Miliary Tuberculosis Presenting as Hepatic and Renal Failure

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A 67-year-old man developed hepatic and renal failure over a six-day period. Despite full supportive care, he died on his 11th day of hospitalization with fulminant DIC and hepatic, renal, and respiratory failure. Postmortem examination revealed acid-fast bacilli in virtually all organ systems. Miliary tuberculosis should be considered as a potentially treatable cause of hepatic failure.

(Chest 1991; 99:752-54)

DIC = disseminated intravascular coagulation; PT = prothrombin time; PTT = partial thromboplastin time; AST = aspartate-aminotransferase; GMS = Gomori methenamine silver

Hepatic and renal involvement in miliary tuberculosis is frequent but usually not of major clinical consequence. To our knowledge, the present patient represents the first report of miliary tuberculosis presenting as fulminant hepatic and renal failure.

Case Report

A 67-year-old white man, who had been previously well, developed malaise, myalgias, watery diarrhea, and upper respiratory symptoms three days prior to his presentation at a local hospital. Jaundice was noted, and he was admitted for evaluation of suspected viral hepatitis. Six days following admission, renal function had deteriorated and required hemodialysis. The patient was transferred to our critical care service.

Physical examination on admission showed a toxic-appearing, jaundiced lethargic man with a respiratory rate of 34/min. Blood pressure was 118/58 mm Hg, the pulse rate was 100 beats per minute, and his temperature was 37.7°C (99.9°F). The sclerae were icteric. Chest examination revealed bibasilar inspiratory rales. The liver was palpable with a 10-cm to 12-cm span.

The hematocrit reading was 32.5%; the leukocyte count was 4,000/cu mm, with 99 percent neutrophils; and the platelet count was 59,000/cu mm, with a PT of 21.3 seconds and PTT of 41.2 seconds. The fibrin split products were >10<40, with a fibrinogen level of 57 mg/dl. Other data were as follows: serum sodium, 140 mmol/L; BUN, 98 mg/dl; creatinine, 7.6 mg/dl; albumin, 1.8 g/100 ml; total bilirubin, 15.9 mg/dl; alkaline phosphatase, 158 IU/ml; lactic acid dehydrogenase, 2,345 IU/ml; and serum AST, 417 IU/ml. The results of urinalysis were normal.

A chest roentgenogram showed bilateral alveolar infiltrates. An abdominal CT scan showed minimal hepatosplenomegaly. Renal ultrasonography showed no hydronephrosis, and an abdominal ultrasonogram demonstrated a minimally enlarged gallbladder without stones.

Cultures of blood remained sterile. Hepatitis B surface antigen was negative. Agglutinins were negative on cerebrospinal fluid. Three separate smears of sputum for AFB were negative. The Western blot test for the human immunodeficiency virus was negative.

On transfer to our service, the patient was begun on therapy with penicillin and doxycycline for suspected leptospirosis. He became anuric and progressively dyspneic and, two days following transfer, required intubation with mechanical ventilation for hypercapnic and hypoxic respiratory failure.

Despite aggressive resuscitative measures, the patient's hepatic function continued to deteriorate, and he died on the fifth day of hospitalization following his transfer in fulminant DIC secondary to hepatic failure.

Postmortem examination revealed an enlarged (2,400-g) liver. The parenchyma was yellow-brown, and the surface was scattered with numerous areas of hemorrhagic necrosis. Hepatic necrosis was demonstrated microscopically, involving the majority of the parenchyma. Well-formed granulomas were rare, but numerous histiocytic cells were present at the periphery of the necrotic areas, and focal giant cell formation was noted (Fig 1). Special stains, including D-PAS, GMS, and Brown and Brown for fungi and bacteria, were negative. Stains for AFB (Auramin-Rhodamin and Kinyoun's) were strongly positive, with the greatest concentration of AFB noted in the central portions of the necrotic areas.

The kidneys weighed 220 g and 260 g. Microscopic sections demonstrated no parenchymal necrosis or granuloma formation (Fig 2). Stains demonstrated numerous AFB within the renal parenchyma.

The lungs were congested. On cut surface, numerous firm white nodules (less than 0.75 cm in diameter) were present. Microscopically, the nodules were well-formed histiocytic granulomas of varying size with central caseous necrosis. Stains were strongly positive.

FIGURE 1. Liver, showing dead hepatocytes, nuclear fragments, and necrotic debris (hematoxylin-eosin, original magnification ×200).

FIGURE 2. Kidney, showing no parenchymal destruction or granuloma formation. Arrows indicate AFB (hematoxylin-eosin, original magnification ×200).

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positive for AFB and negative for fungi and bacteria. Cultures grew Mycobacterium tuberculosis. Leptospiral cultures were negative.

Stains of splenic and adrenal tissue were positive for AFB. Numerous AFB were present within the bone marrow, but granulomas were absent. No AFB were demonstrated in the central nervous system.

**DISCUSSION**

The present case of miliary tuberculosis would be extremely unusual if the presentation was with hepatic failure alone, but the associated renal failure makes it, to the best of our knowledge, unique. There are select case reports of miliary tuberculosis presenting as hepatic failure, but renal failure was not a comorbid condition. Although renal failure may have been due to tuberculous involvement of the kidney, Simon et al suggest that extensive renal cavitation must be present to implicate tuberculosis as the primary etiology. The renal failure was most likely secondary to the fulminant hepatic failure and a part of the hepatorenal syndrome.

While hepatic failure is an extremely rare presentation for miliary tuberculosis, mild elevation of hepatic enzymes is a frequent finding. One out of three patients with miliary tuberculosis will have an elevated concentration of alkaline phosphatase. Munt reported that 14 of 15 patients with miliary tuberculosis had mild increases in the level of AST, but none demonstrated a bilirubin level greater than 2.0 mg/dl. Sulfobromophthalein (Bromsulfalein) retention of greater than 5.0 percent has been reported as one of the most frequent hepatic abnormalities. Mild decreases in the serum albumin level (2 to 3 g/dl) and hypergammaglobulinemia (greater than 3.5 g/dl) have been noted.

The finding of granulomas in the liver of patients with miliary tuberculosis approaches 100 percent but is nonspecific, as granulomas may be found in sarcoidosis, brucellosis, histoplasmosis, infectious mononucleosis, Behçet's, Sjögren's, and Mikulicz's syndromes, systemic lupus erythematosus, and multiple myeloma. While a liver biopsy is a sensitive test for miliary tuberculosis, its lack of specificity must be compensated for by the remainder of clinical data associated with each case.

Miliary tuberculosis may affect not only mature blood cells but also the bone marrow. Granulomas are found in the bone marrow of about 50 percent of the patients with miliary tuberculosis. The reported yield of bone marrow aspirates and biopsies for positive smear or culture (or both) of tubercle bacilli in patients with miliary tuberculosis ranges from 16 to 90 percent.

Miliary tuberculosis less commonly affects the kidney than the liver and hematopoietic system. Simon et al reported the findings in 20 patients with miliary tuberculosis, and five had urine cultures positive for tubercle bacilli. Larger series of patients have demonstrated positive urine cultures in 14 to 24 percent of the patients. In one postmortem series, 62 percent of the patients with miliary tuberculosis had renal lesions consisting of early cortical granulomas. Hyponatremia is well recognized in miliary tuberculosis as with isolated pulmonary involvement, but other serum markers for renal abnormalities have not been documented. Munt described 15 of 51 patients with a serum sodium level of less than 130 mg/dl. In the series of

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*ALT, alanine transaminase

Gelb et al of 109 patients with miliary tuberculosis, 80 percent had a normal BUN level, and 90 percent demonstrated a normal serum glucose level.

The term, hepatorenal syndrome, has been in use for about 50 years and originally denoted unexplained renal failure following biliary tract surgery. Cirrhosis is the most common etiology, but acute hepatitis and fulminant hepatic failure can also trigger the syndrome. To our knowledge, the present case is the first description of miliary tuberculosis as causative of hepatic failure with associated renal failure.

A compilation from the literature of hepatic and renal abnormalities associated with miliary tuberculosis is presented in Table 1.

The present case is a reminder of the myriad of ways that tuberculosis can present. Even in endemic areas, the diagnosis can be evasive. Miliary tuberculosis should be considered as a potentially treatable cause of acute hepatic failure.

**REFERENCES**

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Paradoxic Air Embolism in the Absence of an Intracardiac Defect*  
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A 58-year-old man experienced paradoxic air embolism with passage of air from the systemic venous to the systemic arterial circulation with subsequent stroke and death. No intracardiac shunt was present. Pulmonary fibrosis concomitant with severe pulmonary arterial hypertension appears to have been responsible for the air traversing the pulmonary capillary bed. This unusual outcome of a complicated central venous catheterization must be borne in mind and guarded against in similar patients.  

(Chest 1991; 99:754-55)

The systemic and pulmonary venous and arterial systems are being accessed increasingly for a myriad of invasive diagnostic and therapeutic procedures. As a result, unusual forms of iatrogenic morbidity and mortality present themselves. Such a case in which a "routine" central venous catheterization was complicated by air embolism, subsequent paradoxic embolism with resultant stroke, and death is described herein. The paradoxic embolism occurred in the absence of an intracardiac shunt, and the possible mechanisms of this are discussed.

Case Report

A 58-year-old man was admitted to the hospital with idiopathic pulmonary fibrosis. History included dermatomyositis and hepatitis in the distant past. The patient was initially treated with prednisone and azathioprine (Imuran) with a substantial improvement, but during the last six to seven months, he had worsening shortness of breath. The patient was found to have tricuspid regurgitation, rightsided heart strain, and pulmonary hypertension. He was scheduled for a three-day serial drug testing program. Invasive monitoring was accomplished using an intra-arterial catheter as well as a pulmonary arterial thermodilution catheter (Swan-Ganz). Pulmonary artery pressure was 85/40 mm Hg (with mean of 60 mm Hg), pulmonary capillary wedge pressure was 3 mm Hg, and cardiac output 5.8/l/min. Pulmonary vascular resistance was 872 dynes/sec cm

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before treatment with diltiazem and 493 dynes/sec cm after.

The Swan-Ganz catheter was removed at the end of the study. The obturator was not returned to the sheath which was still in place. The patient was sitting and a large "sucking" sound was heard, and within ten minutes the patient developed left hemiparesis. An emergency echocardiogram revealed air within all cardiac chambers, especially the right ventricle. A right-to-left shunt with paradoxic embolism to the cerebral arterial circulation was suspected. However, this intracardiac defect could not be documented echocardiographically. The patient was too unstable for transfer to a facility with a hyperbaric chamber. The patient manifested a large right middle cerebral arterial distribution stroke and suffered severe hypoxic encephalopathy. Complications thereafter included sepsis and disseminated intravascular coagulopathy. The patient died of a cardiac arrest four days after the catheterization.

At autopsy a large recent right cerebral hemorrhagic infarct was found, with subentorubial herniation and changes of severe anoxic-ischemic encephalopathy. The cerebral vasculature was unremarkable, and the findings from the neuropathologic examination were compatible with air embolism. The lungs had extensive parenchymal fibrosis especially of the lower lobes and basal segments of the upper lobes, consistent with the effect of dermatomyositis. There were changes of marked pulmonary arterial hypertension with medial hypertrophy and intimal hyperplasia of smaller pulmonary arteries, marked dilatation of large pulmonary arteries, marked right-sided heart dilatation and hypertrophy, and changes of marked chronic passive venous congestion of vicesa. The terminal event was a severe aspiration bronchopneumonia probably precipitating a cardiorespiratory arrest. Careful examination of the great vessels of the heart and lungs, of the pulmonary parenchyma, and of the heart revealed no pulmonary arterial-systemic arterial defect. The puncture site in the jugular vein, through which catheterization took place, was identified and was locally uncomplicated.

Discussion

Air embolism is most often venous, but may be arterial and encountered in the settings of head and neck trauma and surgery, obstetric and gynecologic procedures, pneumothorax, decompression sickness, positive pressure ventilation, and a number of cardiothoracic procedures such as needle biopsy and open cardiac surgery. Venous air embolism is also a hazard of the use of central venous catheter systems. The upright position and cyclical negative

FIGURE 1. Representative illustration of the emergency echocardiogram done, showing echogenic "speckles" of air in each of the cardiac chambers (r = right atrium; r = right ventricle; l = left atrium, and l = left ventricle).