Systemic Vasculitis: Review Questions

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QUESTIONS

Choose the single best answer for each question.

Questions 1 to 3 refer to the following case.

A 74-year-old man with a history of benign prostatic hyperplasia, hypertension, type 2 diabetes mellitus, and glaucoma presents to the emergency department with a 2-week history of paroxysmal fevers up to 101°F, decreased appetite with sudden neck and tongue pain when chewing food, and new-onset progressive blurry vision in his right eye. Laboratory testing reveals a hemoglobin A_{1c} (HbA_{1c}) of 5.5%, hemoglobin level of 14 g/dL, prostate-specific antigen level of 2.1 ng/mL, and an erythrocyte sedimentation rate (ESR) greater than 115 mm/hr. Blood and urine cultures are negative. Urinalysis is unremarkable.

1. What is the most appropriate action at this time?
(A) Administer intravenous (IV) antibiotics and antifungal medications
(B) Administer IV methylprednisolone 1000 mg
(C) Call ophthalmology to perform an urgent tonometric study
(D) Repeat blood cultures with the next fever spike
(E) Start prednisone 20 mg daily

2. Which of the following should be performed to establish the diagnosis?
(A) Computed tomography (CT) angiogram of the thorax
(B) Cranial ultrasound
(C) 2-Dimensional Doppler echocardiogram
(D) Fundoscopic examination
(E) Temporal artery biopsy

3. How should this patient be treated?
(A) IV infliximab every 8 weeks
(B) Methotrexate 25 mg/wk with folic acid 1 mg/day
(C) Prednisone 60 mg/day
(D) Prednisone 60 mg/day and aspirin 81 mg/day
(E) Timolol 0.5% gtt twice daily

Questions 4 and 5 refer to the following case.

A 38-year-old man with newly diagnosed hypertension presents to his primary care physician with multiple lesions on his lower extremities, a 10-lb weight loss over the past 4 months, and dull discomfort of his right testicle. The lesions started out as dark hyperpigmented areas, which ulcerated and healed, leaving a crater-like scab (**Figure 1**). The lesions are not pruritic or painful. He has been seen by a wound care specialist, but the recommended treatments have not helped. Cultures taken on several occasions have been unremarkable. The patient has recently developed some new dark spots on the tips of his fingers and toes, with increasing tingling and numbness in these areas. On physical examination, blood pressure is 160/94 mm Hg, heart rate is 88 bpm, respiratory rate is 14 breaths/min, and temperature is 100.5°F. Laboratory results reveal a hemoglobin level of 15.5 g/dL, platelet count of 247,000 cells/μL, blood urea nitrogen (BUN) of 47 mg/dL, serum creatinine of 1.8 mg/dL, aspartate aminotransferase of 25 U/L, alanine aminotransferase of 29 U/L, alkaline phosphatase of 220 U/L, and ESR of 88 mm/hr. Antineutrophil cytoplasmic antibody (ANCA) staining is negative, and hepatitis A and C serologies are negative. Serologic testing for hepatitis B surface antigen is positive, and testing for HIV is negative. The patient drinks alcohol occasionally and does not smoke.

4. This patient's symptoms are most consistent with which of the following conditions?
(A) Churg-Strauss syndrome (CSS)
(B) Henoch-Schönlein purpura
(C) Polyarteritis nodosa (PAN)
(D) Thromboangiitis obliterans
(E) Wegener's granulomatosis

5. Which of the following should be performed to confirm this patient's diagnosis?
(A) Kidney biopsy
(B) Muscle biopsy
(C) Peripheral nerve biopsy
(D) Renal angiogram
(E) Testicular ultrasound

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6. **A 42-year-old woman presents to her physician with shortness of breath, fatigue, mild fevers, and a 12-lb weight loss over the past 8 weeks. She has had asthma since she was a teenager, with mild attacks occurring every 2 to 3 months, usually alleviated with an albuterol inhaler. She notes an ongoing dry cough during these attacks. The patient reports lost sensation in her right arm approximately 2 weeks ago as well as in her left arm approximately 2 months ago. She has had atopic dermatitis and eczema on several occasions. Laboratory testing reveals a hemoglobin level of 14 g/dL; white blood cell count of 98,000 cells/μL, with a differential of 28% neutrophils, 7% lymphocytes, 24% eosinophils, and 1% basophils; BUN of 12 mg/dL; and serum creatinine level of 1.4 mg/dL. The ESR is 65 mm/hr, and C-reactive protein is 3.2 mg/dL. P-ANCA staining is positive with confirmed myeloperoxidase reactivity. Urinalysis shows numerous white and red blood cells. Urine cultures are negative. Chest radiograph demonstrates bilateral diffuse interstitial infiltrates. This patient's symptoms are consistent with which of the following?**
   (A) Allergic bronchopulmonary aspergillosis
   (B) CSS
   (C) Eosinophilia-myalgia syndrome
   (D) Pulmonary sarcoidosis

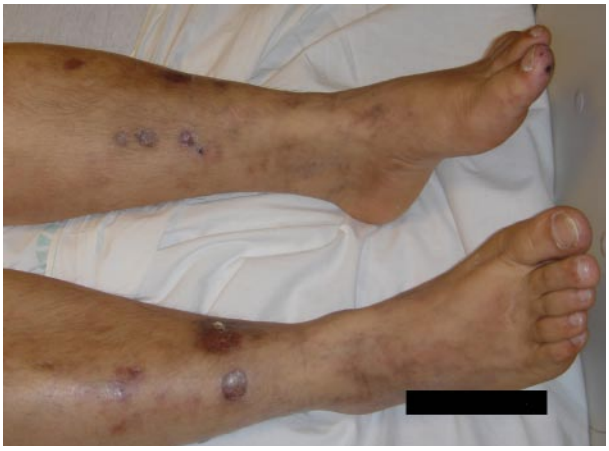

Figure 1. Photograph of the lesions on the lower extremity of the patient described in questions 4 and 5.

ANSWERS AND EXPLANATIONS

1. **(B) Administer IV methylprednisolone 1000 mg.** The patient has active signs of giant cell arteritis (GCA), such as fever, weight loss, jaw claudication, and an elevated ESR. The most concerning sign is the visual change. This is a true emergency, as blindness can occur in 1 or both eyes if not treated promptly. Initiating IV methylprednisolone 1000 mg for 3 days and then switching to oral prednisone is the most appropriate treatment to possibly prevent loss of vision.[1] This patient's normal HbA_{1c} level suggests that his diabetes is under control and that the visual changes are not due to diabetes. Waiting for repeat blood cultures as well as starting antibiotics in a patient with negative blood cultures is not indicated. Measuring hydrostatic pressure within the eye with tonometry is important; however, the results would not explain the patient's painless visual disturbances.

2. **(E) Temporal artery biopsy.** Given this patient's high probability of having GCA, there is no need for a fundoscopic examination or a 2-dimensional Doppler echocardiogram. Several available modalities may help establish the diagnosis, including temporal artery ultrasound, CT, positron emission tomography, magnetic resonance imaging, and angiographic studies. However, the gold standard for diagnosing GCA remains a temporal artery biopsy demonstrating granulomatous inflammation with intimal hyperplasia and central narrowing (**Figure 2**).[1] A temporal artery biopsy will still show histologic changes after corticosteroids have been administered (7–14 days), but radiologic findings may change.

3. **(D) Prednisone 60 mg/day and aspirin 81 mg/day.** Corticosteroids are the only proven treatment for GCA. They should be started at 60 mg/day for the first few weeks and then tapered. Treatment often lasts many years, and relapses are common once corticosteroids are stopped. The addition of an antiplatelet agent, such as aspirin, can reduce the odds of cerebral ischemic events and visual loss.[2,3] The addition of aspirin should be considered in light of the patient's medication history and in conjunction with gastrointestinal prophylaxis, especially in the elderly. Although useful as steroid-sparing agents for many other conditions, methotrexate and infliximab are not useful in the treatment of GCA.

4. **(C) PAN.** This patient has PAN, a necrotizing vasculitis that affects small- and medium-sized arteries but without glomerulonephritis or vasculitis in arterioles, venules, or capillaries. This condition most prominently affects the neurologic, musculoskeletal, gastrointestinal, and dermatologic systems. PAN is not usually associated with ANCA but can be associated with hepatitis B. Testicular pain or unilateral orchitis is due to ischemia of the testicular artery and is found in less than 10% of patients with PAN. In Wegener's

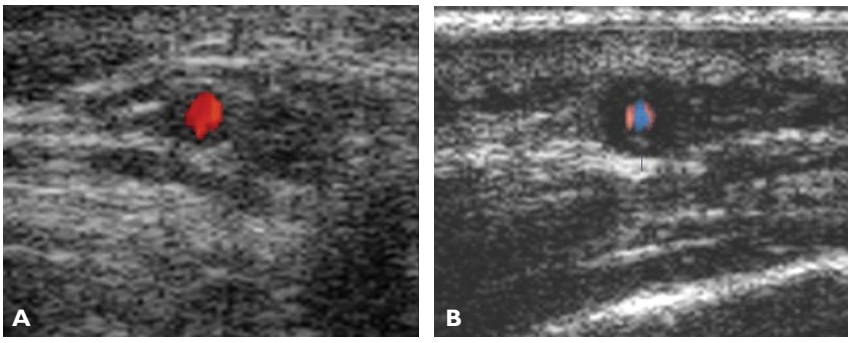

Figure 2. Cross-section of the temporal arteries in (**A**) a normal patient and (**B**) a patient with biopsy-confirmed giant cell arteritis. Note the difference in the vessel walls and the "halo sign" on color Doppler ultrasonography (B), significant for probable arterial wall edema.

granulomatosis, the patient usually presents with signs or symptoms of upper and lower airway disease, and c-ANCA staining is usually positive with confirmed targeting of proteinase-3. Thromboangiitis obliterans usually presents in a patient who is a heavy smoker. Henoch-Schönlein purpura is usually found in children but can occur in adults, often after an infectious process. It frequently presents with palpable purpura of the lower extremities and not with large open ulcerative lesions. Absence of prominent eosinophilia in this patient makes the diagnosis of CSS unlikely.

5. **(C) Peripheral nerve biopsy.** Based on this patient's hypertension, skin lesions, and neurologic disturbances, sural nerve biopsy is most appropriate to confirm the diagnosis of PAN.[4] In PAN, the biopsy will show a necrotizing pattern of vasculitis in medium-sized vessels in the epineurium as well as vessels in various stages of the disease process, such as with fibrinoid necrosis with acute inflammation and scarring and organizing thrombi. A muscle biopsy has a sensitivity of 50% in diagnosing PAN.[5] Renal biopsy has a lower specificity for diagnosing PAN and is associated with an increased risk of bleeding as a result of microaneurysms in the kidney.[6] Angiographic studies should only be performed if there is no dermatologic or renal involvement and are not the best option in this patient given his elevated serum creatinine level.

6. **(B) CSS.** This patient presents with the classic findings of CSS, including allergic rhinitis, asthma, and eosinophilia. The eosinophilia affects different organ systems, causing inflammation. The lungs, peripheral nerves, sinuses, and skin are most commonly involved; however, cardiovascular, renal, gastrointestinal, and the central nervous systems can also be affected. The patient's neurologic manifestations are likely due to mononeuritis multiplex. The 3 phases of CSS are the (1) prodromal phase, where asthma predominates; (2) the eosinophilic phase, in which eosinophils dramatically increase and pulmonary manifestations become evident; and (3) the vasculitic phase, in which nonspecific findings such as weight loss, fevers, fatigue, and skin lesions predominate. Dermatologic manifestations include a combination of macular papular rashes, subcutaneous nodules, palpable purpura, and raised erythematous lesions. In eosinophilia-myalgia syndrome, the blood eosinophil count is greater than 1000 cells/μL and patients have incapacitating myalgia and no evidence of infection or neoplastic conditions. Several cases of eosinophilia-myalgia syndrome have been attributed to the consumption of products containing L-tryptophan. Pulmonary sarcoidosis is a progressive granulomatous disorder with variable findings on radiography depending on the stage of disease (stage 1, bilateral hilar lymphadenopathy; stage 2, hilar lymphadenopathy; stage 3, parenchymal disease without hilar lymph nodes; stage 4, pulmonary fibrosis). Common symptoms of pulmonary sarcoidosis include cough, dyspnea, and exercise limitation but not marked eosinophilia. Bronchopulmonary aspergillosis is an allergic lung reaction to a type of fungus (most commonly *Aspergillus fumigatus*) that occurs in some individuals with asthma or cystic fibrosis, causing cough and wheezing and sometimes fever. This condition is not associated with neurologic sequelae.

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