A child with fever, cough, and dyspnea

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A 5-month-old boy presented with fever, cough, and tachypnea that he had had for 1 month. There also was a history of poor weight gain for 2 months. The child was born full-term at a private hospital, and the mother's antenatal course was uneventful. There was no postnatal history of bleeding, jaundice, diarrhea, poor feeding, vomiting, or seizures. There was no family history of tuberculosis.

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The physical examination findings included tachypnea, tachycardia, pallor, and fever. Arterial oxygen saturation was 92% on room air and improved to 98% after starting supplemental oxygen therapy. There were multiple variable-sized ulcers with a necrotic base over the trunk and right forearm. Chest examination revealed extensive bilateral crepitations, but air entry was normal. On abdominal examination, the liver was palpable 6 cm below the costal margin, and the spleen could be palpated 2 cm below the costal margin. The results of the remainder of the systemic examination and ophthalmological examination were normal.

Tests showed a hemoglobin level of 8 g/dL; a total leukocyte count of 12,000/μL, with 80% lymphocytes; a platelet count of 1,000,000/μL; and an elevated erythrocyte sedimentation rate (40 mm/h). Serum biochemistry profile findings showed elevated oxaloacetate and aspartate transaminase levels (200 U/L [normal, less than 50 U/L] and 250 U/L [normal, less than 50 U/L], respectively). The TORCH profile (toxoplasmosis, rubella, cytomegalovirus infection, and herpesvirus infection) findings were negative except for an elevated IgG antibody level against cytomegalovirus. The patient's chest radiograph is shown in the Figure.

What is the likely diagnosis?

Answer on next page.

ANSWER:

The patient's chest radiograph showed bilateral, diffuse, tiny, round shadows ranging from 1 to 2 mm in size. Three consecutive early-morning gastric aspirate samples were negative for Mycobacterium tuberculosis, and the tuberculin test result was nonreactive. A biopsy specimen from the edge of a skin lesion showed epithelioid cell granulomas with Langerhans giant cells and central caseation necrosis. A diagnosis of miliary tuberculosis was made. A 4-drug antituberculosis regimen was started (isoniazid, 5 mg/kg; rifampicin, 10 mg/kg; pyrazinamide, 30 mg/kg; and ethambutol 15 mg/kg). There was significant improvement in both skin and pulmonary lesions, and the patient was discharged after 3 weeks of hospitalization.

Discussion

Miliary tuberculosis arises as a result of widespread lymphohematogenous dissemination of tubercle bacilli. The lesions are small (1 to 2 mm) foci of yellow-white consolidation scattered throughout the lung parenchyma and organs such as the liver, bone marrow, adrenal glands, and spleen, and the meninges. Miliary disease is usually a complication of primary pulmonary tuberculosis and occurs within 6 months of initial infection. The onset is usually insidious, and common presenting symptoms and signs include fever, night sweats, weight loss, and anorexia. Specific symptoms depend on the organ systems involved, but almost half of the patients with miliary tuberculosis have hepatosplenomegaly and lymphadenopathy. Pulmonary involvement may manifest initially as dyspnea, wheezing, and cough, but as the disease...
A child with fever, cough, and dyspnea progresses, an alveolar-air block syndrome may develop and patients may have frank respiratory distress, hypoxemia, and pneumothorax.\textsuperscript{3,5} Meningitis and peritonitis are found in 20\% to 40\% of patients with miliary tuberculosis.\textsuperscript{3} Choroidal tubercles are rare but are highly specific for miliary tuberculosis.\textsuperscript{3} Fulminant disease presenting as septic shock, acute respiratory distress syndrome, and multiorgan failure rarely occurs.\textsuperscript{6,7} The patient’s immune competence plays a key role in the pathogenesis of miliary tuberculosis, and this form of tuberculosis is more common in infants\textsuperscript{8,9} and in malnourished and immunosuppressed persons.\textsuperscript{3,10}

Microscopic demonstration of mycobacteria and histopathological and radiographic findings are the mainstay of diagnosis of miliary tuberculosis. Chest radiographs typically reveal multiple bilateral diffuse opacities between 1 and 3 mm. Approximately two thirds of patients with a miliary pattern on a chest radiograph have additional abnormalities, such as pleural effusion, lymphadenopathy, consolidation, cavitation, or calcified granulomas. Chest radiographs have high specificity and good interobserver agreement but allow identification of miliary tuberculosis in only 59\% to 69\% of cases.\textsuperscript{11}

High-resolution CT (HRCT) also can be used to diagnose miliary tuberculosis. Miliary nodules and ground-glass opacities are the predominant HRCT findings, and the extent of ground-glass opacities on HRCT scans correlates with the severity of disease.\textsuperscript{12}

Gastric aspirates can be useful for diagnosis of tuberculosis in children because of the difficulty in obtaining sputum specimens in the pediatric population. Ideally, 3 early-morning gastric aspirate samples should be cultured for acid-fast bacilli in every child in whom tuberculosis is suspected. The results are positive in 20\% to 40\% of children with tuberculosis.\textsuperscript{13,14} There is evidence that the yield is higher in infants.\textsuperscript{15} However, polymerase chain reaction assay of gastric aspirates has low sensitivity and is not currently recommended.\textsuperscript{16} Tuberculin test results can be negative in approximately half of patients with miliary tuberculosis.\textsuperscript{17,18} Biopsies of liver, bone marrow, and skin specimens and microbiological and histological findings can yield early diagnosis.\textsuperscript{3}

Resolution of miliary tuberculosis is slow after starting therapy, and fever takes about 2 to 3 weeks to respond. The current recommendation is to treat for 12 months,\textsuperscript{19} with daily administration of isoniazid, rifampin, pyrazinamide, and streptomycin for 1 to 2 months, followed by isoniazid and rifampin daily or twice weekly for another 10 months.\textsuperscript{20}

An efficient tuberculosis control program with early detection of infectious adults and their cure is the best long-term approach to the reduction of tuberculosis in children. The directly observed therapy strategy advocated by the World Health Organization has the potential to have a significant impact on the epidemiology of tuberculosis by achieving high cure rates and thereby decreasing community transmission.\textsuperscript{21}

Protective efficacy of the BCG vaccine varies from 0\% to 80\% across various trials.\textsuperscript{22} One trial in south India found the protective efficacy to be as low as 31\%.\textsuperscript{23} However, evidence shows that the BCG vaccine protects against severe forms of pediatric tuberculosis, such as disseminated disease and meningitis.\textsuperscript{9,24}

References: REFERENCES


Links:
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