

Case Reports

Pancytopenia in Disseminated Tuberculosis

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Patients with disseminated tuberculosis have varied presentations, including pyrexia of unknown origin, hepatosplenomegaly, lymphadenopathy and meningitis. Hematologic aberrations like anemia, monocytosis, leukopenia, and leucocytosis are also commonly associated(1-3). However, major

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hematologic changes like pancytopenia are rare. In view of its extreme rarity, we report a patient of disseminated tuberculosis presenting with prolonged pyrexia and pancytopenia which reversed with antitubercular therapy.

Case Report

A 5-year-old boy was admitted with high grade continuous fever of 4 weeks duration with non-productive cough and diffuse abdominal pain. A day prior to admission, he had malena and vomiting. There was no history of bleeding from any other site, diarrhea, rash, dysuria and exposure to toxins or chemicals. There was no history of tuberculosis in the family and the patient was not immunized.

On examination he was malnourished, febrile, pale and had tachycardia. There were six lymph nodes measuring 1-2 cm, non-tender and non-matted, palpable in the inguinal region. There were no petechiae or ecchymosis.. The liver and spleen were palpable 3 cm and 2 cm, respectively below the costal margin. Rest of the systemic examination was normal.

Investigations revealed hemoglobin of

5.9 g/dl, total leukocyte count of 1800/cu mm, differential count of 60% polymorphs and 38% lymphocytes, platelet count of 40,000/cu mm and reticulocyte count of 1%. The peripheral blood smear examination showed no abnormal cells, hemoparasites, or evidence of hemolysis. The bleeding time was 10 minutes. The clotting time, prothrombin time and partial thromboplastin time were normal and fibrin degradation products were absent. The urine and stool examination did not show any abnormality. Urine and blood cultures did not grow any organisms. The direct and indirect Coomb's tests were negative. Blood Widal and VDRL were non-reactive. ELISA for *Brucella* was negative and for A60 antigen of *Mycobacterium tuberculosis* revealed IgM titres of 260 U/ml and IgG of 670 U/ml (normal IgM <100 U/ml and IgG <120 U/ml). X-ray chest showed right paratracheal lymphadenopathy and the Mantoux test revealed an induration of 20 mm after 48 h. Gastric lavage did not grow any acid fast bacilli. Ultrasound examination of abdomen did not reveal any abnormality except enlarged liver and spleen. Bone marrow aspiration yielded hypocellular marrow and numerous non-caseating granulomas (Fig. 1). The bone marrow staining and culture for acid fast bacilli, fungi and bacteria was negative.

A diagnosis of disseminated tuberculosis was made and the child treated with isoniazid, rifampicin and pyrazinamide for two- months followed by isoniazid and rifampicin for another ten months. He was given blood transfusion twice. Peripheral blood examinations revealed pancytopenia for next seven weeks. After seven weeks of therapy, hemoglobin, total leukocyte count and platelet count increased to 9.5 g/dl, 9600/cu mm and 200,000/cu mm, respectively and reticulocyte count to 6.6%. The

bone marrow biopsy revealed a normocellular marrow with no blast cells or granulomas. The hepatosplenomegaly resolved by 7th month of therapy. The child is doing well after one year of treatment.

Discussion

The hematologic alterations described in patients with miliary or disseminated tuberculosis include anemia, granulocytosis, leucopenia, leucocytosis, thrombocytosis and monocytosis(1-4). Pancytopenia as the presenting feature of disseminated tuberculosis is extremely rare both in children(5,6) and adults(1).

The occurrence of pancytopenia in disseminated tuberculosis is attributed to hypersplenism(7), histiocytic hyperplasia and indiscriminate phagocytosis of blood cells by histiocytes in bone marrow(8), maturational arrest(5,6), or infiltration of the bone marrow by caseating or non-caseating tubercular granulomas(3,4, 9-12). Tubercular granulomas may cause pancytopenia by replacement of marrow cells or suppression through release of interferon and lymphotoxin(12,13). However, despite presence of tuberculous granulomas in a high proportion of patients

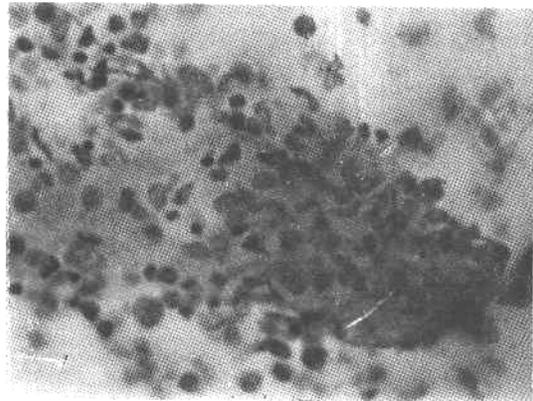


Fig. 1 Microphotograph showing granulomas in bone marrow ($\times 400$).

with disseminated tuberculosis, pancytopenia is uncommon (1,3). In our case the diagnosis of disseminated tuberculosis was established on clinical features, positive Mantoux test, hilar adenopathy, positive ELISA and numerous non-caseating granulomas in the bone marrow. The granulomas disappeared and the peripheral blood picture became normal following anti-tubercular therapy, supporting the diagnosis of tuberculosis induced reversible pancytopenia. The other causes of pancytopenia including leukemia, exposure to drugs, chemicals, radiation, aplastic anemia, immune cytopenias and granulomas secondary to leprosy, syphilis, sarcoidosis and brucellosis were excluded on clinical and laboratory evaluation. This case suggests that disseminated tuberculosis may be considered as a cause of reversible pancytopenia.

Patients of miliary tuberculosis with pancytopenia and granulomas in the bone marrow have a variable outcome. Most of the patients with caseating granulomas in the bone marrow died (10-12), whereas those with non-caseating granulomas, as in our case, survived (9,12). The precise reason for the variable outcome is not clear but may be attributed to the virulence of the bacteria, immunity of the host and delay in initiation of appropriate treatment.

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