International Journal of Infectious Diseases 32 (2015) 87–93

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Review

Imaging in tuberculosis

Evangelia Skoura [a], Alimuddin Zumla [b], Jamshed Bomanji [a,*]

[a] Institute of Nuclear Medicine, University College Hospitals NHS Trust, London NW1 2BU, UK
[b] Division of Infection and Immunity, Centre for Clinical Microbiology, University College London, and NIHR Biomedical Research Centre, University College London Hospitals, London, UK

ARTICLE INFO

Article history:
Received 14 November 2014
Received in revised form 28 November 2014
Accepted 1 December 2014

Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Pulmonary tuberculosis
Extrapulmonary tuberculosis
Computed tomography
Positron emission tomography
Fluorodeoxyglucose
Magnetic resonance imaging

SUMMARY

Early diagnosis of tuberculosis (TB) is necessary for effective treatment. In primary pulmonary TB, chest radiography remains the mainstay for the diagnosis of parenchymal disease, while computed tomography (CT) is more sensitive in detecting lymphadenopathy. In post-primary pulmonary TB, CT is the method of choice to reveal early bronchogenic spread. Concerning characterization of the infection as active or not, CT is more sensitive than radiography, and ^{18}F-fluorodeoxyglucose positron emission tomography/CT (^{18}F-FDG PET/CT) has yielded promising results that need further confirmation. The diagnosis of extrapulmonary TB sometimes remains difficult. Magnetic resonance imaging (MRI) is the preferred modality in the diagnosis and assessment of tuberculous spondylitis, while ^{18}F-FDG PET shows superior image resolution compared with single-photon-emitting tracers. MRI is considered superior to CT for the detection and assessment of central nervous system TB. Concerning abdominal TB, lymph nodes are best evaluated on CT, and there is no evidence that MRI offers added advantages in diagnosing hepatobiliary disease. As metabolic changes precede morphological ones, the application of ^{18}F-FDG PET/CT will likely play a major role in the assessment of the response to anti-TB treatment.

1. Introduction

Tuberculosis (TB) remains a global emergency despite substantial investment in health services over the past two decades. Patients with sputum-negative pulmonary TB (PTB) and extrapulmonary TB (EPTB) are difficult to diagnose and may be missed at all points of care. Diagnostic imaging is challenging because signs of TB may mimic those of other diseases such as neoplasms or sarcoidosis. Clinical signs and symptoms in affected adults can be non-specific and a high level of pre-test clinical suspicion based on history is fundamental in the diagnostic work-up. The global impact of TB is extremely important, considering that an estimated 9.0 million people developed TB in 2013 and 1.5 million died from the disease, according to the recent World Health Organization (WHO) global tuberculosis report 2014.

Early diagnosis promotes effective treatment and leads to a reduced onward transmission of TB. This article gives a review of imaging patterns of chest TB as may be detected on conventional radiography and computed tomography (CT). The main aim is to improve the radiologist's familiarity with the spectrum of imaging features of this disease in order to facilitate timely diagnosis. Furthermore, we consider the emerging role of alternative methods of imaging, such as magnetic resonance imaging (MRI), which can be helpful and highly accurate for a better definition of some of the signs of TB.

Although new imaging methods are now being used, conventional radiography remains the initial modality for suspected PTB and for mass screening purposes.[1] CT and MRI are the modalities of choice for the evaluation of specific body parts.[1] Positron emission tomography/computed tomography with the use of ^{18}F-fluorodeoxyglucose (^{18}F-FDG PET/CT) is a non-invasive imaging method that has been used widely for the differentiation of malignant from benign lesions. However, ^{18}F-FDG also accumulates in inflammatory cells such as neutrophils, activated macrophages, and lymphocytes at the site of inflammation or infection.[2] Consequently, ^{18}F-FDG uptake is observed in PTB, in tuberculoma, and in other TB-related lesions.[3,4] Using PET/CT, pulmonary and extrapulmonary TB involvement is assessed simultaneously, with time- and cost-saving implications.

Although any organ of the body can be involved, the lung remains the most commonly involved organ in TB. The imaging appearances of TB are described below for both pulmonary and extrapulmonary involvement.

* Corresponding author.
E-mail address: jamshed.bomanji@uclh.nhs.uk (J. Bomanji).

http://dx.doi.org/10.1016/j.ijid.2014.12.007

2. Pulmonary tuberculosis

Classically, PTB can be divided into a primary and a post-primary pattern, each presenting with characteristic radiological features. In practice, however, it is very difficult to draw distinct lines between these radiographic patterns, and there is considerable overlap in the radiological manifestations.[5]

2.1. Primary tuberculosis

Primary TB is due to first-time exposure to *Mycobacterium tuberculosis*. At radiology, primary PTB manifests as four main entities – parenchymal disease, lymphadenopathy, pleural effusion, and miliary disease – or any combination thereof.[1]

Chest radiography continues to be the mainstay of diagnosis. Typically, parenchymal disease manifests as consolidation in any lobe, with predominance in the lower and middle lobes.[6] In these cases, the bacterial infections are much more likely to be the cause of such radiological features and hence the findings are non-specific, although primary infection should be suspected in individuals at risk of exposure to TB. Multilobar consolidation can be seen in almost 25% of cases.[1] In approximately two-thirds of cases, the parenchymal lesion resolves without sequelae on conventional radiography.[6] In the remainder, a radiological scar persists that can be calcified in up to 15%, while persistent mass-like opacities called tuberculomas are seen in approximately 9% of cases.[6] Frequently, the only radiological evidence suggestive of previous TB is the so-called Ranke complex: the combination of a parenchymal scar, calcified or not (Ghon lesion), and calcified hilar and/or paratracheal lymph nodes.[5] Destruction and fibrosis of the lung parenchyma result in the formation of traction bronchiectasis within the fibrotic region.[5]

The most common abnormality in children is lymph node enlargement, which is seen in 90–95% of cases; by comparison, in adults the percentage reaches up to 43%.[7] Right paratracheal and hilar lymph nodes are the most common sites of nodal involvement, although involvement is bilateral in about a third of cases. CT is more sensitive than plain radiography in detecting tuberculous lymphadenopathy. It reveals nodes often measuring more than 2 cm, with a very characteristic, but not pathognomonic, 'rim sign' that consists of a low-density centre, representing caseous necrosis, surrounded by a peripheral enhancing rim due to granulomatous inflammatory tissue.[8,9]

In contrast to lymphadenopathy, the prevalence of radiographically detectable parenchymal involvement is significantly lower in children up to 3 years old (51%) than in older children, among whom the prevalence is similar to the reported percentage in adults (80%).[7,8] Also, evolution to cavitary disease is rare in children.[5]

Concerning the role of ^{18}F-FDG PET/CT, two distinct patterns of PTB have been described: (1) the lung pattern, related to a restricted and slight hypermetabolic infection, with ^{18}F-FDG uptake in areas of lung consolidation ± cavitation surrounded by micronodules and mild uptake within lymph nodes, and (2) the lymphatic pattern, related to a systemic and intense infection, with more enlarged and ^{18}F-FDG-avid hilar and mediastinal lymph nodes.[10]

A limitation to the use of ^{18}F-FDG PET/CT for the assessment of a single pulmonary nodule, especially in endemic areas, is the inability to distinguish tubercular from malignant lesions (Figure 1).[11] Studies investigating the diagnostic value of dual time-point ^{18}F-FDG PET/CT imaging have shown limited promise, but further investigations in larger series of patients are warranted.[12,13]

2.2. Post-primary tuberculosis

Post-primary PTB is one of the many terms (including reactivation, secondary, or adulthood) applied to the form of TB that develops and progresses under the influence of acquired immunity.[5] The most common radiographic manifestation of post-primary PTB is focal or patchy heterogeneous, poorly defined consolidation involving the apical and posterior segments of the upper lobes and the superior segments of the lower lobes (Figure 2).[14,15] In the majority of cases, more than one pulmonary segment is involved.[6] Cavitation, the radiological hallmark of PTB, is radiographically evident in 20–45% of patients (Figure 3), while air-fluid levels in the cavity occur in 10% of cases.[14,15] Cavitation may progress to endobronchial spread and results in a typical 'tree-in-bud' distribution of nodules in addition to cavitation; this is considered a reliable marker of active TB.[16] High-resolution CT is the method of choice to reveal early bronchogenic spread, with 2- to 4-mm centrilobular nodules and sharply marginated linear branching opacities around terminal and respiratory bronchioles (tree-in-bud sign).[16] The tree-in-bud sign is the constellation of small centrilobular nodules and concomitant branching opacities, which mimics the branching pattern of a budding tree.[17] The centrilobular nodules are peripheral, spare the subpleural lung, and denote the inflammatory lesions in the bronchioles and peribronchial alveoli.[16,17] Hilar or mediastinal lymphadenopathy is uncommon in post-primary PTB, seen in only 5–10% of patients (Figure 4).[18,19]

Although pulmonary tuberculomas are most often the result of healed primary PTB, a pulmonary tuberculoma is the main or only abnormality on chest radiographs in approximately 5% of patients with reactivation.[20] The CT scan shows a round or oval granuloma, measuring from 0.4 to 5 cm in diameter, with a wall lined by

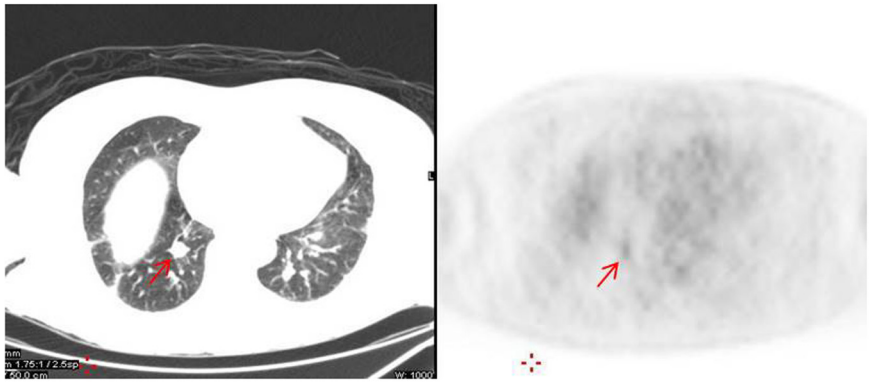

Figure 1. Arrows indicate a mildly ^{18}F-FDG avid right lower lobe nodule measuring 1.5 cm (SUV_{max} 2). The differential diagnosis for this nodule would include cancer or tuberculosis.