A 40-year-old African-American man with a 20-pack-year history of smoking was admitted to the hospital with acute abdominal pain. Physical examination revealed bilateral upper quadrant abdominal pain associated with splinter hemorrhages and finger clubbing. An abdominal radiograph was normal, but CT of the abdomen showed splenic and renal infarctions. The liver, pancreas, large bowel, and small bowel appeared normal. A chest radiograph showed increased interstitial markings. Six blood cultures showed no bacterial or fungal growth. A transesophageal echocardiogram was consistent with prolapse and myxomatous changes of the mitral valve but revealed no vegetations. Bronchoscopy showed no endobronchial lesions. BAL fluid was negative for cytologic study, and stains and cultures were negative for bacteria and fungi. He denied IV drug abuse. He was discharged to a long-term care facility and given 6 weeks of antibiotic therapy for culture-negative bacterial endocarditis. He was readmitted to the hospital because of persistent radiographic infiltrates.

**Physical Examination**

Vital signs: temperature, 36.9°C; pulse, 100/min; respirations, 18/min; BP, 140/86 mm Hg. General: thin and cachectic. Chest: clear to auscultation. Cardiac: grade 1-2/6 murmur at apex and left lower sternal border. Extremities: finger clubbing and splinter hemorrhages. Rectal: stool negative for occult blood.

**Laboratory Findings**

WBC count, 6,500/mm³ with normal differential; hematocrit, 32%; platelet count, 313,000/mm³. Calcium, liver function test results, and electrolytes:

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normal. Prothrombin time: 15 s; partial thromboplastin time: 25 s; fibrinogen, 689 mg/dL; D-dimer varied from 1,000-2,000 (upper limits of normal=500). HIV antibody: negative. Chest radiograph: diffuse interstitial infiltrates, more prominent in the right upper lobe, and right hilar adenopathy (Fig 1). CT of the chest: peripheral consolidation in the right upper lobe and bilateral hilar and mediastinal adenopathy (Figs 2 and 3).

Hospital Course

Repeated bronchoscopy with the addition of transbronchial biopsy specimens showed poorly differentiated adenocarcinoma. A workup for metastatic adenocarcinoma disclosed no abnormalities. He developed a nonhemorrhagic cerebral infarct and aspiration pneumonia requiring mechanical ventilatory support. A transthoracic echocardiogram showed thickening of the mitral and tricuspid valves but no definite vegetations.

An acute abdomen developed requiring an exploratory laparotomy. Necrotic areas involving the small and large bowel were resected and the superior mesenteric artery was opened; a white clot was removed. Cultures of the clot were negative. Histologic study revealed agglutinated blood and platelets but no inflammatory cells. IV heparin therapy was started.

What diagnosis can explain the constellation of clinical and laboratory findings?
Diagnosis: Nonbacterial thrombotic endocarditis (NBTE) secondary to adenocarcinoma (probably lung).

NBTE is characterized by the presence of fibrinous vegetations on the heart valves. These vegetations contain platelets with an absence of associated inflammation or organisms. NBTE is also known as marantic or terminal endocarditis. The prevalence of NBTE in autopsy populations has varied from 0.3 to 9.3%. NBTE most commonly affects patients in the fourth through the eighth decades of life but has been observed in all age groups and in both sexes. The victims are commonly patients with malignant neoplasms, particularly those with adenocarcinomas of the lung and pancreas. Any valve can be affected but the left-sided valves are more commonly involved. Microscopically, the vegetations are composed of agglutinated blood and platelet thrombi without inflammatory cells. In most instances, the underlying valves are normal but the disease can occur on previously damaged valves.

The pathogenesis of NBTE is not fully understood. Some authorities believe that the formation of NBTE requires a damaged valvular surface; other investigators contend that the hypercoagulable state associated with disseminated intravascular coagulation (DIC) and malignancy predisposes to NBTE.

There are no pathognomonic symptoms or signs of NBTE. Systemic emboli are usually the first symptoms. These patients may present with stroke or encephalopathy, myocardial infarction, mesenteric artery occlusion, limb arterial occlusion, renal infarcts, splenic infarcts, pulmonary emboli (if the vegetations are right-sided), and subungual hemorrhages. Of these embolic phenomena, splenic and renal infarcts are the most frequent, but cardiac and cerebral infarctions are the most dangerous in terms of morbidity and mortality. Heart murmurs may be noted but many investigators have emphasized their rarity.

The antemortem diagnosis of NBTE is problematic. There are three cardinal clinical features of the disease: (1) the presence of heart murmurs; (2) the presence of an underlying disease process known to predispose to NBTE; and (3) evidence of multiple systemic emboli.

If the clinical diagnosis is suspected, the following laboratory and diagnostic studies should be performed: (1) multiple blood cultures to exclude infective endocarditis; (2) coagulation profiles to establish the presence of a hypercoagulable state; and (3) a two-dimensional echocardiogram to assess for the presence of vegetations.

There is no specific treatment for NBTE. Treatment of the underlying disease responsible for valvular damage or hypercoagulable state and control of the thromboembolism, and sometimes accompanying DIC, with anticoagulants are the mainstays of therapy. IV heparin is the most effective agent. Warfarin and aspirin are not beneficial.

The present patient clinically had lung cancer of the right upper lobe (Fig 3) with NBTE manifested by a heart murmur, thickened heart valves, systemic emboli, and DIC with negative blood cultures.

He responded to IV heparin with an improvement in his coagulopathy. No bleeding episodes occurred. He subsequently developed septic shock and died. An autopsy was refused.

**Clinical Pearls**

1. The diagnosis of NBTE should be considered in any patient with a malignant neoplasm, especially adenocarcinoma, in the setting of multiple systemic embolic episodes.

2. If multiple blood cultures fail to grow bacteria or fungi, coagulation profiles and a two-dimensional echocardiogram should be performed.

3. Since the pathogenesis of NBTE is not understood, there is no specific prophylactic or curative treatment.

4. Heparin is the only available therapy.

**Suggested Readings**


