Chameleon behaviour of Tuberculosis

Abstract
Tuberculosis (TB) is a diagnostic “chameleon” and can mimic different pathologic conditions. In countries with a high incidence of lung cancer or sarcoidosis, TB often gets mis-diagnosed with the result of delayed treatment.

Keywords: CT; Lung; Tuberculosis; Atypical; Sarcoidosis; Malignancy; Lymphoma

Introduction
Pulmonary tuberculosis (TB) is nowadays one of the most common causes of infectious disease-related morbidity and mortality worldwide. The differential diagnosis between TB and some other pathologic conditions is an emerging problem, as pulmonary TB may easily show heterogeneous aspects. Differential diagnosis can be particularly challenging when TB mimics sarcoidosis, lymphoma and pulmonary neoplasms.

TB vs. Sarcoidosis and Lymphoma: The Dilemma of Lymph Nodes
Changes in epidemiology characteristics of the disease can be one of the causes of challenges in the differential diagnosis. While in the past primary TB was mainly a pediatric disease, nowadays it is more common in young adults (age 18 to 25). This new scenario account dilemma about differential diagnoses because other diseases, more frequently encountered in young adults, show similar radiologic findings.

The differential diagnosis with systemic diseases such as sarcoidosis, Hodgkin lymphoma (HL) and some respiratory viral diseases, on occasion, may represent a real challenge for the radiologist and the clinician.

Indeed, pathologic findings of these conditions are characterized by the presence of pathological hilar and mediastinal enlargement lymph nodes that can be hardly differentiated from TB manifestations. In a study published in 2012, Tang et al. [1] compared the Computed Tomography (CT) features of mediastinal TB adenitis with those of untreated lymphoma (both HD and NHL). Tuberculous adenopathies do not exceed 4 cm in diameter, while lymphomatous can be larger and polylobulated. Region 10R (right hylar) is interested more frequently in TB, while region 6 (paraaortic) in lymphomas. Nearly half of the patients with TB showed concomitant pulmonary or pleural disease. On the other hand TB, CT findings of adenopathies with central low attenuation and peripheral rim enhancement is a typical aspect of an active disease [2-4]. However, these findings are not fully specific and, especially in cases of TB without parenchymal lesions, lymphonodal biopsy is often the only way to reach a reliable diagnosis [4]. Even if literature describes sarcoidosis as the “great masquerade”, the association of peripheral “pseudoplaque” opacities (adjacent to the pleura, with a rounded shape, well defined margins and regular edges), of small nodules in a perilymphatic distribution and of ground-glass opacities with fine reticulation, is the key to a diagnosis of sarcoidosis.

TB vs Sarcoidosis: The Question of Nodules Distribution
Tuberculosis, on a CT, demonstrates a variety of both poorly defined and sharply 1–4 mm nodules (1,2).

Nodules are randomly distributed relative to structures of the lung and secondary lobule sometimes associated with interlobular or intralobular septal thickening (5). The intra-lobular network or interlobular septal thickening that is visible on thin-section CT scans in miliary TB is suggestive of the presence of tubercles localized inside the interlobular septa and alveolar walls. Also, in
patients with active post-primary disease, centrilobular nodules and branching linear structures with a “tree-in-bud” pattern may be patent (1-2-6). However, some atypical patterns of nodules distribution have been reported in TB on thin-section CT. Ortega et al. (7) described the “Sarcoid Cluster Sign” as a new CT sign, observed in cases of sarcoidosis. The “sarcoid cluster” correlates to, oval-shaped or “tree in bud” clusters of multiple small nodules in the lung parenchyma that are not confluent but very close to each other’s.

In one case, of a woman affected by tuberculosis, published by Cardinale et al, (8) are also reported some zones where these nodules are so confluent to produce a near ground-glass aspect. These small nodules represent non-caseating tubercolous granulomas with and without connection. They concluded that definition of “sarcoid cluster sign” must be expanded to confluent micro-nodules generating a ground-glass appearance.

**TB vs. Lung Cancer: The Problem of Masses and Solitary Nodule**

TB findings can also determine a further differential diagnostic problem with lung solid neoplasms, especially when caviting lung masses are also accompanied by negative sputum. Lung imaging of tuberculosis is often represented with the cavity involving the upper lobes, although it may be radiographically revealed also with a mass appearance suggesting lung or pleural neoplasms (2,3,9,10).

In a series of 597 subjects diagnosed as tuberculosis, evaluated by Cherian et al. (11), 11 patients who presented with a solitary mass lesion were detected. Rolston et al. (12) attended a retrospective study, covering a 3-year period, of patients with supposed lung cancer, who turned out to have lung infection instead. Of the 2908 patients who underwent a diagnostic evaluation, 2713 (93%) were documented as having lung neoplasms; 11 patients (0.4%) had a benign process; 37 patients (1.3%) had a documented infection; and 147 fungal infections accounted for 46%, mycobacteria for 27%, bacteria for 22%, and parasitic lesions for 5% of these infections. A differential diagnosis according to the radiological findings cannot be provided. The final diagnosis was confirmed by pathological and microbiological analysis. Indeed, the presence of Acid Fast Bacilli (AFB) in sputum or a positive skin test didn’t rule-out the coexistence of TB and cancer. CT imaging is helpful for the accurate evaluation of the morphologic and densitometric aspects of the lesion, detection of lymph nodes enlargement and the possible presence of metastases.

**What about lung solitary nodule?**

Diffuse, central, or lamellar calcifications may be clues to the imaging diagnosis of TB over malignancy. Positron Emission Tomography CT (PET-CT) could be another useful tool in case of a challenging differential diagnosis, however, TB still remains a common cause of false positive diagnoses on PET-CT because tuberculomas may even show high F18-FDG uptake raising problems of overlapping findings with tumor masses. Surgery or biopsy may occasionally be the only solution to obtain a correct diagnosis.

**Conclusion**

Tuberculosis can mimics malignancy, like lung cancer / lymphoma and sarcoidosis both radiologically and clinically, despite the use of the advanced imaging techniques. In these cases, the correct diagnoses can be made with certainty only with trans-bronchial or CT guided biopsy.
References


