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TEACHING FILES (GRAND ROUNDS)

MILIARY SHADOWS IN PULMONARY TUBERCULOSIS: HOW SOON CAN THEY DEVELOP?

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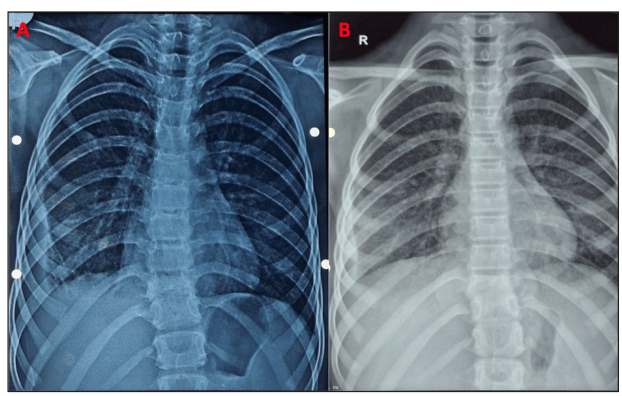
KEYWORDS
Chest X-ray, Chest CT, Disseminated tuberculosis, Pediatric tuberculosis, Radiological diagnosis of tuberculosis, TB diagnosis.

Clinical Problem:

An 11-year-old girl presented in November 2024 with fever and dry cough for 2 days. There was no loss of weight or appetite. She was treated for microbiologically-diagnosed multidrug-resistant (MDR) miliary, abdominal and central nervous system tuberculosis (TB) 3 years ago for which she received 18 months of second-line antitubercular therapy (ATT). On presentation, her weight was 27.3 kg (between 10th-25th percentile according to the Indian Academy of Pediatrics growth charts). General and systemic examinations were normal. Peripheral smear for malaria and Widal test were negative. Other investigations are shown in Table 1. She was started empirically on oral amoxicillin-clavulanate, however, there was no symptomatic improvement after 5 days of therapy. Chest X-ray performed in November 2024 showed right lower zone opacities and obliteration of the right costophrenic angle suggestive of a syn-pneumonic effusion (Figure 1A) and mycoplasma IgM was positive with a titre of 12 units/mL (normal: <10 units/mL). She was shifted onto oral clarithromycin for 14 days during which her cough improved, however, fever spikes were persistent. On day 14 of clarithromycin, chest ultrasound showed a loculated mild right-sided pleural effusion with septations measuring about 5 mL and a thickened pleura measuring 2 mm. She was started on oral levofloxacin, following which the fever spikes reduced. However, even after 14 days of levofloxacin, the fever did not subside completely and she developed a new-onset backache. Chest X-ray performed in December 2024 showed bilateral miliary pulmonary opacities (Figure 1B). Contrast-enhanced computerized tomography (CT) chest showed miliary pulmonary nodules, mediastinal lymphadenopathy and T10-T11 vertebral end-plate destruction with periosseous collections. Gastric lavage Xpert MTB/Rif detected rifampicin-resistant Mycobacterium tuberculosis (MTB) and Xpert MTB/XDR showed resistance to isoniazid and fluoroquinolones. She was diagnosed with pre-extensively drug-resistant TB (preXDR-TB) and was started on second-line ATT.

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Figure 1. (A) Chest X-ray PA view done in November 2024 showing opacities in the right lower zone and obliteration of the right costophrenic angle. (B) Chest X-ray PA view done in December 2024 showing bilateral miliary pulmonary shadows.



How soon can miliary shadows develop in pulmonary TB?

Discussion:

Miliary TB is characterised by lympho-hematogenous dissemination of MTB which results in the formation of tiny, discrete "millet seed-like" tubercules of granulomatous tissue in various organs of the body.[1,2] The diagnosis criteria of miliary TB relies on clinical findings consistent with TB such as fever, night sweats, loss of weight and appetite and evening rise of temperature; along with microbiological/histopathological diagnosis of TB; and most importantly, the appearance of characteristic radiological findings on chest imaging.[2] Chest X-ray is the initial radiological investigation used to detect and diagnose miliary TB. The classical presentation of miliary TB is the appearance of miliary infiltrates on a radiograph.[2] These miliary opacities may be classified as typical (1-3 mm discrete nodules throughout the lung fields) or atypical (nodules larger than 3 mm or a reticulonodular miliary pattern).[3] However, this classic miliary pattern on chest X-ray is only seen in half the cases. In upto 30% cases, chest X-ray may show asymmetrical nodular lesions, coalescing nodules, mottled or snow-storm appearance and lobar consolidation resembling typical or atypical pneumonias. In a small category of patients (about 5%), chest X-ray may even show segmental consolidation and pleural involvement

Table 1. Investigations of the patient.

Parameters	At presentation	Day 14 of clarithromycin	Day 10 of levofloxacin	Start of ATT	Reference Ranges
Hemoglobin (gm/dL)	11.2	10.5	10.5	10.5	11.5-15.5
White blood cell count (cells/cumm)	5400	5480	5180	6290	5000-13,000
Absolute neutrophil count (cells/cumm)	2970	-	3212	3460	2000-8000
Absolute lymphocyte count (cells/cumm)	2200	-	1502	2246	1000-5000
Platelets (10^5 cells/cumm)	3.50	3.76	3.26	3.78	1.50-4.50
ESR (mm/hr)	10	58	45	-	0-10
CRP (mg/dL)	-	9.3	11.7	-	0.3-1

Note: ESR- Erythrocyte sedimentation rate, CRP- C-reactive protein.

(effusion, empyema, pneumothorax), as in our patient.[2] In addition to the variable radiographic appearance of miliary TB, due to the delayed appearance of miliary nodules or due to the presence of nodules below the threshold of perceptibility, initial chest X-ray may be normal.[1] The deposition of collagen and/or caseous material in the nodules is responsible for the appearance of miliary shadows on chest X-ray. This deposition is progressive and thus a typical miliary pattern may be delayed, evolving over the course of the disease.[2] Studies have found that the detection of miliary nodules radiologically may be delayed upto 2.5 weeks from the onset of fever.[3] CT chest is known to be more sensitive than X-rays for the identification of miliary opacities.[1] Choe et al.[4] found that initial CT chest missed the identification of miliary patterns in about 10% of the patients. In these 10% patients, classical miliary nodules appeared on the follow-up CT scan at a median duration of 29 days (range: 15-55 days). They found that ill-defined nodules and smaller-sized nodules less than 2 mm were independently and significantly associated with missed miliary TB.[4] Our patient had a past history of treated miliary TB and her initial X-ray did not show the classical miliary nodules. However, since she did not clinically respond to antibiotic therapy, suspecting a recurrence of miliary TB, we decided to repeat a chest X-ray for her. Her subsequent X-ray and chest CT showed characteristic miliary nodules. Thus, due to the delayed appearance of miliary opacities, if the disease is suspected, repeat chest imaging should be obtained.

Compliance with ethical standards

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Conflict of Interest: None

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