Pediatric Tuberculosis: pictorial review of radiologic findings

Poster No.: C-1667
Congress: ECR 2013
Type: Educational Exhibit
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Keywords: Thorax, Lung, Lymph nodes, CT, Plain radiographic studies, Computer Applications-Detection, diagnosis, Cavitation, Infection
DOI: 10.1594/ecr2013/C-1667

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Learning objectives

- To provide an overview of the possible spectrum of pediatric tuberculosis (PTB) findings in Chest X-Ray (CXR) and Computed Tomography (CT), in particular focusing on intrathoracic PTB.
- To correlate the radiological findings with a new classification of PTB.
- To emphasize the role of imaging in the evaluation of treatment response.

Background

Increased international travel and immigration have seen PTB rates increase even in traditionally low burden, industrialized settings, with roughly a million cases estimated globally each year. Children are particularly vulnerable to severe disease and death following infection, and those with latent infection become the reservoir of disease reactivation in adulthood, fueling the future epidemic [1]. For these reasons, today PTB is considered a public health emergency.

The changing landscape in which tuberculosis occurs, as well as the global resurgence, and the changed spectrum of the clinical and radiological presentation, justify a renewed interest of radiologists for the imaging features of pulmonary tuberculosis.

While intense scientific and clinical research efforts into novel diagnostic, therapeutic and preventative interventions have focused on tuberculosis in adults, PTB has been relatively neglected. This is the result of challenging diagnoses which physician have to cope with in children population, because of the rareness of clinical features (60% asymptomatic) and complexity of bacteriologic exams [Fig. 1 on page 3]. In particular, the greatest diagnostic challenge is represented by intrathoracic disease, the most common type of PTB.

In this setting, imaging findings associated with patient's history are very useful to reach a final diagnosis, to characterize the severity of disease, to identify complications and to evaluate treatment response.

PTB has conventionally been classified as pulmonary and extrapulmonary, without a clear correlation to the severity of disease. Thus, Wiseman CA et al [2] have recently proposed a new classification which may more accurately reflect the clinical disease spectrum and severity in children, relevant to clinical management and treatment strategies.
Fig. 1: Bacteriologic diagnosis of PTB: characteristics of the main laboratory exams.
Imaging findings OR Procedure details

The clinical spectrum of childhood TB reflects differences in the balance between the pathogen and the host immune response, with more severe disease resulting from either poor or 'over-exuberant' attempts to contain the disease. It remains largely unknown what determines the differences in the host/pathogen interactions that leads to successful containment as opposed to progressive disease, however age and immunodeficiency represent important factors, strictly correlated each other.

Two different types of PTB have been described in the extremes of childhood according to differences in host immunity: **infant disease** and **adult-type disease**. The former (typical of infants, 0-3 months) is due to poor cell mediated immunity which leads to unrestrained proliferation of bacilli with progressive parenchymal lung damage (with or without cavity formation) and dissemination [Fig. 2 on page 12]. The latter, adult-type disease, occurs in children major than 10 years old, representing the dominant disease manifestation following recent primary infection. This is due to an exuberant immune response in immunocompetent adolescents which tends to result in cavitating disease [Fig. 3 on page 13, Fig. 4 on page 14]. The initial presentation of adult-type disease may be with cloudy opacification in apical lung zones, before coalescence and parenchymal breakdown. Most commonly the apical and posterior segments of the upper lobes and the apical segment of the lower lobes are affected. Complications may result from progressive cavity formation and intra-bronchial spread with bronchopneumonic consolidation.

Apart from these particular types of PTB, radiologic manifestations of other forms of disease affecting children with normal immune function can be categorized into the two distinct forms of **primary** and **post-primary disease**, in individuals without and with prior exposure and acquired specific immunity, respectively.

The most common form in childhood is primary, whose hallmark is represented by **lymphadenopathies** [Fig. 5 on page 15].
Lymphadeopathies may be accompanied by parenchymal involvement, with age-related differences in pattern of presentation: children from 0 to 3 years old usually have higher prevalence of lymphadenopathy and lower prevalence of parenchymal involvement, whereas children 4-15 years old present lower prevalence of lymphadenopathy and higher prevalence of parenchymal involvement [5]. Parenchymal involvement in primary pulmonary TB most commonly appears as an area of homogeneous consolidation, though patchy, linear, nodular and masslike forms have also been described. Consolidation typically occurs in a segmental or lobar distribution.

_Less common findings_ of PTB are represented by multifocal parenchymal involvement, pleural effusion, obstructive atelectasis and obstructive overinflation (resulting both from compression by adjacent enlarged nodes). Right side is more commonly affected than left side (reflecting presumably the greater statistical probability of an airborne infection involving the right lung), without relevant differences between upper and lower pulmonary zones.
Although **CXR** is the first exam performed in children with respiratory symptoms and/or suspicion of PTB, **CT** is the imaging of choice to diagnose the presence, location and characteristics of mediastinal adenopathy, to detect PBT in patients with normal CXR (higher incidence of lymphadenopathies on CT scans - 85% - compared to CXR - 70%) [6], to identify miliary forms and eventual complications. Finally, CT allows the classification of TB disease severity.

**CLASSIFICATION OF PTB SEVERITY**

One of the obstacles in childhood TB is the lack of standard descriptive terminology to classify the diverse spectrum of disease. Definite disease classification is important to allow an accurate evaluation of patient prognosis [7].

Conventionally PTB has been classified into **pulmonary** and **extrapulmonary** forms (which include miliary disease and TB meningitis), without correlation with clinical disease severity.

Although no approach to comprehensively classify the observed clinical disease spectrum and severity in children has been developed yet, Wiseman CA et al [2] have recently proposed a new classification that more accurately reflect the clinical severity of TB in children. Clinical severity is important to determine, as it strictly correlates to bacterial load (thus infectivity), patient's prognosis and treatment response.

Based on the site primarily involved, on the extent of disease and on the presence of complications, the different disease entities may be classified at first as **intrathoracic** or **extrathoracic** and then as either severe or non severe.
**Fig. 7**: Classification of PTB.

*References*: Radiology, Catholic University of Sacred Heart, Agostino Gemelli Hospital - Rome/IT

**Severe** disease implies either poor host control of *Mycobacterium tuberculosis* (uncontrolled disease) or some forms of complicated disease manifestation, often with severe sequelae.

**Non Severe** disease implies that the host has managed to control the pathogen so that the disease pattern is limited (controlled), non-disseminated and uncomplicated.

**INTRATHORACIC PTB**
Fig. 8: Classification of intrathoracic PTB.

**References:** Radiology, Catholic University of Sacred Heart, Agostino Gemelli Hospital - Rome/IT

**Non severe forms**

- **Ghon focus or non-expansile single lobar opacification**, which may be accompanied by uncomplicated intrathoracic lymph nodes (Ranke complex) [Fig. 9 on page 16]

- **Pleural effusion** without severe underlying lung disease [Fig. 10 on page 17]

Pleural effusion may be due to a hypersensitivity phenomenon after rupture of uni- or bilateral subpleural foci, or from hematogenous spread. It is classified as non severe if there is no evidence of severe underlying lung disease. Large effusions in young children are uncommon, usually occurring in adolescence. Pleural effusions complicate 2-38% of cases of pulmonary TB in children, usually unilaterally [8].
Severe forms

- **Expansile alveolar opacification, tuberculous bronchopneumonia** [Fig. 11 on page 18]

- **Multilobar alveolar opacification** [Fig. 12 on page 19]

- **Cavitary disease** [Fig. 13 on page 20, Fig. 14 on page 21]

Cavitation in single or multiple sites is evident radiographically in 40%-45% of cases of postprimary TB. Walls of cavities may range from thin and smooth to thick and nodular; air-fluid levels have been reported to occur in 9%-21% of tuberculous cavities [5].

- **Complicated intrathoracic lymph nodes, including "lymphobronchial TB"** [Fig. 15 on page 22]

The wide spectrum of endobronchial or "lymphobronchial" TB includes different entities: extrinsic bronchial compression, actively caseating lesion in the tracheobronchial tree, granuloma formation, polypoid mass lesions and lymph node protrusion through mucosal erosion with ulceration. Although these lesions are observed during bronchoscopy, large airway compression can often be suspected based on CXR findings. CT scans may show irregular or smooth circumferential bronchial narrowing associated with mural thickening [Fig. 4 on page 14-d], airway compression by lymphadenopathies, polypoid masses on the wall of the tracheobronchial tree and also lymph nodes into the bronchial lumen.

- **Pleural effusion with severe underlying lung disease** [Fig. 16 on page 23]

Occasionally, an air-fluid level may be also demonstrable within the pleural cavity, indicating the presence of a broncho-pleural fistula.

- **Empyema** [Fig. 17 on page 24]

Contrast-enhanced CT evaluation of post-primary tuberculous effusions typically reveals smooth thickening of visceral and parietal pleural surfaces separated by a variable amount of fluid: the "split pleura" sign [5].

Tuberculous effusions are typically loculated and may be stable in size for years; detection of persistent fluid within a calcified fibrothorax at CT should raise concern for active disease and chronic tuberculous empyema.

- **Tuberculous pericarditis** [Fig. 18 on page 25]

Usually develops when a subcarinal lymph node erupts into the pericardial space. However, it is also the result of hematogenous bacillary spread. If unrecognized, it may have severe sequelae, including death, due to its mechanical effects.
• **Miliary pulmonary form** [Fig. 19 on page 26]

Innumerable, 1-3-mm non-calcified nodules scattered throughout both lungs, with mild basilar predominance, often associated with intra and interlobular septal thickening.

Typical miliary lesions may not be visible until 3-6 weeks after hematogenous dissemination.

**EXTRATHORACIC PTB**

![Classification of extrathoracic PTB in children](image)

**Fig. 20:** Classification of extrathoracic PTB in children.

**References:** Radiology, Catholic University of Sacred Heart, Agostino Gemelli Hospital - Rome/IT

**Non severe forms**
• Peripheral lymphadenitis, without infiltration/compression of adjacent structures [Fig. 21 on page 27]

No evidence of contiguous spread and infiltration or compression of adjacent neural, vascular, lymphatic duct, or osteal tissues. Isolated sinus or fistula formation from a diseased node, although reflecting uncontrolled disease, is classified as non severe, as its complications do not usually result in any functional deficits.

• Uncomplicated abdominal TB [Fig. 22 on page 28]

It is thought to be due to retrograde lymphatic spread from a pulmonary focus, hematogenous spread, or ingestion of organisms during primary infection or disease.

• Otitis media (if not complicated by deafness)

• Hypersensitivity forms of arthritis, synovitis and osteitis in isolation

Severe forms

• All forms of central nervous system disease [Fig. 23 on page 29]

They are represented by tuberculous meningitis, vasculitis, granulomata and brain abscess, reflecting hematogenous organism dissemination.

• Complicated forms of abdominal TB

These forms include enteritis, solid organ disease, and peritoneal spread, which reflect either bowel wall infiltration from ingested organisms at primary infection, hematogenous organism dissemination, or rupture of abdominal nodes into the peritoneal cavity.

• Mastoiditis [Fig. 24 on page 30]

It may occur from hematogenous dissemination or contiguous spread from uncontrolled otitis media.

• Genito-urinary tract TB

It is assumed to arise from hematogenous spread of bacilli.

• Spondylitis, arthritis, synovitis and osteitis
They are the result of hematogenous TB dissemination.

This classification seems to correlate quite directly with clinical disease severity, allowing a more rapid prognostic evaluation.

**TREATMENT RESPONSE**

The aim of anti-TB treatment in children is to cure the patient of TB, reduce spread to others and avoid the development of drug resistance within the community. Although national recommendations still vary considerably in treatment duration and drug regimens used, TB treatment consists generally of two phases: an intensive phase, using a combination of bactericidal drugs to kill the rapidly growing bacilli, and a continuation phase, using fewer drugs to eradicate the slower growing persistent bacilli [9].

Owing to the lack of bacteriologic confirmation in most cases, radiologic and clinical evaluation become the major indicators of response to anti-TB therapy in children.

*Regression* of radiologic abnormalities is a slow process, involving in parallel parenchymal consolidations and lymphadenopathies [Fig. 25 on page 31, Fig. 26 on page 32].

*Resolution* of parenchymal abnormalities may require from 6 months to 1 year. Lymphadenopathy may persist for several years after treatment.

During the first 3 months of therapy, *worsening* of radiologic signs (i.e. extension of parenchymal involvement, development or enlargement of existing nodes) may be observed in up to 1/3 of patients. It has been attributed to an hypersensitivity reaction which normally occurs 2-10 weeks after initial infection.

After treatment, lymph nodes in regression usually appear discrete, reduced in size, homogeneous, with visible surrounding perinodal fat and sometimes with calcifications [Fig. 5 on page 15]. However, residual sizable nodes after 6 months of therapy do not necessarily indicate disease activity: it's the clinical scenario along with the trend of regression of nodes which suggest if the disease is active or not [10].

**Images for this section:**
Infant disease

- In infants (<3 months) there are some differences:
  - More symptomatic
  - Tuberculin skin test is frequently negative
  - Airways are smaller and more easily compressed by enlarged hilar lymph nodes than older children → obstructive overinflation
  - Higher risk of severe and life-threatening complications

![Fig. 2: Infant disease. CXR anteroposterior view (a) shows a large cavity (star) within consolidation in right upper lobe (RUL). Axial CT scan at lung window setting (b) confirms the cavitating process in RUL, showing various cavities in the same lobe and an inner air-fluid level (arrow). Sagittal MPR image allows a better characterization of the cavity, which is unique and presents thick internal septa.](image)
Fig. 3: Adult-type cavitating disease (1). CXR posteroanterior view (a) shows multiple cavitations (asterisks) over both upper lobes, with a significant decrease in volume of RUL, as demonstrated by minor fissure elevation (yellow arrows). Poorly defined consolidations associated with cavitations (asterisks) and bronchiectasis in the upper third of the left hemithorax are also present. Coronal MPR image at lung window setting (b) confirms consolidations (short arrow), cavitations (asterisks) and bronchiectasis (long arrows) over both upper lobes.
**Fig. 4:** Adult-type cavitating disease (2). In the same boy of Fig. 3 axial CT scans at lung window setting (c-d) demonstrate cystic and cylindrical bronchiectasis (asterisks) surrounded by parenchymal consolidations over both upper lobes, more evident at right side. Bronchial wall thickening (yellow arrow), poor defined small solid nodules and little cavitations (green arrow) are also present. Coronal minIP reformation image (e) exalts bronchiectasis, helping radiologist to distinguish between true cavities and cystic bronchial dilation.
Fig. 5: Different types of TB lymphadenopathies in children.

**Conglomerate necrotic lymph nodes**
Multiple enlarged nodes in the right upper paratracheal region, with low attenuation areas indicating central necrosis. The right anonymous vein is compressed (arrow) by the bulky nodes.

**Calcified nodes (pre-treatment)**
Right hylar and subcarinal lymphadenopathies with inner little calcifications (arrow) and central low attenuation areas (arrowhead).

**Calcified node (post-treatment)**
Right upper paratracheal lymph node with coarse calcification of the entire node.
Fig. 9: Axial CT image at lung window setting (a) shows a multilobulated consolidation of the lateral basal segment of right lower lobe (RLL). Axial CT image at mediastinal window setting (b) shows an hylar enlarged lymph node (yellow arrow). Oblique MPR image (c) better depicts the consolidations along the bronchovascular bundle (orange arrows), suggesting a bronchogenic spread. Bronchogenic spread of disease occurs when an area of caseous necrosis liquefies and communicates with the bronchial tree. Typically it involves lower lung zones, as in this case.
**Fig. 10:** Chest CT scan at mediastinal window setting (a) shows right pleural effusion (arrow). Axial CT scan at lung window setting (b) shows only a linear parenchymal consolidation in the posterior basal segment of RLL, without a severe lung disease.
Fig. 11: Chest CT scans at lung window setting (a) show consolidation of the apicodorsal segment of LUL (star). Axial enhanced CT scans at mediastinal window setting (b-c) show hylar enlarged lymph nodes (arrow in b) and the inhomogeneous low attenuation of the expansile pneumonia (c).
**INTRATHORACIC TB: SEVERE FORMS**

- Multilobar alveolar opacification

![Image](image-url)

**Girl, 3 y-o**

**Fig. 12:** CXR (a) shows mild opacifications in the right lung (stars). Axial CT scans at lung window setting localize the alveolar consolidations (asterisks) in different lobes: lateral and posterior basal segment of RUL with air-bronchogram (b), medial segment of middle lobe (ML) (c) and anterior basal segment of RLL (d). Axial enhanced CT scan at mediastinal window setting (e) shows mild calcifications within a consolidation and hylar lymph nodes calcifications (arrow).
**Fig. 13:** Axial CT scans at lung window setting (a) and at mediastinal window setting (b) show the typical apical cavitation (star), with thick wall (purple arrow) and an inner air-fluid level (green arrow), consistent with superinfection. Enlarged and inhomogeneous hylar and subcarinal nodes are also evident (yellow arrows) (c). Sagittal MPR (d) shows the cavitation within expasile consolidation in the apicodorsal segment of left upper lobe (LUL), with fissural buldging (orange arrow) and other parenchymal consolidations in the left lower lobe (LLL).
Fig. 14: CXR anteroposterior view (e-f) 1 week after CT scan [Fig. 13] shows reduction of consolidation and cavitation of LUL (arrow), even more reduced 1 month later.
Fig. 15: Axial CT scans at lung window setting (a-c) show compression of trachea (orange arrow) and carina (green arrow) associated to atelectasis of the apical and anterior segment of RUL (star). Axial enhanced CT scan at the same levels (b-d) show large, conglomerate enhancing nodes with central low attenuation areas, as for central necrosis (yellow arrows). (e-f) Other pathologic lymph nodes are also present in the supraclavicular and hylar regions (pink arrow).
**Fig. 16:** CXR anteroposterior view (a) shows complete opacification of left hemithorax, with mild shift of mediastinal structures to the right (yellow arrow). Axial CT images at lung window setting (b-c) show: a wide cavity with internal septa in the left apex (b), lingular and LLL consolidation with air-bronchogram (orange arrow), loculated pneumothorax in the anterior part of the right hemithorax (star). Axial non-enhanced CT scan at mediastinal window setting (d) shows pleural effusion (green arrow) and consolidation of the adjacent parenchyma.
**Fig. 17:** Axial enhanced CT images at mediastinal window setting (a-b) show thickening of visceral and parietal right pleural surfaces (arrows) separated by the presence of fluid (star), representing the "split pleura" sign. Axial CT image at lung window setting (c) shows no underlying parenchymal abnormalities.
**Fig. 18:** Axial enhanced CT scan at mediastinal window setting demonstrates a thickened pericardium (arrows) and bilateral pleural effusions (stars). Atelectasis of basal-posterior segment of both lower lobes (RLL>>LLL) is also present.

✓ Tuberculous pericarditis
**Fig. 19:** CXR anteroposterior view (a) shows multiple disseminated nodules in both lungs, calcified right hylar nodes (arrow) and the loss of sharpness of the right cardiac profile (star), due to partial consolidation of the ML. Chest CT scans at lung window setting (b-c) better depict the diffuse involvement of both lungs through multiple 2-3 mm nodules. A partial consolidation of the ML with inner calcifications is also present. Axial non-enhanced CT scans at mediastinal window setting (d-e) show calcified nodes in hylar, subcarinal and right lower paratracheal regions (arrows).
**EXTRATHORACIC TB: NON SEVERE FORMS**

- Peripheral lymphadenitis, without infiltration/compression of adjacent structures

*Fig. 21:* CXR anteroposterior view (a) shows a right latero-cervical opacity (arrows), due to laterocervical adenopathies, confirmed at CT scan (b). No signs of compression/infiltration of adjacent structures are present.
Fig. 22: Axial CT images at abdominal window setting (a-b) show enlarged lymph nodes in the intercavo-aortic and left paraaortic regions (yellow arrows). A calcified Ghon focus in the superior lingular segment (green arrow) associated with calcified hylar and subcarinal nodes is also present (orange arrows) (c-d). These features are typical seen in post-primary tuberculosis.
**EXTRATHORACIC TB: SEVERE FORMS**

- All forms of central nervous system disease

*Fig. 23:* T1-weighted MRI after contrast administration show florid leptomeningeal enhancement along the right middle cerebral artery (yellow arrow) and anteriorly to the tip of temporal horns of lateral ventricula (green arrows). High-intensity signals in the right basal ganglia (orange arrow) are also noted.
**Fig. 24:** Bilateral tuberculous mastoiditis. High-resolution CT scan of the temporal bone demonstrates bilateral destructive lesions in the mastoid processes (straight arrows). There is an accompanying cold abscess overlying the right temporo-occipital region (curved arrow).
Hyperinflation may be the result of a check-valve effect due to partial airway obstruction by lymph nodes!!!
Fig. 26: CXR anteroposterior view (a) performed after 1 month of anti-TB therapy shows initial regression of LLL consolidation (arrows) and reduction of LUL hyperinflation. This finding indirectly indicates a reduction of size of lymph nodes. Axial CT scan at lung window setting (b) shows residual little subpleural consolidations in the LLL (arrowhead), without differences in parenchymal attenuation between the two lungs. Axial CT images at mediastinal window setting (c-d-e) highlight the presence of soft calcifications (arrow) within consolidations and the regression of necrotic lymphadenopathies previously seen in left hylar and subcarinal regions.
Conclusion

- **CXR and CT are essential diagnostic tools** in PTB because of the rarity of clinical signs and complexity of bacteriologic tests in childhood.

- **Primary TB** is the most common form of pulmonary TB in children and lymphadenopathy represents the most common finding.

- The **new classification** of pediatric TB better correlates with disease severity than the traditional distinction in pulmonary and extrapulmonary TB. CXR and CT are helpful in distinguish severe from non-severe forms of PTB, leading to different clinical management.

- Imaging represent also a valuable tool for **treatment evaluation**, though radiologic signs have always to be correlated to the clinical scenario.

References


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