she developed a similar rash on her face. The skin lesions were bilateral, in a mandibular distribution on her left side and on a maxillary distribution on her right side. She noted associated symptoms of malaise, high fever, and decreased vision. The patient was hospitalized for management with intravenous (IV) acyclovir. After 14 days of treatment, she was discharged with instructions to follow up at this institution's Retina- Vitreous service. There, she was diagnosed with progressive outer retinal neuropathy (PORN) and was begun on oral acyclovir. One week later, the patient's retinal disease was found to have worsened and she was admitted for more aggressive treatment.

On admission she was noted to have resolving skin lesions consistent with varicella zoster, along with bilateral involvement of her retina with progressive outer retinal neuropathy (PORN) and a right lateral rectus palsy. All other cranial nerves were intact. Her CD4 count and viral load were 21 cells/mL and 331,486 copies/mL, respectively. The patient was begun on a regimen of IV foscarnet, 1920 mg Q8 hr for a total of 14 days. On the 7th day of treatment she was begun on IV ganciclovir at 5 mg/kg. She was discharged on day 18 on continued ganciclovir treatment at 5 mg/kg/d. While her PORN had improved somewhat during the hospital admission, her right lateral rectus paralysis persisted.

Comment

Herpes zoster ophthalmicus is a common manifestation of varicella zoster disease with a distinct set of complications. It results when the latent virus, present in the trigeminal ganglia, is reactivated. Because of the numerous delicate structures in the vicinity of the infection, many clinically significant complications can occur.¹ Extraocular muscle paralysis can manifest with both primary varicella and zoster.^{2,5} Reports have varied with regard to prevalence of extraocular muscle paralysis among patients with HZO. Marsh et al. reviewed a series of 69 patients and found an incidence of 58 cases of extraocular muscle paralysis among 146 cases of herpes zoster ophthalmicus. In this group of patients, 42% experienced CN III involvement, 44% with CN VI involvement, and 30% with CN IV involvement. Isolated CN VI nerve paralysis accounted for 25% of cases.⁶ Ragozzino et al. noted 6 cases of motor deficits among 55 cases of herpes zoster ophthalmicus, none of which involved the extraocular muscles.³ Other reports have demonstrated an 11% to 29% incidence of extraocular muscle paralysis among patients with HZO.⁷ The order of prevalence is greatest for the third nerve and least for the trochlear nerve.⁶

There have been documented cases of abducens nerve paralysis in patients with herpes zoster ophthalmicus. Goldsmith documented a case of a lateral rectus muscle paralysis which resolved within 6 months.⁴ Nemet et al. documented a case of primary varicella.⁵ Archambault et

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Quantitative tests of copper are useful in suggesting a diagnosis. Serum free copper levels are typically elevated. Urinary copper levels may also be elevated. It should be noted, however, that any disease with hepatocellular necrosis can result in elevated urinary copper levels. Liver biopsy with quantitative analysis for copper is considered the gold standard, but in patients with coagulopathy or ascites, this modality may not be an option. Hepatic copper concentrations are typically greater than 250 mcg/gm (dry weight) and can approach 3000 mcg/gm. Elevated hepatic copper content can be elevated in neonates and young children, as well as patients with chronic cholestasis or copper overload.

Liver biopsy allows for quantitative analysis of copper, and assessment of the extent of organ involvement. Pathology can demonstrate changes anywhere along the spectrum of steatosis to cirrhosis. Analysis of DNA for mutations can also play a role in diagnosis, while also identifying presymptomatic siblings of patients.

The goal of treatment in Wilson's disease is to reduce the total body amount of copper. Copper-rich foods such as organ meats, chocolate, nuts, shellfish, and mushrooms, should be eliminated from the diet. Instituting therapy as early as possible is critical in avoiding long-term complications of the disease.

First-line treatment is with D-penicillamine. This agent acts as a copper chelator and increases urinary copper excretion. Its effects can be seen within weeks to months of initiation of therapy. Typical starting dose is at 250 mg a day, with titration to 1000-1250 mg a day. There are numerous reports of acute hemolysis or neurologic deterioration shortly after initiation of therapy, particularly in those patients with neurologic symptoms. D-penicillamine is associated with a large number side

effect profile, including rashes, leukopenia, thrombocytopenia, nephritic syndrome, and a lupus-like reaction. There is a 30% intolerance rate.

Trientine (triethylene tetramine dihydrochloride) is another copper chelating agent that can be used as first-line therapy in those patients with allergies or intolerance to D-penicillamine. It has a more favorable side effect profile and is not associated with the potential worsening of neurological symptoms. It has been associated with sideroblastic anemia and colitis, upon cessation. The typical dose is 500 mg three times a day. Oral zinc is a newer treatment modality. Zinc interferes with the absorption of copper from the gastrointestinal tract and increased the amount of copper excreted in stool. Other treatment options include ammonium tetrathiomolybdate, an antioxidant which inhibits gut absorption of copper by binding copper-albumin complexes.

Screening for Wilson's disease should be conducted in all siblings of affected individuals, as well as those relatives with a history of consanguinity. A complete physical examination should be done with slit lamp ophthalmologic exam, along with liver function testing, and determination of serum ceruloplasmin and copper levels. Family members should be re-evaluated every 5-10 years.

References

- 1 Pfeil SA, Lynn DJ. Wilson's disease: Copper unfettered. *Journal of Clinical Gastroenterology* 1999; 29(1): 22-31.
- 2 Ferenci P. Wilson's disease. *Clinics in Liver Disease* 1998; 2(1): 31-49.
- 3 Feldman M, Friedman LS, Sleisenger MH. Sleisenger and Fordtran's *Gastrointestinal and Liver Disease*. 2002. Philadelphia: Saunders.

Training Residents in ACLS/Code Response Using a Computerized Medical Simulator: Improving Resident Comfort and Preparedness

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John Caruso MD⁺⁺, *Salvatore Mangione MD^{***}*, and *Gregory C. Kane MD^{***}*

Internal Medicine residents are responsible for leading the code response team at most teaching hospitals, yet many graduating interns (PGY1s) may feel unprepared to run codes. Currently, the only formal training for house staff is the two-day American Heart Association's Advanced Cardiac Life Support (ACLS) course, generally required at the beginning of internship, with recertification necessary every two years. This course does not address leadership skills or a resident's self-reported sense of comfort with leading a code team within a teaching hospital. Prior investigations have highlighted the deterioration in knowledge of important ACLS protocols, with knowledge levels at or near ACLS training levels within 6 months.^{1,2} Schwid and Sivarajan showed that the use of computerized ACLS simulator on CD-ROM improves retention of the guidelines better than textbook review alone.³ Others have shown that refresher courses can enhance performance in a mock resuscitation setting, with improvements maintained, in part, over several months.⁴ The use of more life-like simulation training has recently come into favor, through a variety of commercially available medical simulators. We designed an ACLS training program with such a medical simulator for interns preparing for their PGY2 year, namely those residents about to assume responsibility for leadership of the code team. Prior to the simulation training sessions, we collected baseline data regarding interns' experiences in code situations and comfort with the anticipated transition to leading the code team, as they advance to the PGY2 year of training.

Our investigation involved the use of a computerized Medical Simulator (MedSim[®]) to better prepare house staff to lead a code response team. We believed that such practical training was lacking, while certainly important for housestaff about to transition to a leadership role in running resuscitation efforts in our institution. The goal of our project was to give our interns some practical experience in a life-like simulation of three ACLS scenarios, while assessing improvements in their self-reported level of comfort with the role of team leader and preparedness for dealing with future code situations.

Methods

Thomas Jefferson University Hospital is a 550-bed teaching hospital with 37 categorical residents in each year of training and 6 preliminary medicine residents. The code blue team consists of two upper year residents (PGY2 or PGY3) assigned to lead the resuscitation effort and two interns to provide the actual care. Interns complete 8 blocks of inpatient assignments with time on the code team. PGY2's are assigned to rotations with overnight coverage and leadership of codes during 8 blocks, while PGY3's are assigned to only 2 blocks. All PGY1s were asked to participate in simulation training of code situations during the last quarter of the academic year (April/May 2000), prior to the start of their PGY2 year. Interns participated in teams of three and were asked to complete a questionnaire (QRE) and sign consent before taking part in the training exercise. A follow-up QRE was administered again at the start of their PGY2 year, after the interns had completed training. All responses were confidential and did not have any personal identifying information. A follow-up QRE was completed by residents continuing in the categorical internal medicine residency program.

MedSim[®] was designed to run several simulated Code Blue scenarios that were developed by the residency program leadership. The simulator consists of a computerized mannequin with synthesized heart and lung sounds, palpable pulses, pupillary responses, a functional airway, and IV access. The cardiac rhythm, BP, and oxygen saturation are displayed on an ICU monitor. Medications given by trainees through an electronic stop-cock lead to anticipated physiologic responses. Each resident performed one standard scenario while the other two residents assisted. The scenarios, unknown to the trainees, included tension pneumothorax with pulseless electrical activity, symptomatic bradycardia, and ventricular fibrillation. A primary resident was assigned as code leader. The other residents were assistants, charged with following the code leader's instructions, including airway intubation and ventilation, CPR, and medication administration. For each of the three scenarios, the residents would rotate their responsibilities. Each scenario had a different

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outcome. All sessions were videotaped so that actual performance could be reviewed. After all three scenarios were completed, the residents underwent a debriefing with a Chief Medical Resident or faculty member. These sessions included review of videotapes, review of critical assessments and decision-making of the team leader, and discussion of the correct course of action according to established ACLS protocols.

The QRE used a standard 5-point Likert scale to measure residents' comfort level leading a code team, familiarity with ACLS protocols, and sense of preparedness to run resuscitation efforts. We also collected data regarding the intern's experience with codes over the first 9 months of their PGY1 year of training. Statistical analysis was performed on a PC microcomputer using the SPSS statistical package (SPSS Inc., Chicago, Illinois). Analysis consisted of chi-square tests to relate dichotomous and nominal variables. Paired t-tests were used for pre- and post- intervention comparison on the several scale measures. Data dispersion was expressed as one standard deviation and significance set at a level of 95% or greater ($P < .05$).

Results

Forty-one interns completed the simulation training and pre-QRE. Thirty-six of them completed the post-QRE at the start of their PGY2 year. Two preliminary medicine interns opted not to participate because of career interests that did not include direct patient care. One categorical resident missed the simulation training because of vacation. All participating residents indicated that they were currently certified in ACLS (confirmed by residency program records). On average, the interns had attended between 6–10 codes during the preceding 9 months of training (options for response included 1-5, 6-10, 11-15, etc). Only 4 of 41 (10%) were given an opportunity to lead the resuscitation effort under the guidance of their senior resident prior to the simulation exercise. The 4 interns who indicated that they had led a code, had only done so one time each.

Prior to the intervention, trainees felt uneasy leading the code team. Only 7/41 (17%) interns said they felt "comfortable" running a code.

The simulated training program significantly increased house staff sense of comfort and preparedness in running codes. We observed improvement in their sense of comfort in leading the Code Blue team (1 to 5 scale, with 5 as highest): $2.61 + 0.90$ in the pre-intervention vs. $3.25 + 0.87$ post-intervention questionnaire ($p = .003$). We also observed an increase in their sense of preparedness: $2.67 + 0.79$ pre- vs. $4.03 + 0.97$ post-intervention ($p < .001$). Residents were enthusiastic about the training, and nearly all (33/36, 92%) requested a follow-up simulator session. Figure 1 shows the pre and post intervention comparisons of the resident's response to the question "I am prepared to lead the Code Team".

Discussion

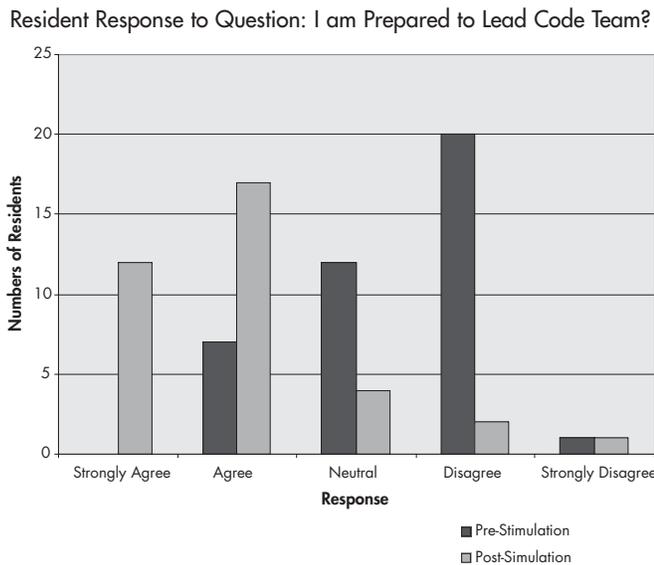
The survival of hospitalized patients with critical arrhythmias is clearly linked to the physician's correct treatment of the potentially deadly arrhythmia, combined with availability of equipment and coordination of care of the resuscitation team.^{5,6} Medical simulation offers a realistic model to train house staff to coordinate and lead a code team, while offering practical exposure to common code situations.

At our institution, we found that interns approaching the completion of their PGY1 year did not feel prepared to run the code team, despite certification in ACLS. Few had actual experience leading the code team as interns and the number of codes attended was quite low (not more than 10 resuscitation efforts). We found that house staff comfort and sense of preparedness was enhanced through lifelike training with a medical simulator and mock scenarios with formal post-simulation debriefing. Interns were overwhelmingly eager to undergo further simulated training.

Our study, based on an educational intervention, did not involve a control group. However, it is unlikely that such an increase in housestaff confidence could have occurred for other reasons. First, our data indicate that individual intern experience with code blue situations was infrequent, less than once per 4-week block. Thus, few interns would have had further significant experience during the last few blocks of their internship. Moreover, we do not require our interns to recertify in ACLS at the end of internship since their certificates are valid for two (2) years. At our

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institution, the majority of inpatient night call and responsibility for leading codes occurs during the PGY2 year prior to required recertification. While requiring ACLS training annually would represent an alternate educational strategy, more formal simulation with a group is the only way to address team leadership skills- a major focus of our simulations and debriefing sessions.

Since we report only on improvements in self-reported measures of comfort and preparedness, the impact of our findings does not extend to knowledge or performance. Arguably, performance would be the ultimate standard to judge such an intervention. Similar practical training, but using a CD-ROM based format, combined with expert debriefing or follow-up has been associated with improvements in knowledge of ACLS protocols.³ The advantage, however, of a true simulated training program such as ours is threefold. In our simulations, interns gained experience in leading a resuscitation team, worked with the necessary equipment utilized in an actual hospital resuscitation, and performed the important manual skills required in codes, including airway control and ventilation, chest compression, and needle decompression of pneumothorax. Faculty or Chief Residents observed the performance and provided direct expert feedback regarding performance of critical aspects of the resuscitation. Moreover, the use of videotape enhanced the reliability and objectivity of the debriefing.⁷

We have found that at our institution, graduating medical interns' sense of comfort with leading the code team is lacking. We have shown that comfort and sense of preparedness can be enhanced through a program of simulation training with expert feedback. Future work will be required to see whether improvements in comfort level or sense of preparedness correlate with increased measures of knowledge or actual outcomes. The availability of new technology in simulation training affords a novel and ethical approach to training housestaff that may yield benefits for hospitalized patients who suffer an arrest.

References

1. Lowenstein SR, Libbey LS, Mountain RD, et al. Cardiopulmonary resuscitation by medical and surgical house-officers. *Lancet* 1981;ii:679-681.
2. Curry L, and Gass D. Effects of training in cardiopulmonary resuscitation on competence and patient outcome. *Can Med Assoc J* 1987;137:491-496.
3. Schwid HA, Rooke GA, Ross BK, Sivarajan M. Use of a computerized advanced cardiac life support simulator improves retention of advanced cardiac life support guidelines better than a textbook review. *Critical Care Medicine* 1999;27(4):821-824.
4. Stross JK: Maintaining competency in advanced cardiac life support skills. *JAMA* 1983;249:3339-3341.
5. Kaye W, Mancini ME, Rallis SF: Advanced cardiac life support refresher course using standardized objective based Mega Code testing. *Crit Care Med* 1987;15:55-60.
6. Tunstall-Pedoe H, Bailey L, Chamberlain DA, Marsden AK, Ward ME, Ziderman DA. Survey of 3765 cardiopulmonary resuscitations in British hospitals (the BRESUS study): methods and overall results. *BMJ* 1992;304:1347-51.
7. Liu P, Miller E, Herr G, et al: Videotape reliability: A method of evaluation of a clinical performance examination. *J Med Educ* 1980;55:713-715.

A Man with Shortness of Breath and Bloating

Matthew E. Levy MD, PGY-3 Internal Medicine

The patient is a 61-year-old male with a past medical history of hypertension and insulin-dependent diabetes mellitus presented to the ED with new onset shortness of breath. He reported a three week progression of dyspnea after one flight of stairs, from a normal baseline. The patient also noticed 2 pillow orthopnea and increased urinary frequency and urgency. He denied fevers, chills, chest pain, palpitations or productive cough. Symptoms began when he ran out of his oral medications three weeks prior to admission (furosemide, enalapril, digoxin, metoprolol, spironolactone, aspirin). Family history was positive for alcoholic cirrhosis. Social history was positive for occasional tobacco and alcohol usage. Review of systems was also significant for a 2 to 3 month history of abdominal fullness and q3 day bowel movements. Upon further review, the patient stated he had a distended abdomen earlier, as an adult, that had somewhat disappeared until recently. He denied decreased oral intake, nausea, emesis, reflux, abdominal pain, diarrhea, melena or hematochezia.

Physical exam revealed an obese African-American male in no distress. Vital signs were pertinent for a resting tachycardia at 128 beats per minute and a blood pressure of 149/93. He had mild jugular venous distension and tachycardia with frequent ectopic heart sounds. Lung exam showed bibasilar crackles higher in the left lung field. His abdomen was massively distended with a rounded appearance, and dull to percussion throughout. Bowel sounds were loudest in the right flank area. There was no pain on palpation, rebound or guarding, and shifting dullness or a fluid wave could not be elicited. His extremities had 1+ pitting edema bilaterally to the knees. Labs including serum chemistry, blood count, liver function panel, PT and PTT, and cardiac enzymes were all within normal ranges. ECG revealed sinus tachycardia with multiple premature ventricular conduction and a left bundle branch block, while chest x-ray was notable for cardiomegaly and bilateral pulmonary vascular congestion, consistent with heart failure.

The patient was admitted with a diagnosis of heart failure, exacerbated by medication non-compliance. He was restarted on his medications and ruled out for

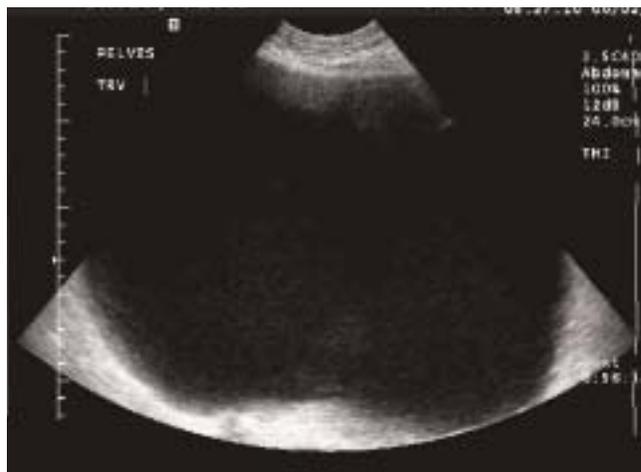


Figure 1.

myocardial infarction. An echocardiogram showed global hypo- to akinesis with an ejection fraction of approximately 15%. His symptoms improved with diuresis and he was asymptomatic by the end of his hospital admission. However, the size of his abdomen did not decrease, despite a negative fluid balance. An ultrasound of his abdomen was performed to evaluate for possible ascites secondary to heart failure. No ascites was seen. Instead, a large cystic space-occupying lesion was appreciated, involving most of the pelvis and abdomen, with mass effect on the left kidney causing moderate to severe left hydronephrosis (Fig 1). Computer tomography confirmed the cystic mass that measured 32 x 25 x 30 centimeters. (Figs 2-3). The massive size of the lesion prevented identification of an exact origin. Surgery was consulted for resection and tissue diagnosis. An uncomplicated open laparotomy was performed, which located the mass beneath the mesentery of the colon with the left ureter draped over it. There was no obvious connection to any of the surrounding organs. Due to the size of the mass, it could not be entirely excised, so it was first aspirated, with the removal of 12,000 ccs of serous fluid, and then resected. Pathology was consistent with benign mesothelial cyst. No further workup was required and the patient was discharged home in stable condition.

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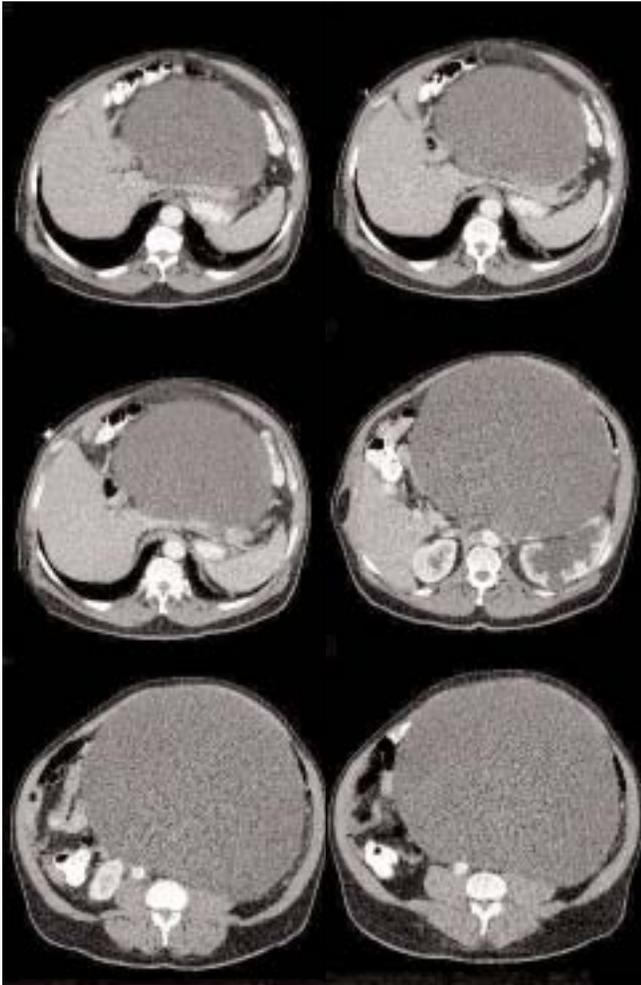


Figure 2.

Discussion

Mesenteric cysts are very rare benign fluid-filled tumors. They account for only 1 in 100,000 acute adult hospital admissions.¹ They're more commonly found in the pediatric population (1 in 20,000 pediatric admissions).² This is probably due to the more rapid progression of symptoms in children, with a greater ratio of cystic volume to intraabdominal volume). The Italian anatomist Benineni reported the first mesenteric cyst in 1507 from an autopsy of an 8-year-old boy.³ P.J. Tallaux performed the first successful resection of a mesenteric cyst in 1850.⁴ Since then 750 to 1000 cases have been reported in the literature.⁵⁻⁶



Figure 3.

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Most mesenteric cysts in adults are asymptomatic. Over 40% are diagnosed incidentally during unrelated surgeries.⁵ Others are found during routine physical or radiological examinations. Physical examination may show a distended abdomen mobile in the transverse plane only, as opposed to mobile in all directions with omental cysts.⁶ The most common symptoms are abdominal pain with distension, anorexia, nausea, vomiting, and malaise. Pain can be caused by infection or torsion of the cyst, hemorrhage into the cyst, mesenteric stretching from the cyst, or compression of surrounding structures causing obstructions.⁷ Occasionally cysts will cause mesenteric volvulus or herniations.⁵⁻⁶

Classification of mesenteric cysts used to be variable and inconsistently applied, lacking pathologic correlation. In 1986, Ros et al collected 41 cases of mesenteric and omental cysts and retrospectively classified them using histology and imaging criteria. Five types of mesenteric cysts were identified. These include lymphangiomas (endothelial lining), enteric duplication cysts (enteric and double-muscle lining), enteric cysts (enteric mucosa only), mesothelial cysts, and non-pancreatic pseudocysts that have a fibrous wall but no lining.⁸ Other non-mesenteric cysts include cystic mesotheliomas, cystic spindle cell tumors, cystic teratomas, and cysts originating from abdominal or retroperitoneal organs.⁹

Lymphangiomas are usually large, thin-walled, multi-loculated cystic masses, formed from small bowel lymphatic tissue that congenitally does not communicate with lymphatic vessels. They are almost always seen in childhood or adolescents.¹² Lymphangiomas are often attached to bowel wall and are more likely to cause partial bowel obstructions.¹⁸ Ultrasound shows lymphangiomas as multi-septated cysts that can be anechoic or contain fluid-filled levels caused by debris.^{8,10} CT scans show a cystic mass with attenuation (Hounsfield units) ranging from water (serous contents) to fat (chylous contents).¹¹

Enteric duplication cysts are thick-walled, unilocular cysts with predominantly serous contents. These cysts probably were once attached to normal bowel, but separated and migrated into the mesentery. Their composition “duplicates” that of the normal enteric wall. On histologic examination, all layers of bowel are seen, including

mucosa, circular and longitudinal muscle layers, and mesenteric plexus. Ultrasound shows a thick-walled, anechoic cyst that internally resembles small bowel. CT scan reveals the thick wall with serous fluid attenuation.⁸⁻⁹

Enteric cysts are thin-walled, unilocular cysts lined with gastric mucosa only, lacking the muscle layers of an enteric duplication cyst. They are formed from small bowel or colonic diverticuli that migrate into the mesentery. Ultrasound shows a hypoechoic mass with occasional septations. CT scan shows a fluid-filled mass without an identifiable wall and attenuation consistent with serous contents.⁸⁻⁹

Mesothelial cysts are thin-walled, unilocular cysts lined with mesothelial cells. They are thought to arise from incomplete fusion of mesothelial layers during development, and are found in mediastinum (pericardial, pleural), omentum, and retroperitoneal areas (splenic). Ultrasound shows an anechoic mass with acoustic enhancement. They appear similar to enteric cysts on CT scan.⁸⁻⁹

Non-pancreatic pseudocysts, like their pancreatic namesakes, arise from local trauma or inflammation. They are thought to be the results of a hematoma or abscess that did not resorb. Pathologically they are thick-walled and septated, with hemorrhagic or purulent contents. Ultrasound shows a thick-walled mass with echogenic debris. CT scan shows a mass that may have a fluid-fluid level differentiating blood from pus.⁸⁻⁹

Other masses in the abdominal cavity can mimic mesenteric cysts. Cystic mesotheliomas are an intermediate formation, between an adenomatoid tumor and a malignant peritoneal mesothelioma. These benign tumors are usually found in middle-aged women. They are usually large and multicystic, and tend to reoccur locally after resection.¹³ Spindle cell tumors, otherwise known as gastrointestinal leiomyomas or leiomyosarcomas, can occasionally undergo necrosis. This causes liquification and hemorrhage into the center of the neoplasm, creating an appearance similar to mesenteric cysts on imaging. Ultrasound and CT scan will show a complex cystic mass with a lot of internal debris.¹⁴ Mesenteric teratomas, usually seen in children,

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have cystic components and resemble mesenteric cysts on physical exam. However, imaging studies will pick up calcifications and accumulations of fat, that do not appear in mesenteric cysts.¹⁵

Treatment

Mesenteric cysts very rarely resolve spontaneously and surgical resection is most often required. Drainage of cysts are not recommended, because they tend to reaccumulate quickly. Marsupialisation of cysts are also not performed, since they increase infection risk from a persistently draining sinus. Complete resection of the cyst usually prevents recurrence. This may require the removal of a bowel segment, if the cyst cannot be separated cleanly, as is the case with lymphangiomas.⁷ Recently, laparoscopy has been used for identification and removal of mesenteric cysts. Like other minimally invasive surgeries, laparoscopic excision of mesenteric cysts significantly reduces hospital duration and complication rates. Mesothelial cysts are usually easier to remove, due to their loose attachments to surrounding tissues.¹⁶ However, our patient's cyst was too large and too close to other vital structures to be safely removed by laparoscopy.

Conclusion

Because of their relative rarity, mesenteric cysts are not commonly considered by most primary care physicians evaluating patients with abdominal complaints. Certainly in cases of appreciable abdominal distention, when physical examination is not consistent with ascites, a work-up to rule out mesenteric cyst pathology could be warranted. Ultrasound should be the first imaging performed because of its ease of use and identification of internal components of the cyst. CT scan and MRI can delineate physical nature and relationship to adjacent structures and should be performed prior to surgery. . New approaches such as laparoscopic removal make mesenteric cysts easy to cure. A definitive diagnosis can only be made after surgical resection and histologic examination.

References

1. Takiff, H., Calabria, R., Yin, L., Stabile, B.E. Mesenteric cysts and intra-abdominal cystic lymphangiomas. *Arch. Surg.* 1985; 120: 1266-1269.
2. Kurtz, R.J., Heiman, T.M., Beck, A.R., Holt, J. Mesenteric and retroperitoneal cysts. *Arch. Surg.* 1986; 203: 109-112.
3. Bearhs, O.M., Judd, E.S., Docherty, M.G. Chylous cysts of the abdomen. *Surg. Clin. North Am.* 1950; 302: 1081-1096.
4. Tallaux, P.J. Cyste du mesentere un homme: ablation par la gastromie: quersion. *Rev. Ther. Med. Chir. Paris.* 1880; 47: 479.
5. Mohanty, S.K., Bal, R.K., Maudar, K.K. Mesenteric cyst - an unusual presentation. *J Pediatr Surg* 1998; 33: 792-793.
6. O'Brien, M.F., Winter, D.C., Lee, G., Fitzgerald, E.J., O'Sullivan, G.C.. Mesenteric cysts - a series of six cases with a review of literature. *Ir. J. Med. Sc.* 1999; 168: 233-236.
7. Mollitt, D.R., Ballantine, T.V.N., Grosfield, J.L. Mesenteric cysts in infancy and childhood. *Surg. Gynaecol. Obstet.* 1978; 147: 182-184.
8. Ros, P.R., Olmsted, W.W., Moser, R.P Jr., Dachman, A.H., Hjermsstad, B.H., Sobin, S.H. Mesenteric and omental cysts: histologic classification with imaging correlation. *Radiology* 1987; 164: 327-332.
9. Stoupis, S., Ros, P.R., Abbitt, P.L., Burton, S.S., Gauger, J. Bubbles in the belly: imaging of cystic mesenteric or omental masses. *Radiographics* 1994; 14: 729-737.
10. Wicks, J.D., Silver, T.M., Bree R.L. Giant cystic abdominal masses in children and adolescents: ultrasonic differential diagnosis. *Am J Radiology* 1978; 130: 853-857.
11. Davidson, A.J., Hartman, D.S. Lymphangioma of the retroperitoneum: CT and sonographic characteristics. *Radiology* 1990; 175: 507-510.
12. Sun, C.C.J., Tank, C.K., Hill, J.L. Mesenteric lymphangioma. *Arch Pathol Lab Med* 1980; 104: 316-318.
13. Katsube, Y., Mukai, K., Silverberg, S.G. Cystic mesothelioma of the peritoneum: a report of five cases and review of the literature. *Cancer* 1982; 50: 1615-1622.
14. Volk, B.A., Scholmerich, J., Farthmann E., Gerok W., Wenz, W. Leiomyoblastoma of the stomach - a case report on ultrasonographic differential diagnosis of cystic lesions in the abdomen. *Hepatogastroenterology* 1983; 30: 33-35.
15. Bowen, B., Ros, P.R., McCarthy, M.J., Olmsted, W.W., Hjermsstad, B.M. Gastrointestinal teratomas: CT and US appearance with pathologic correlation. *Radiology* 1987; 162: 431-433.
16. MacKenzie, D.J., Shapiro, S.J., Gordon, L.A., et al. Laparoscopic excision of a mesenteric cyst. *J. Laparoendosc. Surg.* 1993; 3: 295-296.

A Woman with Headache and Chest Pain

Theresa Pondok MD, PGY-3 Internal Medicine

A 34 y/o woman, with a past medical history significant for asthma, newly diagnosed hypertension, and migraines, presented to the emergency department with complaints of sudden onset chest pain. She was an active young woman, who up until the day of admission, had been able to run several miles without chest pain or shortness of breath. Symptoms began the morning of admission, when the patient reported that she developed a migraine headache, with typical right-sided temporal pain. After administering an injection of Sumatriptan, her headache resolved. Soon thereafter, she noted 5/10 substernal chest pressure occurring suddenly at rest, without radiation to her arms or jaw. It was not associated with nausea, vomiting, diaphoresis or shortness of breath. The patient stated that she had never experienced this type of pain before, which alarmed her enough to come to the hospital. One sublingual nitroglycerin, given in the ED, completely relieved her symptoms.

The patient's medical history included hypertension, asthma, Raynaud's phenomena, and migraine headaches. Hypertension was recently diagnosed, and well controlled off medications with a strict regimen of diet and exercise. Her asthma was stable with very occasional use of an albuterol metered dose inhaler, and she stated that she had never been intubated or required hospitalization for an exacerbation. Her Raynaud's symptoms occurred in her fingertips intermittently during the winter months for the past several years. Migraine headaches were diagnosed 2 years prior, and she had been tried on several different abortive therapies without success. The Sumatriptan had just recently been prescribed, and this instance represented her first use.

The patient had no surgical history. She denied alcohol, tobacco, or intravenous drug abuse. She lived at home with her husband and four children. Both parents were still alive, her father with atrial fibrillation and her mother with hypertension. There was no family history of sudden death or coronary artery disease. The patient took no regularly prescribed medications, only prn albuterol MDI and sumatriptan injections. Her allergies included aspirin and shellfish, both of which exacerbate her asthma symptoms. Review of systems was positive only for the chest pain described above, occasional palpitations and migraine headaches.

On physical examination the patient was afebrile with a pulse of 112, respirations of 20, blood pressure of 111/66, and O₂ saturation of 100% on 3 liters nasal cannula. She was alert and oriented, in no acute distress. Her oropharynx was clear, and heart regular with a normal S₁ and S₂, and no audible murmurs, gallops, or rubs. There was no detectable jugular venous distention. Lungs were clear, and her abdomen soft, nondistended, and non-tender. No peripheral edema was appreciated.

Laboratory data is shown in Table 1.

Table 1. **Outpatient Laboratory Values**

WBC	8.0
Hgb	15.9
PLT	228
Sodium	138
Potassium	4.1
Bicarbonate	25
BUN	9
Creatinine	0.8
Glucose	189
Total cholesterol	193
LDL	113
HDL	50
TG	79
CK	321
Troponin	1.9

The admission chest film showed clear lungs. The ECG, however, revealed sinus rhythm with ST elevations in leads II, III, and aVF, as well as ST depressions in the anterior leads. An echo showed normal chamber sizes, with distal lateral and mid to distal posterior wall hypokinesis.

Hospital Course

The patient was admitted to the medical CCU for management of an ST elevation myocardial infarction, presumed to be secondary to coronary artery vasospasm. The vasospasm was attributed to her recent use of Sumatriptan. She was started on intravenous nitroglycerin for relief of ongoing chest pain. A continuous infusion of diltiazem was also started for control of the vasospasm. Given the patient's allergy to aspirin, clopidogrel was initiated. Cardiac enzymes were

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followed and the troponin I peaked at 27 ng/mL. The patient continued to have episodic chest pain during her stay in the CCU and consequently four days after her admission, the patient underwent cardiac catheterization. Catheterization showed luminal irregularities in the left main, left anterior descending, left circumflex and right coronary arteries. The second obtuse marginal, however, showed 99% occlusion. The left ventriculogram revealed posterolateral akinesis. Given the tortuosity of the vessel, the OM2 lesion was not stented. The location of the occlusion, however, did correspond with the area of akinesis. It was thought that the patient had underlying occlusion of the OM2, with superimposed vasospasm secondary to use of Sumatriptan, and this precipitated her acute myocardial infarction. The final decision was to optimize medical management with clopidogrel, diltiazem and a statin.

Coronary Vasospasm

Coronary vasospasm has also been referred to as Prinzmetal or variant angina. Prinzmetal originally described it in 1959 as a “temporary increased tonus” in areas of high-grade coronary artery occlusion. Vasospasm is a syndrome of cardiac pain secondary to myocardial ischemia. The spasm itself can occur in normal or diseased vessels and usually occurs within one centimeter of an atherosclerotic plaque. The resultant ischemia will appear as ST elevations on ECG, and this can typically be reversed with nitroglycerine or calcium channel blockers.

The patients suffering coronary vasospasm are commonly younger than those who present with other forms of angina. They often lack the cardiovascular risk factors typically associated with heart disease. As in the above case, these patients often have other systemic signs and symptoms of vasospasm, including Raynaud’s phenomenon and migraine headaches. Interestingly, there appears to be an increased incidence of symptoms in the hours between midnight and early morning. The most common cause of mortality associated with vasospasm involves arrhythmias, including ventricular tachycardia.

Although the precise mechanisms have not been clearly defined, there are some circulating theories to explain the underlying pathogenesis of coronary vasospasm. One hypothesis involves the autonomic nervous system. It has

been shown that both acetylcholine and methacholine can precipitate vasospasm, thus inferring that the parasympathetic nervous system may play a significant role in the pathogenesis. The discovery that atropine and alpha-receptor blockers can prevent such spasm also supports this theory. In fact, sympathetic denervation (plexectomy) may be therapeutic in refractory patients. Endothelial dysfunction may also play a role in pathogenesis. Decreased levels of the endogenous vasodilator nitric oxide, and increased levels of the vasoconstrictor endothelin have been shown to impair coronary dilatation. These compounds may play an integral role in coronary vasospasm. Finally, patients with areas of diffuse intimal thickening of the coronary vasculature may also be at risk for spasm. With underlying coronary artery disease, episodic vasospasm alters preexisting plaques, leading to intimal disruption and penetration of macrophages or aggregation of platelets. Consequently, vasospasm may contribute to vascular instability in these patients.

Sumatriptan, a serotonin (5-hydroxytryptamine [5-HT]) receptor agonist, causes vasoactive constriction of cerebral vascular beds, making it useful as an abortive therapy for migraine headaches. However, it has also been shown to exhibit vasoactive activity in the systemic, coronary, and pulmonary vascular beds. Three to five percent of patients experience chest tightness, heaviness, pressure, or pain after its administration. Occasionally, the chest pressure or pain radiates to the left arm and hand, imitating angina pectoris. ECG evidence of myocardial ischemia, however, is rare. Recently, Welch reported that while over 3 million migraine attacks have been treated with sumatriptan, there have only been 4 reported patients with myocardial ischemia due to coronary vasospasm, 1 of whom also had cardiac arrhythmia. All four patients had underlying cardiovascular disease. Sumatriptan has a mild constrictive effect on coronary arteries. MacIntyre et al found 10 patients undergoing diagnostic coronary angiography who had a 14 percent reduction in the diameter of the coronary arteries. Based on such evidence and more recent case reports, sumatriptan is contraindicated in patients with coronary artery disease or vasospastic angina.

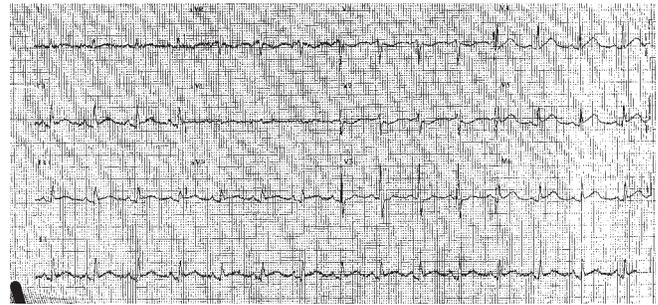
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The typical ECG findings in patients with variant angina are transient ST elevations associated with chest pain, that then return to baseline with resolution of symptoms. Cardiac catheterization plays a major role in diagnosis. In patients presenting with the typical signs and symptoms of variant angina, including non-exertional chest pain and ST elevations, angiography may reveal normal vessels or, as in this case, a proximal fixed obstruction in one or more of the coronary arteries. It is in this latter group of patients that vasospasm should be suspected. Two provocative tests can help confirm this condition. The most sensitive and specific test involves injection of intravenous ergonovine, a vasoconstrictor, during catheterization. The test is positive if drug administration replicates symptoms or ECG findings. The effects should be reversed with intracoronary nitroglycerine. Ergonovine can also be used in conjunction with echocardiography. Wall motion abnormalities after injection indicate a positive test. Hyperventilation is a less sensitive test that can also be performed during coronary catheterization. The patient is instructed to hyperventilate for six minutes and if acute ST changes are seen on ECG, coronary vasospasm is inferred.

The image below shows cardiac catheterization with hyperventilation-induced vasospasm of the proximal left circumflex artery that resolved with the administration of intracoronary nitroglycerine and diltiazem.

As with all types of coronary artery disease, risk factor modification is essential. Cessation of smoking must be enforced. Medical management includes lipid-lowering medications, and calcium channel blockers or nitrates to maintain coronary vasodilatory effects. Medical treatment has shown favorable responses in female patients and patients with ST-segment elevation during selective spasm provocation tests. However, patients with either a longer history of episodic chest pain or a history of diffuse spasms do not improve with medical treatment alone. Nonselective beta-blockers should be avoided, as they may exacerbate vasospasm. Angioplasty is helpful if there is a discrete area of occlusion, however its utility is limited by the fact that many patients have multivessel spasms. It has been recommended that calcium channel blockers be continued after percutaneous revascularization for this very reason. In refractory patients, surgical denervation with plexectomy may be an option.



References

1. Chen H.S. V., Pinto D. S. Prinzmetal's Angina. *N Engl J Med* 2003; 349:e1, Jul 3, 2003.
2. Johnson S. M., Mauritsen D. R., Willerson J. T., Hillis L. D. A controlled trial of verapamil for Prinzmetal's variant angina. *N Engl J Med* 1981; 304:862-866, Apr 9, 1981.
3. MacIntyre PD, Bhargava B, Hogg KJ, Gemmill JD, Hillis WS. Effect of subcutaneous sumatriptan, a selective 5HT_{1B/1D} agonist, on the systemic, pulmonary, and coronary circulation. *Circulation* 1993;87:401-405.
4. Meredith IT, Yeung AC, Weidinger FF, et al. Role of impaired endothelium-dependent vasodilation in ischemic manifestations of coronary artery disease. *Circulation* 1993;87:Suppl V:V-56.
5. M. L. Main, K. Ramaswamy, and T. C. Andrews. Cardiac Arrest and Myocardial Infarction Immediately after Sumatriptan Injection. *Ann Intern Med*, May 15, 1998; 128(10): 874 - 874.
6. Sueda, S., Kohno, H., Fukuda, H., Watanabe, K., Ochi, N., Kawada, H., Uraoka, T. (2003). Limitations of Medical Therapy in Patients With Pure Coronary Spastic Angina. *Chest*. 123: 380-386.
7. Welch K.M.A. Drug Therapy: Drug Therapy of Migraine. *N Engl J Med* 1993; 329:1476-1483, Nov 11, 1993.
8. Yeghiazarians Y., Braunstein J. B., Askari A., Stone P. H. Unstable Angina Pectoris. *N Engl J Med* 2000; 342:101-114, Jan 13, 2000.

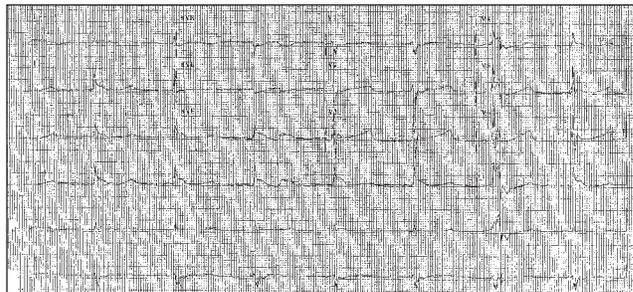
An Unresponsive Woman Found Down

Murliya Gowda MD, PGY-3 Internal Medicine

A middle-aged unidentified female presented by fire rescue to the emergency department after being found unconscious in the snow. Her identity, familiar contacts, and medical history were not known, but the patient was presumed to be homeless.

On examination, the patient was found to have a core body temperature of 75 F, an accucheck of 75, a palpable systolic blood pressure of 60, heart rate of 39, and shallow but spontaneous respirations. Pulse oximetry was not obtainable secondary to her cold peripheral extremities. In general, she was a thin disheveled female dressed in multiple layers of clothes with damp boots, and unresponsive to voice and tactile stimulus. The patient had a dry oropharynx, anicteric sclera, but equal and reactive pupils bilaterally. There was no evidence of facial droop, jugular venous distension, or thyromegaly. Her heart rate was slow but regular and there were no audible murmurs. Lung exam revealed mostly clear breath sounds, although decreased at the bases. Abdomen was nontender and soft, with mild to moderate distention and no organomegaly. Extremities were cold, with severe sloughing of the skin over both feet and ankles (trench foot and wet gangrene). Dorsalis pedis pulses were intact by Dopplers. Neurological exam revealed symmetric reflexes throughout with downgoing plantar reflexes. She was immediately intubated for airway protection and started on warmed intravenous fluids, with warming blankets and warmed oxygen. She was taken to the CCU for further monitoring and care.

Laboratory data revealed a WBC 6,000/ml³, hemoglobin 9.5 grams/dL, and 154,000 platelets. Coagulation profile was abnormal with a PTT of 60, PT of 27.7, and INR of 2.42. Urinalysis was significant for 4+ blood and 20 RBCs. A post-intubation arterial blood gas revealed a serum pH of 7.45, pCO₂ of 34, PO₂ of 150 and 100 % oxygen saturation. BUN was elevated at 36 with a normal creatinine, and both blood alcohol and urine drug screens were negative. Amylase, lipase, and chemistries were normal. Chest x-ray revealed a normal cardiomeastinal silhouette and no consolidation. Head CT on admission showed no acute intracranial abnormalities. Echocardiogram showed normal right and left ventricular function, no pericardial effusion and trace mitral regurgitation, tricuspid regurgitation and mild



pulmonary regurgitation. ECG showed sinus bradycardia with a heart rate of 44, borderline intraventricular conduction delay, prolonged QT interval, and Osborne waves (J waves).

The patient was later identified as a 55 year-old homeless female with past medical history significant for schizophrenia, HIV, alcohol and tobacco abuse. The patient was treated for severe hypothermia compounded by MSSA bacteremia, sepsis, frostbite and wet gangrene of the lower extremities, eventually requiring bilateral below the knee amputations.

Brief Discussion

Approximately 700 people die in the United States each year as a result of hypothermia. Risk factors include homelessness, mental illness, older age, and alcohol and drug addiction. Hypothermia is a core body temperature less than 35 C (95 F). It can be additionally categorized into mild hypothermia (32 C to 35 C or 90 F to 95 F), moderate hypothermia (28 C to 32 C or 82 F to 90 F), and severe hypothermia (below 28 C or 82 F). At these temperatures, the systems responsible for thermoregulation begin to fail. Temperature regulation includes the balance between heat production and loss. Heat is generated through various cellular mechanism and is lost through evaporation, radiation, conduction (transfer of heat to another object) or convection (transfer of heat to air currents). Temperature is regulated in the nuclei of the preoptic anterior hypothalamus. Activation of thermostats in the nuclei and peripheral cold receptors initiate compensatory mechanisms, which eventually leads to progressive depression of metabolism in each organ system. In cold temperatures, the hypothalamus stimulates heat production through shivering and

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increases catecholamine, thyroid and adrenal activity. Other compensatory mechanisms include vasoconstriction, which reduces heat loss by decreasing flow to peripheral tissues. As metabolism in each organ system slows, complications such as cardiac arrhythmias, confusion, lethargy, hypoventilation, pulmonary edema, muscle rigidity, metabolic derangements, and bleeding diatheses, including DIC, can ensue.

Cold exposure is the most obvious cause of hypothermia, but there are also many other conditions that can exacerbate or precipitate it. Altered pituitary/adrenal/thyroid axes can predispose, along with hypoglycemia, sepsis, pancreatitis, uremia, and neurological diseases. Illicit drugs or iatrogenic medications can also alter body temperature fairly rapidly.

Medical approach for hypothermic patients primarily focuses on airway protection, volume resuscitation, careful monitoring of core body temperature, rewarming techniques, and management of complications. Endotracheal intubation is important in these patients for airway protection, particularly in those with altered mental status or a diminished cough reflex. Many develop bronchorrhea with copious secretions, progressing to frank pulmonary edema in some patients. Volume resuscitation and pressor support are also important elements in the management of hypothermic patients. As core temperature rises, peripheral vasodilatation occurs, leading to profound hypotension. Aggressive intravenous hydration with warmed saline is crucial.

Hypotension can contribute to cardiac arrhythmias, which can be refractory to conventional therapies. Specifically, the bradyarrhythmias are typically unresponsive to atropine and pacing is not indicated, unless they persist after adequate rewarming. Classic ECG findings show a sinus bradycardia with elevation of the J-point (J or Osborne wave), representing distortion of membrane repolarization. Ventricular arrhythmias occur when core temperature is less than 82 to 90 F (28 to 32 C). At these temperatures, the myocardium becomes more susceptible to hypoxia, movement, and hypovolemia. Caution must be taken not to jostle the patient, as sudden movement can predispose them to instantaneous arrhythmias. Often, ventricular

arrhythmias are treatment-refractory until core body temperature has returned to normal. Standard ACLS protocol is quickly initiated (defibrillation and appropriate pharmacological agents); if initially unsuccessful, rewarming techniques with CPR must be instituted first, and after core body temperature has reached 86 F to 90 F (30 C to 32 C), defibrillation should be reattempted. In some studies, ventricular arrhythmias in animal models have shown a response to bretylium, which has even been used prophylactically at some institutions. Life-supporting measures are continued, unless the body is completely frozen and chest compressions cannot be performed adequately, or there is ice in the airways. There have been case reports describing resuscitation efforts lasting several hours, until the patient has been sufficiently rewarmed.

Monitoring core body temperature is a crucial element in the management of hypothermic patients. The goal is to increase core body temperature 1 to 2 degrees per hour, and temperature should be monitored at more than one site. Standard thermometers can give readings as low as 93 F, and in these situations cannot reliably be used. It should also be noted that rectal and bladder probes have temperature readings that tend to lag behind true core body temperature, while esophageal temperature probes can be falsely elevated due to inhalation of warmed air. Rewarming techniques include intrinsic heat production (shivering), removal of wet clothing, and the use of heating blankets and pads/insulation. Active internal warming techniques, including pleural, peritoneal, and bladder irrigation with warm saline, continuous veno-veno or arterio-veno hemodialysis, and cardiopulmonary bypass with warmed oxygen are more invasive options. Pleural and peritoneal lavage is recommended only in patients with a normal cardiac rhythm and a stable blood pressure. During the rewarming process, a unique phenomenon known as afterdrops can occur. Afterdrop occurs when the extremities and trunk are warmed simultaneously and cold acidotic blood from the periphery returns to core circulation, causing acute temperature drops.

Complications of hypothermia are of particular concern. Skin damage from both cold exposure (i.e. frostbite and trenchfoot) or from heating pads are common. Care must

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be taken not to rub or massage the skin and induce further friction-related injuries. Compartment syndrome and gangrene are frequently seen, which can lead to limb or digit amputation. Metabolic derangements such as rhabdomyolysis, acidosis, hyperglycemia, hypoglycemia, and adrenal suppression can also occur. In severe progression, renal failure, DIC, pancreatitis, sepsis and shock liver can lead to death. Initial work up should always consist of chest x-rays, ECG and complete laboratory studies including TSH, cortisol, electrolytes, CBC, LFTs, pancreatic enzymes, serial arterial blood gases, and coagulation studies. Head CT, urine drug screen and blood alcohol level in the unresponsive patient can help rule out other etiologies of syncope. Empiric antibiotics, thiamine, dextrose, and naloxone for patients with altered mental status should also be considered.

In summary, the management of the hypothermic patients focuses on combined resuscitative and rewarming techniques. Resuscitation efforts should be continued until the patient is adequately rewarmed, as arrhythmias can be refractory to standard therapies until the core body temperature is reached. The low temperatures do have a protective effect on neurological function, allowing for patients to recover after a prolonged arrest. Complications can still occur long after rewarming, and careful monitoring of the patient in a critical care setting is essential.

References

- 1 Antretter, H., Bonatti, J., Dapunt, O. E., Hernández, E., Praga, M., Alcázar, J. M., Murray, P. T., Fellner, S. K., Mülleneisen, N., Danzl, D. F., Pozos, R. S. (1995). Accidental Hypothermia. *NEJM* 332:1033-1035.
- 2 Danzl, D. & Pozos, R. S. (1994). Accidental hypothermia. *NEJM* 331:1756-1760.
- 3 Grinspoon, S. K., Hedley-White, E. T. (2001). Case 35-2001 81 year-old male with hypothermia, bradycardia, and confusion . *NEJM* 2001 345:1483-1488.
- 4 Jolly, B., Ghezzi, K. (1992). Accidental hypothermia. *Emergency Medical Clinics of North America* 10:311-327.
- 5 Lazal, H. L. (1997). The treatment of hypothermia. *NEJM* 337:1545-1547.
- 6 McNerney, J., Breakell, A., Madira, W., Davies, T., Evans, P. (2002). Accidental hypothermia and active rewarming: the metabolic and inflammatory changes observed above and below 32{degrees}C. *Emergency Medical Journal* 19: 219-223.
- 7 Mechem, C., *Accidental Hypothermia. Up to Date* 2003.
- 8 Offenstadt, G., Harries, M., MacKenzie, M. A., Walpoth, B. H., Mattle, H. P., Althaus, U. (1998). Accidental Deep Hypothermia. *NEJM* 338:1160-1162.

A Man with Shortness of Breath and an Abnormal ECG: A Short Case

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An 80 year-old Chinese male with a history of tobacco use and asthma presented to the ER complaining of shortness of breath that was unresponsive to bronchodilator use. The patient's ECG on admission was sinus rhythm at 95 beats per minute with minimal ST elevations in V2-V4. Laboratory results were significant for a troponin of 7.7. The patient was started on anticoagulation with heparin. A transthoracic echocardiogram revealed an ejection fraction of 25%. The patient underwent coronary catheterization, which revealed luminal irregularities of his coronary arteries. Figures 1 and 2 show the end diastolic and end systolic left ventriculograms from the catheterization, respectively.

The end systolic ventriculogram demonstrates anterolateral and apical akinesis in a pattern similar to a "tako-tsubo," or octopus pot. Tako-tsubo-like left ventricular dysfunction is a transient process that can be brought on by "stressful" circumstances, including strong emotions and bronchoconstriction. Typically, the patients have elevations in troponin levels, but do not have evidence of coronary artery disease on catheterization. The left ventricular dysfunction resolves in two to six weeks. In this patient, a transthoracic echocardiogram demonstrated normal left ventricular function two weeks after the initial echocardiogram.



Figure 1.



Figure 2.

Effects Of Walnut Consumption As Part Of Heart Healthy Diet On Atherogenic Lipoprotein Subclasses

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Nutritional therapy is fundamental in the treatment of cardiovascular disease. Studies that utilized a low-fat diet supplemented with 64 grams/day of walnuts have shown a significant reduction in serum levels of total and LDL cholesterol, and triglycerides. This study was designed to see if lipoprotein subclasses varied in patients eating a low-fat walnut supplemented diet.

Methods/Design

Frozen aliquots of serum samples from a single center, randomized, open-label, crossover study were tested to evaluate the effects of walnut intake on lipoprotein subclass distribution. Sixty-seven outpatients with high total cholesterol followed a standardized low-fat, low-cholesterol diet for six weeks before random assignment to continue the same diet or to ingest 64grams/day of walnuts as part of the diet. A registered dietitian instructed the patients on various ways to substitute walnuts in their diet to maintain the same amount of total energy, carbohydrates, protein and total fat content as the control diet. After 6 weeks, the patients were crossed over to the opposite treatment arm.

Results/Conclusions

Serum samples obtained pre- and post-treatment from the walnut diet arm of the study from 42 patients were available for analysis by Lipoprint for VLDL and LDL particle size distribution. VLDL particles were distributed among large (C), medium (B), and small (C) subclasses, while LDL particles were distributed among 3 major subclasses sizes (L1-L3) ranging from the largest (L1) to the smallest (L3). The walnut diet demonstrated significant reduction in both the total cholesterol (5%) and LDL-C (9%). Although the observed changes among VLDL and LDL particle size did not significantly change from baseline, a clear trend of -14% was observed for the small (L3) subclass of LDL. An additional trend in reduction of the large VLDL particle subclass (C) of 20% was also observed. Therefore, patients whose total and LDL cholesterol levels decreased by adherence to a low cholesterol, low fat diet enriched by 64grams/day of walnuts also demonstrated a potentially beneficial trend in subclass size distribution of the major atherogenic lipoproteins classes in this study group.

Effect Of Intravenous Pulse Cyclophosphamtoe (CYC) Therapy On Systemic Sclerosis (Ssc) Inflammatory Lung Disease

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Deterioration of lung function is the most frequent cause of death in SSc. Alveolitis is considered the initiating event of SSc lung fibrosis. Effective therapy of SSc alveolitis is, therefore, of paramount importance. Here we assessed the use of intravenous CYC on pulmonary function testing (PFT) and high resolution computerized tomography (HRCT) abnormalities in 15 patients with SSc and alveolitis.

Methods

Fifteen patients with SSc and alveolitis diagnosed by clinical, bronchoalveolar lavage, or HRCT findings were treated with intravenous pulse CYC (750 mg/m² of body surface area) monthly for 6 months. If there was no improvement on PFT or HRCT findings, patients were continued with 6 monthly pulses. If the condition was stable or improved, patients received 3 additional bimonthly pulses. After the first year, patients continued with CYC pulses every 3 months for one year. PFT and HRCT of the chest were obtained during and following therapy to determine the efficacy of CYC treatment. Seven patients received low-dose oral corticosteroids for reasons other than interstitial lung disease.

Results

A regression analysis was performed after normalizing the DLCO (diffusion capacity of the lung for carbon monoxide), FVC (forced vital capacity), and TLC (total lung capacity) values to the values obtained immediately prior to initiation of treatment. This analysis revealed a 61% improvement in the DLCO at 36 months, following initiation of CYC therapy. The FVC and the TLC improved by 28% and 27%, respectively, during the same period. These results were in contrast to a 35% decline in DLCO during the 36 months prior to therapy. FVC and TLC were essentially unchanged in the pre-treatment period. HRCT showed improvement in the ground glass appearance in 80% of the cases, while 20% were unchanged. Fibrosis improved in 67% and remained unchanged in 33%. Honeycombing, if present, disappeared in every case.

Conclusion

Intravenous pulse CYC treatment alone or accompanied by low dose corticosteroid therapy was an effective and well tolerated treatment of SSc inflammatory lung disease. The greatest improvement was observed in DLCO, although there was improvement in FVC and TLC values, as well.

Clinical Quiz



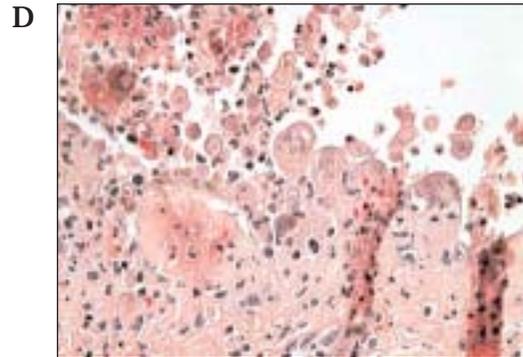
An asymptomatic 14 y/o female with a history of Peutz-Jeghers syndrome and prior small bowel intussusception had the above finding during screening with capsule endoscopy. What is the next step?



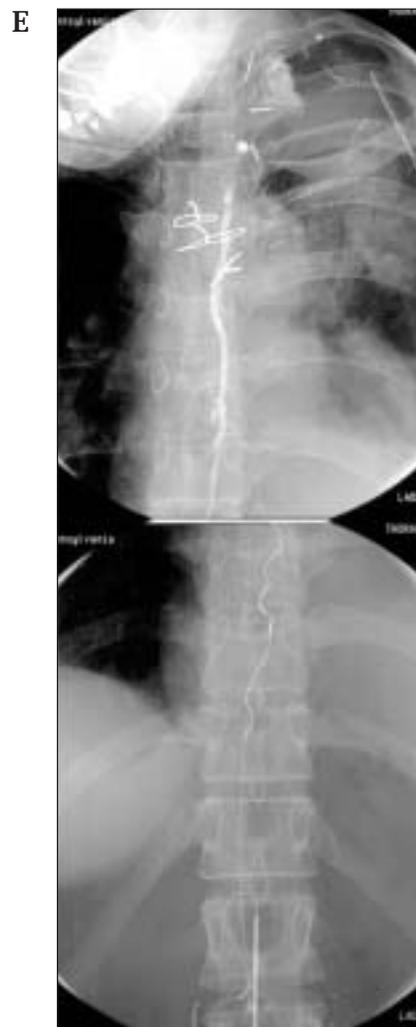
A 33 y/o female with intermittent right upper quadrant pain and an abnormal abdominal ultrasound underwent ERCP evaluation. What abnormality is seen and what would you recommend to this patient?



A 54y/o male with a history of sarcoidosis, in remission from AML after recent chemotherapy and XRT, presents with elevated LFTs and liver nodules on ultrasound. What is shown above?

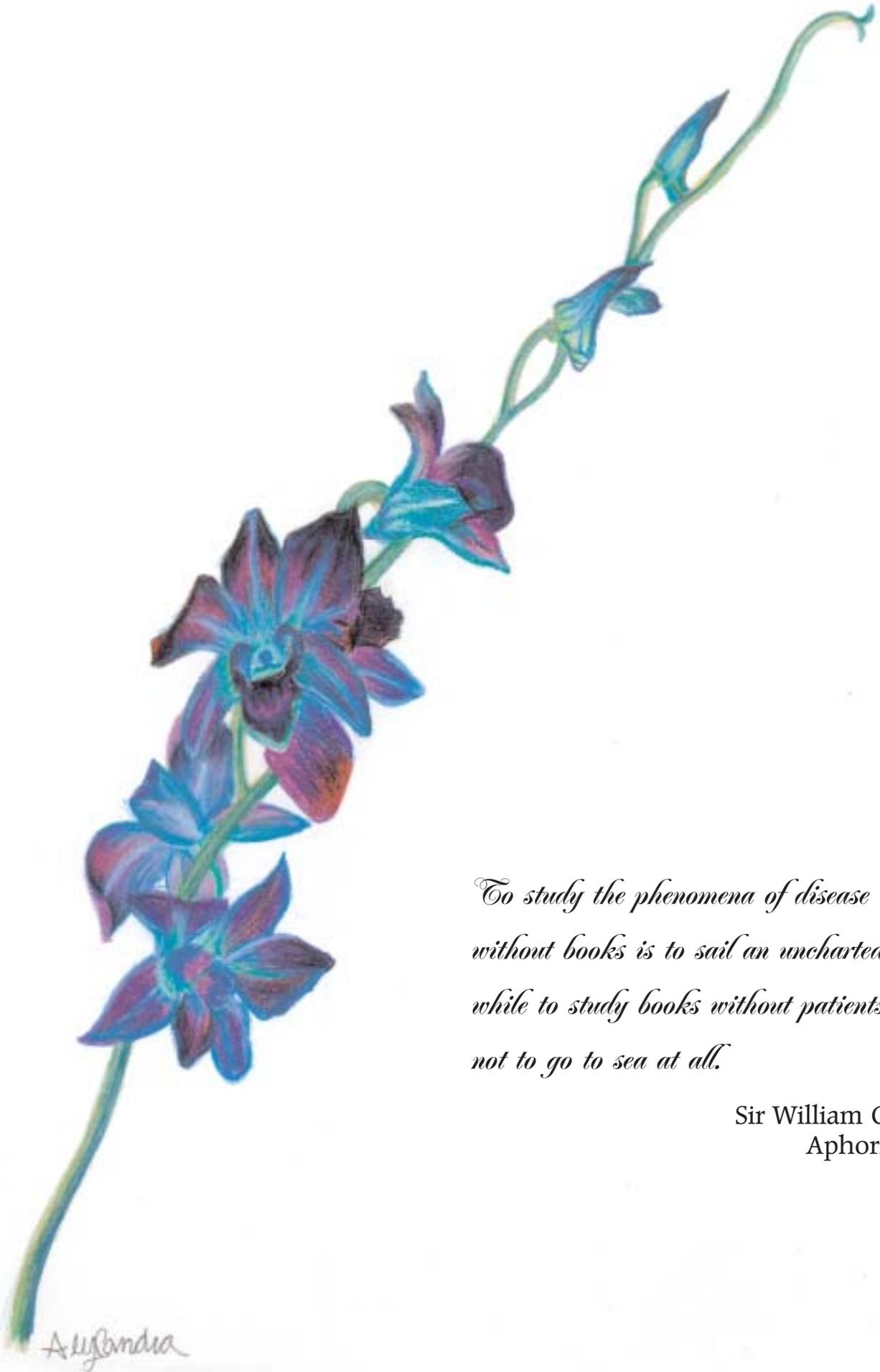


A 21 y/o healthy male acutely decompensates and presents with a total body punctate rash and fulminant liver and renal failure. What is the diagnosis, based on the histologic slide above?



A 68 y/o woman, status post left upper lobe pneumonectomy for squamous cell cancer of the lung, presents with a 2 week history of heaviness in her chest and dyspnea. Thoracentesis revealed a milky discharge. A therapeutic fluoroscopic procedure is shown above. What is your diagnosis? What is the procedure?

Answers on page 12



*To study the phenomena of disease
without books is to sail an uncharted sea,
while to study books without patients is
not to go to sea at all.*

Sir William Osler
Aphorisms