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Case Report

Hepatosplenic Tuberculosis Mimicking Disseminated Candidiasis in Patients With Acute Leukemia

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Abstract

Two cases of hepatosplenic tuberculosis in patients with acute leukemia during or after chemotherapy following prolonged neutropenia are presented. Tuberculosis should be considered as one cause of hepatosplenic abscesses during prolonged neutropenia, especially in countries where the disease is endemic. *Int J Hematol.* 2001;73:119-121.

Key words: Leukemia; Hepatic tuberculosis; Splenic tuberculosis

1. Introduction

Multiple hepatosplenic microabscesses following neutropenic periods are a major problem in patients with acute leukemia and are often attributed to fungal infections such as hepatosplenic candidiasis (HSC) or disseminated candidiasis [1]. Here we describe 2 cases of hepatosplenic tuberculosis mimicking HSC confirmed by laparoscopy-guided biopsy and culture.

2. Case Reports

2.1. Case 1

A 44-year-old woman with a 2-month history of acute leukemia (mixed lineage type) was transferred to our institution because of persistent high fever. She had received induction chemotherapy with idarubicin and cytosine arabinoside. The postinduction phase was complicated by prolonged neutropenia (>50 days) and unexplained fever. Empirical treatment consisted of ceftazidime and amikacin. Because of persistent fever after 3 days of treatment, antimicrobials were empirically changed to imipenem, vancomycin, and, amphotericin B. After administration of these antimicrobials, microbial cultures of blood and urine showed no growth.

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After transfer to our institution, the patient complained of right upper quadrant pain and fever in spite of antimicrobial therapy over 20 days. On physical examination, her abdomen was soft without enlarged liver or spleen. She denied any history of pulmonary tuberculosis. Laboratory studies disclosed the following values: total leukocyte count, 1.8×10^9/L (89% polymorphonuclear leukocytes); C-reactive protein, 51 mg/L; total bilirubin, 0.75 mg/dL (direct bilirubin, 0.28 mg/dL); serum aspartate aminotransferase, 23 IU/L (normal range, 0 to 38 IU/L); serum alanine aminotransferase, 30 IU/L (normal range, 0 to 49 IU/L); and alkaline phosphatase, 455 IU/L (normal range, 96 to 254 IU/L). Serum protein levels and renal function were within normal limits. Chest x-ray did not reveal any abnormal findings. Absolute neutrophil count (ANC) was recovered to 1.8×10^9/L on day 2, 2.5×10^9/L on day 3, and 4.7×10^9/L on day 4. Repeated blood cultures were all negative. Fever continued intermittently in spite of therapy with antimicrobials, and amphotericin B was continued up to a total cumulative dose of 2280 mg.

On day 6, computed tomography (CT) of the abdomen revealed multiple tiny poorly enhancing hypodense foci scattered throughout the liver and spleen. The patient underwent laparoscopy-guided liver biopsy on day 12. Ziehl-Neelson staining showed numerous acid-fast bacilli (Figure 1A), later identified as *Mycobacterium tuberculosis* by culture. Histologic examination revealed granuloma and focal abscess surrounded by a granulomatous response without definite evidence of caseating necrosis (Figure 1B). No fungi were identified, and there was no evidence of leukemic infiltration.

On day 15, antituberculosis therapy with isoniazid, rifampicin, ethambutol, and pyrazinamide was started. The patient died 3 months later, however, because of relapsed

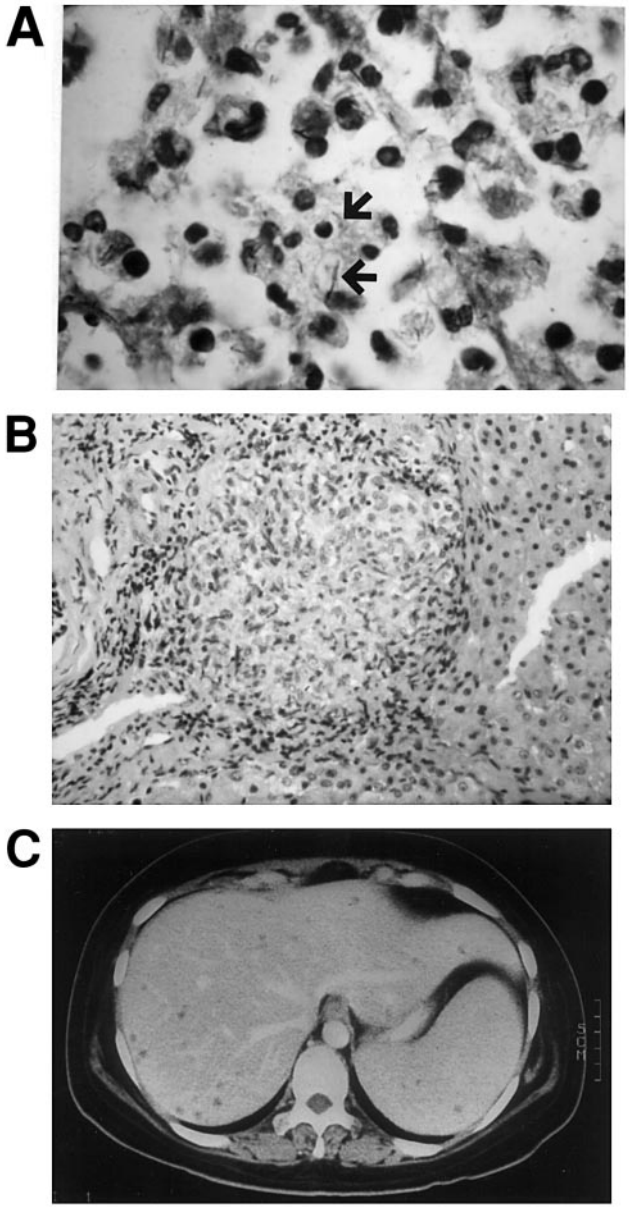

Figure 1. A, Numerous acid-fast bacilli (arrows) (Ziehl-Neelson stain, original magnification ×1000). B, Granuloma and focal abscess surrounded by a granulomatous response without definite evidence of caseating necrosis (hematoxylin-eosin stain, original magnification ×400). C, Abdomen computed tomography scan that shows multiple tiny nodular lesions on liver and spleen with peripheral rim enhancement.

leukemia. The isolated organism had been susceptible to all administered medication.

2.2. Case 2

A 35-year-old woman with a 5-month history of acute myelogenous leukemia (M5) was transferred to our institution because of leukemic cells found in her cerebral spinal fluid. After consolidation chemotherapy with idarubicin and cytosine arabinoside, profound neutropenia (ANC, <500/mm^3) developed. During the intrathecal chemotherapy with methotrexate, the patient was treated with antibiotics for *Staphylococcus epidermidis* Hickman catheter–related bacteremia. She also received empiric amphotericin B therapy because of persistent fever and neutropenia.

On hospital day 25, despite the return of leukocyte count to the normal range, a fever up to 40°C persisted. Her only symptoms were recurrent nausea and vomiting. Other than a leukocyte count of 12.8 × 10^9/L and alkaline phosphatase of 880 IU/L, laboratory values were unremarkable. A CT scan of her abdomen showed multiple tiny nodular lesions on liver and spleen with peripheral rim enhancement (Figure 1C). A laparoscopy-guided liver biopsy was done a week later, which showed multiple white nodules. The biopsy showed chronic granulomas with aggregates of histiocytes and central necrosis without evidence of fungal yeast, pseudohyphae, or leukemic cells. Cultures of a biopsy specimen for bacteria and fungi were also negative.

Although smears and cultures for tuberculosis were negative, antituberculosis therapy was started, which resulted in resolution of the fever after 2 weeks. During the period of fever, systemic chemotherapy was withheld. Because leukemic cells reappeared in microscopic examination of cerebrospinal fluid, another course of reinduction chemotherapy was performed. However, the patient died 2 months later because of Omaya shunt infection.

3. Discussion

Current intensive chemotherapy for acute leukemia is often associated with profound and protracted neutropenia and the risk of serious infections. Of uncommon opportunistic infections that involve the liver or spleen, candida infections, HSC were most frequent [1,2]. The combination of persistent fever not responsive to broad-spectrum antibiotics, abdominal symptoms, and an elevated serum alkaline phosphatase level in a patient who has recently recovered from an episode of neutropenia is highly suggestive of HSC [1].

Other rare opportunistic infections, such as those from Aspergillus, mycobacteria, or coagulase-negative staphylococci, should be taken into account in the differential diagnosis [2-5]. Our cases illustrate very rare cases of hepatosplenic tuberculosis presented during the recovery phase of neutropenia, similar to cases of HSC.

Ultrasonography, CT, or magnetic resonance imagery commonly demonstrates the focal lesions. However, the definite confirmation of hepatic lesions from microbiological source usually requires an invasive procedure, such as ultrasound-guided fine-needle aspiration or laparoscopy-guided liver biopsy, especially when targeted at white nodules [1,5,6]. In these cases, we safely performed laparoscopy-guided liver biopsy within a period of 7 to 10 days after recovery from neutropenia.

Korea is a country where tuberculosis is still endemic. Because tuberculosis should be considered in the differential diagnosis of fever of unknown origin in immunocompetent hosts, it should also be considered a cause of hepatosplenic abscesses during prolonged neutropenia, especially in countries in which the disease is endemic.

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