

Tuberculosis of the chest

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Abstract

The relationship between tuberculosis and mankind has been known for many centuries, with the disease being one of the major causes of illness and death. During the early 1980s, there was a widespread belief that the disease was being controlled, but by the mid-1980s, the number of cases increased. This change in the epidemiological picture has several causes, of which the AIDS epidemic, the progression of poverty in developing countries, the increase in the number of elderly people with an altered immune status and the emergence of multidrug-resistant tuberculosis are the most important.

Mainly due to this epidemiological change, the radiological patterns of the disease are also being altered, with the classical distinction between primary and postprimary disease fading and atypical presentations in groups with an altered immune response being increasingly reported.

Therefore, the radiologist must be able not only to recognize the classical features of primary and postprimary tuberculosis but also to be familiar with the atypical patterns found in immuno-compromised and elderly patients, since an early diagnosis is generally associated with a greater therapeutic efficacy. Radiologists are, in this way, presented with a new challenge at the beginning of this millennium.

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1. Introduction

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*, which was isolated by Robert Koch in 1882, but has been affecting the world population for thousands of years. In western countries, the highest mortality and morbidity occurred in the late 1700s and early 1800s, due to the crowded environments and generalized poverty during and after the industrial revolution [1]. Because of the improved social and economic situation of people in the late 1800s, a spontaneous decrease of TB was observed [2]. Improvement in diagnosing the disease (due to discovery of X-rays), isolation of infectious cases in sanatoria, introduction of effective antituberculous therapy and control programs initiated after World War II, lead to an

annual decrease of 5% in TB cases over the past 30 years [3], so that, by the early 1980s, there was a strong conviction that the disease was being controlled [2]. By the mid-1980s, however, the number of cases was again increasing. At the same time, in developing regions of the globe, where 90% of TB cases of the whole world occur, the number of cases continued to increase by more than 20% between 1984–1986 and 1989–1991 [4]. Also, the human immunodeficiency virus (HIV) infection and the epidemics of acquired immunodeficiency syndrome (AIDS), together with the problem of multidrug-resistant (MDR) TB, may have contributed to the resurgence of the disease [5]. In 1993, the World Health Association declared TB a “global emergency” [6], since almost one-third of the world population is infected with *M. tuberculosis*. Largely because it has been neglected as a public health issue for many years, it is estimated that between 1997 and 2020 nearly 1 billion people will become newly infected and 70 million will die from the disease at current control levels [7].

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2. Pathogenesis

2.1. Primary tuberculosis

M. tuberculosis is a strictly aerobic, acid-fast, Gram-positive bacillus [8], transmitted via airborne droplet nuclei, laden with a few organisms, produced when persons with pulmonary or laryngeal TB cough, sneeze or speak [9]. These particles, being 1–5 µm in diameter, can remain airborne for long periods of time [7], and infection occurs when a susceptible person inhales those droplet nuclei, which in turn deposit most commonly in the middle and lower lobes of the lung [10]. Once in the alveoli, *M. tuberculosis* is ingested by alveolar macrophages. If these cannot destroy the offending organisms, bacilli multiply in this intracellular environment until the macrophages burst and release them, being, in turn, ingested by other macrophages. During this period of rapid growth, *M. tuberculosis* is spread through the lymphatic channels to hilar and mediastinal lymph nodes and through the bloodstream to other sites in the body [7]. This is arrested with the development of cell-mediated immunity and delayed-type hypersensitivity at 4–10 weeks after the initial infection. At this time, the tuberculin reaction becomes positive [11]. The macroscopic hallmark of hypersensitivity is the development of caseous necrosis in the involved lymph nodes and the pulmonary parenchymal focus, the Ghon focus [12], which, together with the enlarged draining lymph nodes, constitutes the primary complex, also known as the Ranke or Ghon complex [11]. In the immunocompetent individual, development of specific immunity is generally adequate to limit multiplication of the bacilli; the host remains asymptomatic and the lesions heal [13], with resorption of caseous necrosis, fibrosis and calcification. The pulmonary focus and the lymph nodes become calcified and minimal haematogenous dissemination may originate calcifications in lung apices (Simon's foci) and in extrapulmonary locations. Some bacilli in these healed lesions remain dormant and viable, maintaining continuous hypersensitivity to tuberculous antigen, and in situations of immunodepression, they can reactivate. In immunocompromised individuals (HIV-positives, alcoholics, diabetics, drug addicts, elderly and patients with chronic renal failure, malignancy or undergoing immunosuppressive medication), more widespread lymphogenic and haematogenous dissemination occurs, resulting in lymphadenopathy and more peripheral locations, respectively [11]. If immunity is inadequate, active disease often develops within 5 years after initial infection, the so-called progressive primary TB, which occurs in about 5% of infected patients [14]. In the patients with little or no host response, disseminated (miliary) TB occurs [15].

2.2. Postprimary tuberculosis

Postprimary disease can result from endogenous reactivation of dormant bacilli in residual foci in the lung apices [11]. Haematogenous spread and reactivation occurs preferentially

in the upper lung zones, due to the higher oxygen tension and impaired lymphatic drainage in those areas [16]. After reactivation, the apical foci reach confluence, liquefy and excavate. Perforation of a lymph node into a bronchus may cause a tuberculous bronchitis with bronchial ulceration, and aspiration of intraluminal bacilli can cause bronchogenic dissemination; a classic finding is an infiltrate in the subapical infraclavicular region. Postprimary disease can also occur, although less frequently, from exogenous reinfection, particularly in countries with low infection risk [11]. Age may often determine the presentation of the disease: whereas neonates and children develop primary disease, adults present with postprimary TB. This picture, however, is altered by the changing epidemiology, with atypical and “mixed” radioclinical patterns occurring in adults, especially in immunocompromised patients, with a consequent fading of the age-related distinction between primary and postprimary TB [17].

3. Clinical findings

Patients with primary TB are often asymptomatic but may experience a symptomatic pneumonia. Young individuals with progressive primary disease may present with cough, haemoptysis and weight loss.

Patients with postprimary disease most commonly experience chronic productive cough and marked weight loss, and sometimes they have haemoptysis and dyspnoea. Chest pain can occur with extension of the inflammatory process to the parietal pleura. Symptoms are often insidious and persist from weeks to months [15].

Clinical features are dependent on the immune status of the patients [18], since persons with relatively intact cellular immune function have their disease localized to the lung, whereas in those with advanced immunosuppression, pulmonary TB is frequently accompanied by extrapulmonary involvement [19,20].

4. Radiological findings

In practice, it is becoming increasingly difficult to differentiate between the classical primary and postprimary patterns based on radiological findings, which show a considerable overlap in radiological manifestations [11]. Because of the decreasing TB incidence in developed countries, many adults have never been infected by *M. tuberculosis* and are at risk for a first tuberculous infection, which may progress in turn to active disease. One can expect a shift from the usual pattern (endogenous reactivation) towards an unusual pattern (progressive primary TB) similar to that observed in children and adolescents [21]. This unusual or “atypical” pattern includes: solitary pleural effusion, isolated mediastinal/hilar lymphadenopathy, lower lobe TB, nodular miliary lesions, diffuse infiltrations, atelectasis but also a normal chest plain film [22].



Fig. 1. Gangliopulmonary TB: on chest plain film, patchy infiltrates in the right upper lobe and right paratracheal lymphadenopathy are detected.

4.1. Primary tuberculosis

This form of disease occurs predominantly in children, but primary TB in the adult is increasing due to public health measures and antituberculous therapy that lead to a decrease in the overall incidence of disease, with a consequent increase in the population of non-exposed adults [23]. Primary TB accounts for 23–34% of all adult cases of the disease [15].

Four entities have been described: gangliopulmonary TB, tuberculous pleuritis, miliary TB and tracheobronchial TB [11].

4.1.1. Gangliopulmonary TB

Gangliopulmonary TB is characterized by the presence of mediastinal and/or hilar lymphadenopathy and parenchymal abnormalities, the Ghon focus [11].

Enlarged nodes occur in 83–96% of paediatric cases, whereas in adult patients they are found in 10–43% [7]. Right paratracheal and hilar stations are the most common sites of nodal involvement in primary TB, although other combinations may also be found (bilateral hilar, isolated mediastinal) [23–25]. Although adenopathy is usually found in association with parenchymal consolidation or atelectasis (Fig. 1), it can be the sole radiographic manifestation of the disease [8], especially in early childhood (49% of cases) [24]. Computed tomography (CT) is more sensitive than chest plain films for detecting intrathoracic tuberculous adenopathy, and lymph nodes greater than 2 cm in diameter may have central areas of low attenuation associated with peripheral rim enhancement and obliteration of surrounding perinodal fat (Fig. 2). This corresponds to caseation necrosis, granulation tissue with inflammatory hypervascularity and perinodal reaction [25–27] and is highly suggestive of active disease [28]. Lymphadenopathy resolves at a slower rate than the parenchymal disease, without significant radiological sequelae; nodes

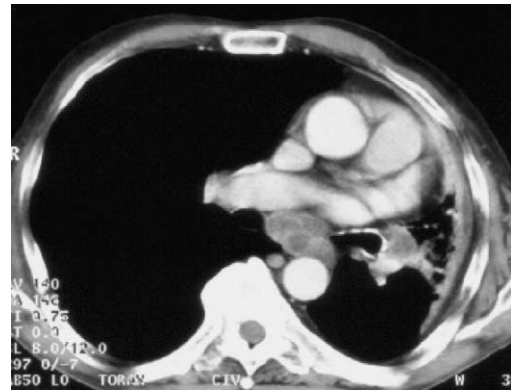


Fig. 2. Tuberculous lymphadenopathy: contrast-enhanced CT shows several low-density center, rim-enhancing lymph nodes in the mediastinum and left hilum.

firstly become homogeneous and finally disappear or result in a residual mass composed of fibrotic tissue and calcification (Fig. 3). This develops 6 months or more after the initial infection and is more common than parenchymal calcification, and also more common in adults than children. It may be present in both active and inactive cases of the disease [28].

Associated pulmonary infiltrates are found on the same side as nodal enlargement in about two-thirds of paediatric cases of primary TB [22]. Parenchymal involvement in the absence of lymphadenopathy occurs in only about 1% of paediatric cases [24], whereas this pattern is much more common in adults with primary disease (38–81%) [23]. Parenchymal opacities are most often located in the periphery of the lung, especially in the subpleural zones. These subtle infiltrates are frequently undetected on plain chest films, so CT may be needed to demonstrate them. Parenchymal involvement in primary disease most commonly appears on plain films as an area of homogeneous consolidation, with ill-defined borders and sometimes air bronchograms (Fig. 4); patchy, linear, nodular and mass-like patterns have also been reported [23,24,29,30]. In 10% of the patients, primary disease is ap-

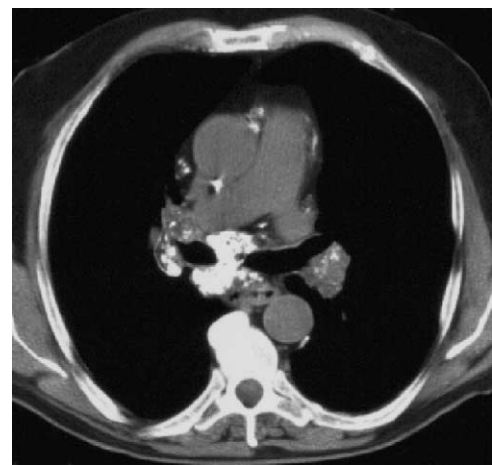


Fig. 3. Calcified lymphadenopathy: CT reveals conglomerates of calcified lymph nodes in the mediastinum and both hila.



Fig. 4. Parenchymal disease: chest plain film shows a patchy consolidation in the right upper lobe with ill-defined borders and air bronchograms.

parent as a single cavitary lesion [22]. Consolidation occurs in a segmental or lobar distribution, with multifocal involvement in 12–24% of the cases [24,29]. Primary TB can cause consolidation of any lobe [8]; the most common sites are areas of greater ventilation, including the middle lobe, the lower lobes or the anterior segments of the upper lobes [31,32]. There is, however, a right-sided predominance in the distribution [23,24]. On CT, a homogeneous, dense, segmental or lobar consolidation is seen [32,33]. In two-thirds of the cases, the parenchymal focus resolves without radiological sequelae, although the resolution is typically slow, usually paralleling that of lymphadenopathy [24]. A calcified scar – the Ghon focus – is seen in 15–17% of the patients, and together with calcified hilar or mediastinal lymph nodes constitutes the Ranke complex, also known as primary or Ghon complex [12] (Fig. 5). Calcified secondary parenchymal foci are called Simon foci [8].

Persistent mass-like opacities predominating in the upper lobes, corresponding to tuberculomas, are uncommon (7–9%



Fig. 6. Tuberculoma: a homogeneous, calcified nodule in the right upper lobe is shown on the chest film.

of cases), and are thought to be a result of healed primary disease (Fig. 6). Cavitation occurs in 10–50% of these nodules, calcification develops in up to 50% and most remain stable in size [31]. Gangliopulmonary TB may also present with perforation of an adenopathy into a bronchus, retroobstructive pneumonia and/or atelectasis (epituberculosis). Obstructive atelectasis or overinflation due to compression by adjacent enlarged lymph nodes occurs in 9–30% and 1–5%, respectively [24], with a typical right-sided predominance.

4.1.2. Tuberculous pleuritis

Pleural TB is most frequently seen in adolescents and adults as a complication of primary TB, being uncommon in young children [12,24,31,34]. Pleural effusions occur in about 10% of all primary infections and, in 5% of the cases, effusions are the sole radiographic feature of the disease [31] (Fig. 7). The effusion generally develops on the same side

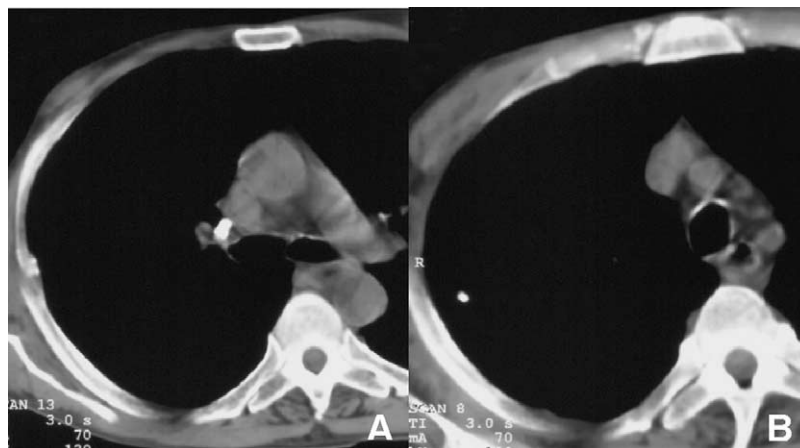


Fig. 5. Ranke complex: CT (A) calcified hilar lymphadenopathy and (B) calcified parenchymal lesion.



Fig. 7. Tuberculous pleuritis: a left pleural effusion is apparent on chest plain film.

as the initial infection and is typically unilateral, most often in association with parenchymal and/or nodal abnormalities [23]. It is often a late finding in primary TB and, usually, resolves promptly with adequate therapy, but the resolution may occur with residual thickening or calcification (Fig. 8). If left untreated, it commonly leads to secondary disease [31]. Complications of pleural tuberculous involvement include empyema formation, bronchopleural fistulae, bone erosion and pleurocutaneous fistulae [35].

4.1.3. Miliary TB

In 2–6% of primary TB cases, the haematogenous dissemination of bacilli results in miliary disease [29]. The elderly, children younger than 2 years old and immunocompromised patients are most frequently affected [12,36]. Chest plain films are usually normal at the onset of symptoms, and the earliest finding, seen within 1–2 weeks, may be hyperinflation [34]. The classic finding of diffuse small (2–3 mm) nodules, evenly distributed, with a slight lower lobe predominance, may not appear until 6 weeks or more after haematogenous dissemination [12] (Fig. 9). Associated adenopathy is



Fig. 8. Tuberculous pleuritis: CT shows a right-sided encapsulated pleural effusion with marked pleural thickening.



Fig. 9. Miliary TB: numerous well-defined, diffusely distributed, small nodules (2–3 mm) are apparent on chest plain film. There is also bilateral hilar lymphadenopathy.

present in 95% of children and 12% of adults with miliary disease, and associated parenchymal consolidation is also more common in children (42% versus 12%) [8]. CT, particularly high-resolution (HR) CT, can detect miliary disease before chest plain film does, demonstrating 1–2 mm nodules in a perivascular and periseptal distribution. A nodular thickening of interlobular septa can result in a “beaded septum” appearance similar to that of carcinomatous lymphangitis [37]; rarely nodules may coalesce into parenchymal consolidation or progress to ARDS and, occasionally, to cavitation [31,36] (Fig. 10). With therapy, resolution is generally faster in children than in adults.

4.1.4. Tracheobronchial TB

Tracheobronchial TB is a complication of primary disease that frequently originates from perforation of an adenopathy into a bronchus; other possible ways of involvement are lymphogenic and haematogenic spread [11]. Chest plain films may be normal or show parenchymal opacities in the upper lobes and segmental or lobar atelectasis. Airway involvement by endobronchial TB in adults presents as areas of segmental atelectasis distal to the involved bronchi and endoluminal or peribronchial masses, simulating a neoplasm (Fig. 11). Endobronchially disseminated TB causes foci of ill-defined

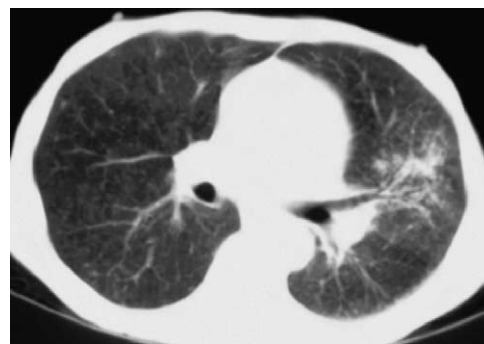


Fig. 10. Miliary TB: CT reveals innumerable 1–3 mm nodules with an even distribution throughout both lungs. In the left upper lobe the nodules coalesce into parenchymal consolidation.



Fig. 11. Tracheobronchial TB: on CT, a nodular density is detected in the right main bronchus (arrow).

nodular densities that may become confluent [30]. On CT, acute tracheobronchial disease causes concentric bronchial narrowing, wall thickening and postobstructive bronchiectasis [38,39]. After healing, cicatricial bronchostenosis may occur. Consolidation of the lower lobes is an atypical radiographic pattern of endobronchial TB [40].

4.2. Postprimary tuberculosis

Also called phthisis, reactivation TB, secondary TB or “adulthood” TB (by opposition to primary or “childhood” TB), this form of disease develops under the influence of acquired immunity. It is the result of reactivation of dormant bacilli in residual foci, spread at the time of primary infection; it is, generally but not always, a disease affecting persons in adulthood [41]. When observed in the paediatric age, it affects adolescents [8,12,24,42].

Postprimary TB usually manifests radiographically as parenchymal disease and cavitation, tracheobronchial TB, tuberculous pleuritis and complications [8].

4.2.1. Parenchymal disease and cavitation

The earliest parenchymal finding is a heterogeneous, poorly margined opacity (the “exsudative” lesion) situated in the apical and posterior segments of the upper lobes and the superior segments of the lower lobes, radiating outwards from the hilum or in the periphery of the lung [31,43]. In about 88% of the cases more than one segment is affected, with bilateral upper lobe disease seen in 32–64% of the cases [29]. The usual progression is towards better-defined reticulonodular opacities (“fibroproliferative” lesions) that may coalesce [31,43] (Fig. 12). These lesions, when healed, may calcify and be related to parenchymal distortion, cicatricial atelectasis and traction bronchiectasis [44]. Severe fibrosis, with upper lobe volume loss and hilar retraction is seen in up to 29% of the cases [29,31]. An apical opacity (the “apical cap”) is seen in 41% of patients, corresponding to pleural thickening, extrapleural fat deposition and subpleural atelectatic and fibrotic lung, as shown by CT studies [29] (Fig. 13). Whereas active infection correlates better with “exsudative” lesions or cavitations [31], “fibroproliferative” lesions may also indi-



Fig. 12. Parenchymal involvement: poorly-margined nodular opacities in the upper lobes, some of them showing confluence, are shown on chest plain film.

cate active disease; the stability of radiographic findings for a period longer than 6 months is the best indicator of disease inactivity, but the radiologist should perhaps use the term radiographically “stable” than “inactive” or “healed” [29]. Sometimes, TB may manifest as a mass-like lesion, usually in the middle or lower lobes, which cannot be distinguished from a neoplasm based solely on imaging studies [15].

Tuberculous cavitation usually indicates a high likelihood of activity [42]. Cavitation is seen on chest plain films in about 50% of the patients at some time during the course of the disease, but chest CT is more accurate in its detection, particularly in cases complicated by architectural distortion [45,46]. Single or multiple cavities are more frequently seen in MDR TB [33]. Cavities are present, in general, at multiple sites, within areas of parenchymal consolidation, and may reach several centimetres in size [31]. Their walls are initially thick and irregular, and progressively become thin



Fig. 13. Parenchymal disease: chest film shows evidence of significant volume loss in the right upper lobe, along with hilar retraction, cavitation and an “apical cap”. There is also calcified mediastinal and hilar adenopathy.

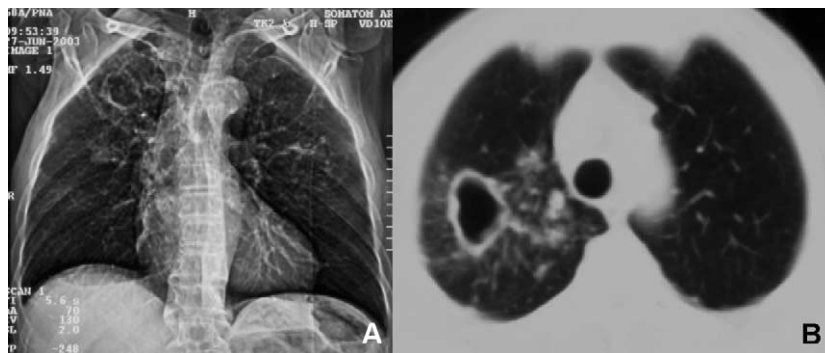


Fig. 14. Parenchymal consolidation and cavitation: (A) CT scout film and (B) CT show multiple small nodules in both lungs, with a thin-walled cavitation in the right upper lobe.

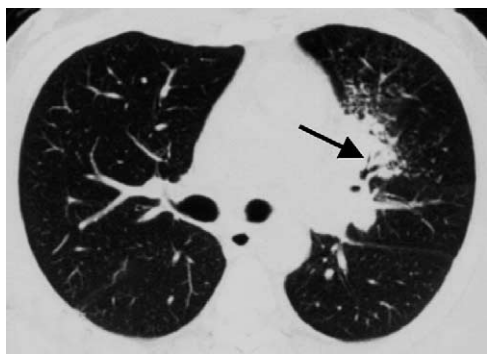


Fig. 15. Bronchogenic spread: HRCT shows wall thickening of the anterior segmental bronchus of the left upper lobe (arrow) and multiple centrilobular nodules. There is also left hilar adenopathy.

and smooth (Fig. 14); with healing, they balloon into large emphysematous spaces [45] and resolve with or without scarring [8]. Air–fluid levels in cavities can be due to superimposed infection by bacteria or fungi [31,46]; however, even in non-complicated, non-infected cavities, air–fluid levels may be found in 9–22% of cases [47]. The differential diagnosis of cavities includes bullae, cysts, pneumatoceles or cystic bronchiectasis [48].

Bronchogenic spread is the most common complication of tuberculous cavitation, being detected radiographically in as much as 20% of cases, and appearing as multiple ill-

defined micronodules, distributed in a segmental or lobar fashion, usually distant from the cavity site and involving lower lung lobes [47] (Fig. 15). HRCT is probably the most sensitive imaging method for the detection of bronchogenic spread of TB, which can be identified in up to 98% of cases. Findings include centrilobular nodules 2–4 mm in size and sharply marginated linear branching opacities (representing caseating necrosis within and around terminal and respiratory bronchioles), the so-called “tree-in-bud” sign, indicating active disease and corresponding to tuberculous bronchitis of the small airways [45] (Fig. 16). The same lesions, however, when surrounded by airless consolidation, may appear as fluid bronchograms [49]. Five to eight-mm poorly marginated nodules, lobular consolidation and interlobular septal thickening are among the other HRCT features in bronchogenic spread [45]. Healing with scarring, residual nodules and parenchymal or endobronchial calcification are found in 30% [44]. Air trapping due to residual bronchiolar stenosis leads to areas of hypoattenuation; when associated with architectural distortion, this finding usually represents paracatricial emphysema [45].

In few cases (3–6%) of postprimary TB, tuberculomas are the predominant parenchymal finding [43] but they represent, most times, healed primary disease. These lesions appear as rounded or oval sharply marginated opacities, measuring 0.5–4 cm in size (the majority remains stable in time), generally solitary and calcified (Fig. 17). Tuberculomas have ad-

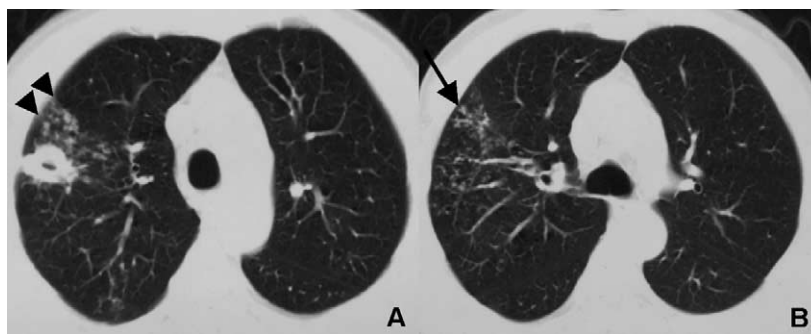


Fig. 16. Bronchogenic spread: CT (A) irregular and thick-walled cavity in the anterior segment of the right upper lobe and scattered small nodules (arrowheads) and (B) branching opacity in the peripheral lung (arrow) corresponding to dilated bronchioli filled with infected material (“tree-in-bud”).

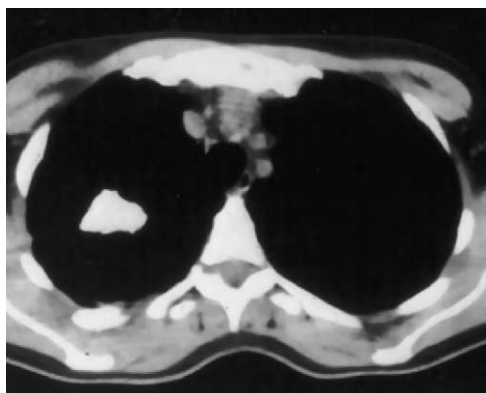


Fig. 17. Tuberculoma: a well-defined, totally calcified nodule with 4 cm in size in the right upper lobe is shown on CT.

adjacent small rounded opacities (“satellite” nodules) in proximity in 30% of the cases [32]. On contrast-enhanced CT, tuberculomas may exhibit a ring-like or a central curvilinear enhancement, with the enhancing area corresponding to a fibrous capsule, whereas the non-enhancing area corresponds to caseating or liquefactive necrosis [33].

Miliary disease is seen less frequently in postprimary than in primary TB [15]. The characteristic radiographic pattern of multiple micronodules, scattered through both lungs, is sometimes unseen until late in the disease, but characteristic features of active TB (consolidation, cavitation, lymphadenopathy) coexist in up to 30% of the patients [50]. HRCT can detect miliary disease before it becomes apparent on chest plain films [51], demonstrating both sharply and poorly defined 1–4 mm nodules, randomly distributed, often with associated intra- and interlobular septal thickening and areas of ground-glass opacity [51,52] (Fig. 18). Differential diagnosis includes carcinomatous lymphangitis, bronchiolitis, pneumoconiosis or metastasis [37,52].

After postprimary TB, cicatricial atelectasis is relatively common. Up to 40% of the patients have a marked fibrotic response, with atelectasis of upper lobes, hilar retraction, hyperinflation of lower lobes, and mediastinal shift towards the affected lung [11]. Extensive parenchymal destruction (the “destroyed lung”) is sometimes the end-stage of postprimary

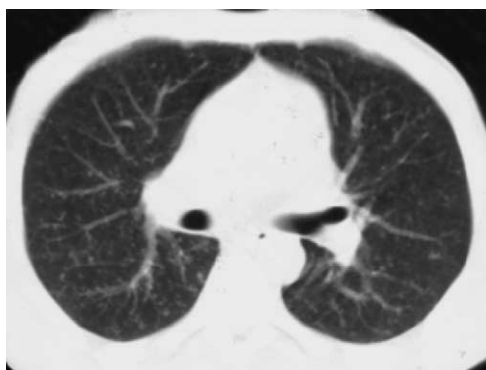


Fig. 18. Miliary TB: HRCT reveals multiple widespread 1–2 mm nodules, some of them in a perivascular distribution.



Fig. 19. Tracheobronchial TB: on CT scout film, a stenosis of the right main bronchus, due to direct extension from tuberculous lymphadenitis, is seen (arrow).

TB, causing some difficulties in the assessment of the disease activity based solely in radiographic criteria [48]. Besides, secondary pyogenic or fungal infection may appear [11].

Mediastinal or hilar lymphadenopathy is also rarer in postprimary disease (5% of patients), usually associated with parenchymal disease and cavitation [29].

4.2.2. Tracheobronchial TB

Tracheobronchial TB is more frequently seen as a complication of primary disease, but also occurs in the setting of postprimary disease. Bronchial stenosis occurs in 10–40% of patients and is caused by direct extension from tuberculous lymphadenitis, by endobronchial spread or by lymphatic dissemination [30] (Fig. 19). Whereas active disease involves right and left main bronchi with equal frequency, fibrotic disease more commonly affects left main bronchus [38]. On plain films, findings include segmental or lobar atelectasis, lobar hyperinflation, mucoid impaction and obstructive pneumonia [30]. CT is more accurate and can show bronchial narrowing (generally of a long segment) with irregular wall thickening, luminal obstruction, and extrinsic compression by lymphadenitis in the setting of acute disease [30,38], whereas in fibrotic disease, the wall becomes smooth and thinner. These findings must be distinguished from bronchogenic carcinoma involving the central airways [38]. Bronchiectasis commonly complicates endobronchial TB, most often occurring as a paracatricial process (traction bronchiectasis), but also due to central bronchostenosis and distal bronchial dilatation. Upper lobes are more frequently involved [44]. Tracheal and laryngeal TB are rarer than endobronchial disease [42].

4.2.3. Tuberculous pleuritis

Pleural disease is most often associated with primary TB, but it may occur in postprimary disease. Small unilateral effusions, associated with parenchymal disease, are detected in up to 18% of patients [29]. Their resolution may occur



Fig. 20. Tuberculous pleuritis: a right-sided, organized pleural effusion is shown on chest plain film.

with residual thickening or calcification, as in primary disease [32]. Contrast-enhanced CT scans in postprimary TB effusions show smoothly thickened visceral and parietal pleural leaflets, the so-called “split-pleura” sign [53]. Effusions are typically loculated and may be stable in size for several years (Fig. 20).

4.2.4. Complications

Bronchiectasis and residual cavities are sequelae typically found in the upper lobes, recognized in 71–86% and 12–22%, respectively [54]. Fungal organisms, especially *Aspergillus* species, can colonize those spaces, particularly the latter. An early radiographic sign of fungal colonization is thickening of the cavity wall or the adjacent pleura [11]. On plain films, an aspergilloma (a fungus ball) appears as a rounded nodule separated from the cavity wall by a crescent-shaped hyperlucent image (“air-crescent sign”) [55]. CT features are those of a spherical intracavitary nodule or mass, partially surrounded by air or occupying the whole cavity [56], that may show mobility towards the dependent position on prone and supine scans [7] (Fig. 21). The most important consequence of aspergillomas, occurring in 50–70%, is haemoptysis [55].

A Rasmussen aneurysm is a pseudoaneurysm of a pulmonary artery caused by erosion from an adjacent tuberculous cavity [57], found in about 5% of patients [11] and presenting with haemoptysis, sometimes massive [58]. Radiographic features include an enlarging mass or a rapidly appearing parenchymal opacity representing haemorrhage [57].

Broncholitiasis is an uncommon complication, resulting from rupture of calcified lymphadenopathy into an adjacent bronchus, with a right-sided predominance. Radiographic manifestations include a change in the position or disappearance of a calcification on serial films, development of airway obstruction, or expiratory air trapping. CT can show, apart from endobronchial or peribronchial calcified nodes, segmental or lobar atelectasis, obstructive pneumonitis, branching linear opacities (obstructive bronchoceles), focal hyperinflation and bronchiectasis [59].

Hilar and mediastinal infected lymph nodes may become fibrocaceous granulomas and coalesce, forming tuberculous granulomas. These, in turn, may lead to reactive fibrous changes and to acute inflammation of the mediastinum. If the first predominate, the result is fibrosing mediastinitis and if the latter is more relevant, tuberculous mediastinitis is the outcome [60]. Both are, however, uncommon [39]. Radiographic findings are similar to those of mediastinal tumours, but there may also be a hilar mass or a pleural effusion. On CT, a cluster of enlarged homo- or heterogeneously enhancing lymph nodes suggests the diagnosis [60] (Fig. 22); sometimes these nodes appear as a mediastinal or hilar mass, often with calcification [39]. Other findings include tracheobronchial narrowing, pulmonary vessel encasement, superior vena cava obstruction and pulmonary infiltrates [39], the latter due to bronchial obstruction (with resulting obstructive pneumonia or atelectasis) or vascular obstruction (leading to infarction) [61]. However, CT cannot always differentiate tuberculous mediastinitis from mediastinal neoplasms [60]. Magnetic resonance imaging (MRI) can demonstrate areas of low signal intensity on T1-weighted images, due to the presence of fibrous and inflammatory tissue. Fibrosis may also be hypointense on T2-weighted sequences, whereas inflammatory and granulomatous tissue enhances on gadolinium-enhanced T1-weighted images [62]. Differential diagnosis

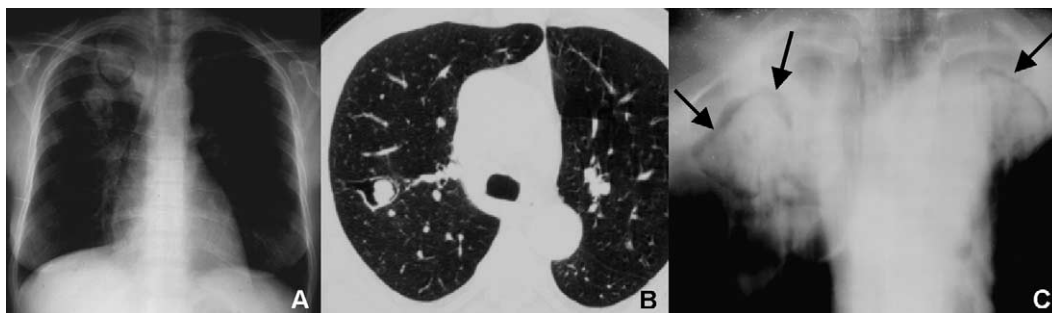


Fig. 21. Aspergilloma: (A) chest film shows two cavities, partially occupied by fungus balls, in the right upper lobe developed within an area of consolidation, (B) HRCT demonstrates a thin-walled cavity in the right upper lobe colonized by an aspergilloma and (C) on conventional tomography (detail), intracavitary nodular opacities are present in both upper lobes, separated from the cavity wall by a crescent of air (arrows).

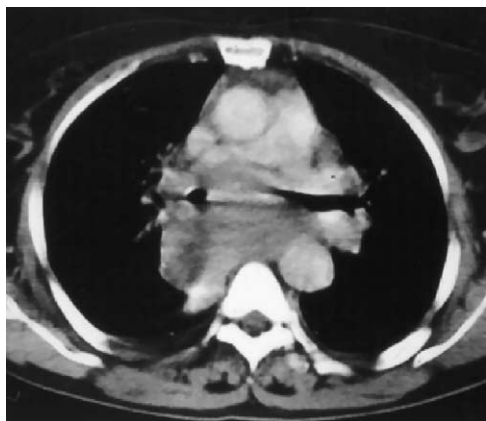


Fig. 22. Tuberculous mediastinitis: a cluster of enlarged homogeneous lymph nodes in the mediastinum is detected on CT.

includes sarcoidosis, lymphoma, metastatic neoplasms, thymoma, thymic carcinoma and malignant teratoma [60].

Tuberculous pericarditis is a complication of about 1% of patients with TB, presenting either as a pericardial effusion, due to exsudation of fluid with cellular proliferation, or pericardial thickening, due to fibrin production and formation of granulation tissue. CT is now the method of choice for the evaluation of the pericardium, but in the near future may be overtaken by MRI [63]. Pericardial thickening (>3 mm) in the suggestive clinical setting indicates the presence of constrictive pericarditis, which occurs in 10% of patients with tuberculous pericardial involvement [39]. Secondary signs include inferior vena cava dilatation (>3 cm in diameter) secondary to right-sided heart failure, and angulation or tortuosity of the interventricular septum probably due to restriction of pericardial expansion. Other associated signs are the presence of pericardial fluid in the acute form, whereas in the sub-acute phase there is gradual absorption of fluid and caseation occurs, resulting in purulent pericarditis and pericardial thickening. Purulent pericarditis is probably secondary to infected lymph nodes, and the lesions predominate along the right border of the heart. In the chronic phase an irregularly thickened and often calcified pericardium, without pericardial fluid, is seen [63] (Fig. 23). Pleural effusions are secondary to the associated haemodynamic abnormality [63] and right atrial thrombi are due to intracardiac stasis of blood.

Pneumothorax occurs in 5% of patients with postprimary disease, usually in the presence of severe cavitation. It heralds the onset of bronchopleural fistula and empyema [11]. When tuberculous pleurisy is localized (1–4% of the cases), a tuberculous empyema ensues, which presents radiographically as a loculated collection of fluid associated with parenchymal disease [29,48]. On CT, a focal fluid collection with pleural thickening and calcification, sometimes associated with extrapleural fat proliferation, is seen [11] (Fig. 24). Empyema may communicate with the skin – pleurocutaneous fistula (empyema necessitatis) – or with the bronchial tree—bronchopleural fistula, manifested by an air–fluid level in the pleural space; CT demonstrates the communication be-



Fig. 23. Tuberculous pericarditis: chest film demonstrates marked pericardial calcification (arrow). There is also bilateral pleural thickening with calcification of the left pleura (arrowhead).

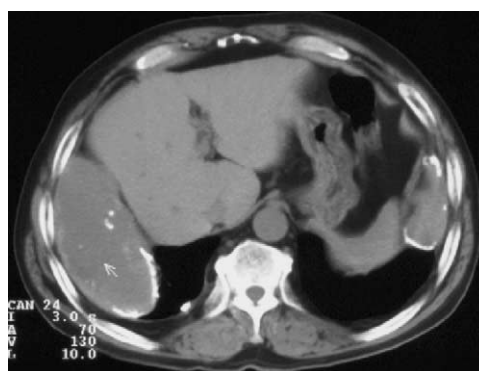


Fig. 24. Empyema: CT shows bilateral organized fluid collections with pleural calcification and extrapleural fat proliferation on the right side.

tween the pleural space and the bronchial tree [64] (Fig. 25). Untreated empyema may also lead to bone destruction, as well as to pleural thickening and calcification [35,48]. There are also reports about the association of chronic empyema and malignancy, more commonly lymphoma, squamous cell carcinoma and mesothelioma, presumably due to the oncogenic action of chronic inflammation and of substances contained

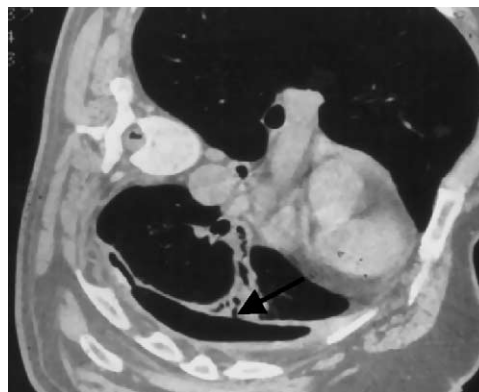


Fig. 25. Bronchopleural fistula: CT demonstrates a dilated airway, which communicates directly with an air–fluid collection in the left pleural space (arrow). Note also thickening of both visceral and parietal pleural leaflets.

in the pleura. Radiographic findings include increased thoracic opacity, soft-tissue bulging and blurring of fat planes in the chest wall, bone destruction and medial shift of the calcified pleura. CT can demonstrate a soft-tissue enhancing mass around the empyema [65].

Pulmonary TB may favour the development of bronchogenic carcinoma due to the oncogenic effects of chronic inflammation and fibrosis (“scar carcinoma”) [44]. Lung cancer, on the other side, may lead to reactivation of TB by eroding quiescent foci or by suppressing cellular immunity. The other possible scenery is that TB and bronchogenic carcinoma might be coincidentally associated [15]. Radiological features that suggest neoplastic disease in patients with postprimary TB include: progressive disease despite adequate anti-tuberculous therapy, hilar and/or mediastinal lymphadenopathy, focal mass larger than 3 cm in size and cavities with nodular walls [66].

5. Atypical patterns

A chronic progressive parenchymal disease is observed in 5–10% of patients with primary disease. It is commonly seen in young children, teenagers, patients with T-cell immunodeficiencies and black people, in which the acquired immunity is inadequate to contain the primary infection. The radiological picture of progressive primary TB is similar to that of postprimary disease [67]. Multilobar involvement with more extensive lesions and lung necrosis is common [8], and in some cases, destruction of a major part of a lung may result [67]. Involvement of the secondary foci within the upper lobes is frequently observed. Endobronchial spread may result from cavitation of the tuberculous pneumonia or rupture of diseased lymphadenopathy into bronchi, and haematogenous spread may also occur [37].

In elderly individuals, in whom the cellular immune response is altered, the presentation of TB shifts away from the expected typical radiographic findings of postprimary disease (apical infiltrates and cavities) towards atypical presentations, similar to those found in children (basal infiltrates,

mediastinal and hilar adenopathy and exsudative pleuritis), which may be due to exogenous reinfection or to a true first infection [68].

Impaired host immunity, predisposing to TB, is also found in diabetic patients or patients who are immunocompromised as a result of corticosteroid therapy or malignancy. In these patients, a higher prevalence of non-segmental distribution and multiple small cavities within a tuberculous lesion than in patients without underlying disease was detected [69]. Some authors also stress that in diabetic patients the involvement of the lower lung zones and the anterior segments of the upper lobes by TB is more frequent than in non-diabetic subjects [47] (Fig. 26).

With the epidemics of AIDS, TB infection is increasing in HIV-positive individuals, since the virus-induced immunosuppression is a potent risk factor for TB [11]. Following primary infection, AIDS patients can have massive haematogenous dissemination and consequently a more fulminant evolution of disease. After infection, the risk of developing progressive primary TB in the first year is about 30%, as compared with 3% in immunocompetent individuals [70]. HIV-infected patients are also predisposed to reactivation of the disease, due to deficient cellular immunity. In fact, even though a fraction of pulmonary TB cases in HIV-positive patients represents primary disease, it is believed that most of TB cases in HIV patients are due to reactivation of latent infection, corresponding to postprimary disease [71]. Radiographic presentation in these patients, however, is more typical of primary than of postprimary disease [20,71,72] and is dependent on the level of immunodepression at the time of overt disease [73,74]. A CD4 T-lymphocyte count of 200 mm^{-3} is considered the cut-off between those subjects who may respond in a typical or atypical manner to *M. tuberculosis* infection and indicates those at risk for atypical radiographic presentation of TB in HIV-positive patients [75]. Patients with a relative preservation of cell-mediated immunity have findings similar to those without HIV infection. Indeed, the typical postprimary pattern of disease is seen less frequently as immunodepression becomes more pronounced [20]. Cavitory disease, pulmonary infiltrates and pleural effusions are usually asso-

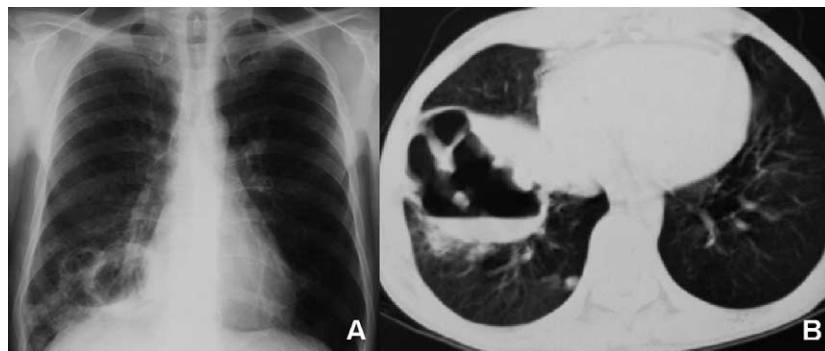


Fig. 26. TB in a 44-year-old diabetic man: (A) chest film and (B) CT show a huge cavity, with thick and irregular walls and an air–fluid level, in the right lower lobe.

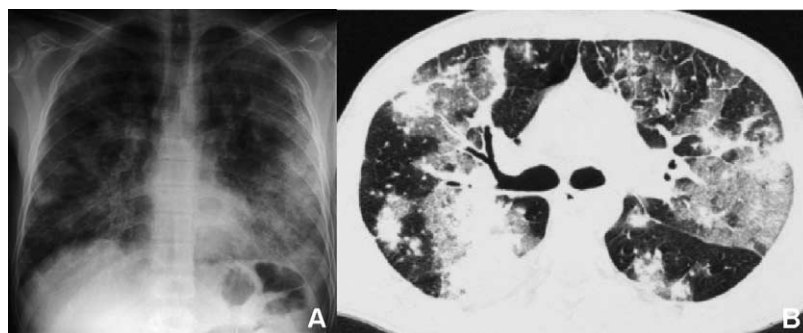


Fig. 27. TB in a 28-year-old HIV-positive man: (A) chest film reveals ground-glass opacities and areas of airspace consolidation and (B) on HRCT, the same abnormalities are found, along with interlobular septal thickening.

ciated with higher CD4 T-lymphocyte counts [73] (Fig. 27). At severe levels of immunosuppression, 10–40% of patients have normal chest plain films [72,75–77]; therefore, normal radiographic findings in patients with AIDS and *M. tuberculosis* infection do not exclude active disease [77]. Other severely immunocompromised patients present with radiographic aspects found in primary disease, regardless of prior *M. tuberculosis* exposition status [71]. A higher prevalence of non-apical parenchymal infiltrates and hilar or mediastinal adenopathy and a lower prevalence of cavitary disease is found in patients with a CD4 T-lymphocyte count of less than 200 mm^{-3} [73,75]. Another feature related to severe immunosuppression is miliary disease [76]. Extrapulmonary locations are common in HIV-infected patients. Those with a normal chest film, positive sputum and disseminated disease are said to have cryptogenic miliary TB [78]. CT features of TB in HIV-positive patients with normal plain films are usually subtle and include single or multiple nodules measuring 1–10 mm in diameter and lymphadenopathy [76], reflecting the low sensitivity of plain films in the evaluation of AIDS-associated TB [77]. Among the most frequent findings in HIV-infected patients are nodular opacities, with an endobronchial or miliary pattern in 57% and 17% of patients, respectively [76]. Lymphadenopathy is found in 19–74% of the cases [71,76,77], most often in the right paratracheal and subcarinal regions [76] and may also exhibit the characteristic peripheral rim enhancement and central hypodense area, as in immunocompetent patients [25,76].

Myelodysplastic syndromes (MDS) are a group of blood disorders characterized by ineffective hematopoiesis and, consequently, pancytopenia. There are also defects in the lymphoid system, resulting in impaired cell-mediated immunity, which may predispose to *M. tuberculosis* infection. Patients with TB and MDS show a radiological pattern similar to that seen in patients with AIDS, commonly exhibiting a primary pattern and frequent extrapulmonary involvement [79].

Silicosis, as any pneumoconiosis, carries an increased risk of TB, possibly due to the saturation of macrophages by silica particles [80]. Radiological differential diagnosis between the two is difficult: in the former, miliary nodules predom-

inate in the upper zones, whereas in TB they may occur everywhere. In cases where the two diseases coexist (silicotuberculosis) it is sometimes impossible to recognize the underlying pathological process. Adenopathy suggests TB, but it is also present in silicosis (with “egg-shell” calcification). Fibrotic conglomerate masses (massive fibrosis) in the upper lung favours silicosis [81]. Some authors also report an increased prevalence of TB in patients with sarcoidosis [46].

6. Follow-up

In patients undergoing adequate antituberculous chemotherapy, a transient worsening of pre-existing lesions or appearance of new ones may occur, what is known as “paradoxical response”. Among the findings are the enlargement or new appearance of lymph nodes, the development of new pulmonary infiltrates or progression of those previously existing and the development of pleural effusions. The transient worsening does not mean a therapeutic failure but instead disappears with continuation of the same medication [82]. It is now recommended that a radiographic evaluation be made at 2–3 months after initiation of therapy [83]. Parenchymal abnormalities can be subsequently evaluated every 2–3 months until clearance, and lymphadenopathy can be followed every year until radiographically stable [84].

7. Specific forms of treatment

Plombage was a type of pulmonary collapse therapy used for treatment of TB prior to the advent of antituberculous drugs and consisted in the insertion of plastic packs (Lucite balls) or polythene spheres in the pleural space [42] (Fig. 28). Injection of oil or paraffin (oleothorax) was also performed [48].

Control of haemoptysis may be achieved with bronchial embolization in cases of cavitary disease, bronchiectasis, Rasmussen aneurysms or aspergillomas. In the latter, the intracavitary injection of antifungal agents under CT guidance is sometimes performed.

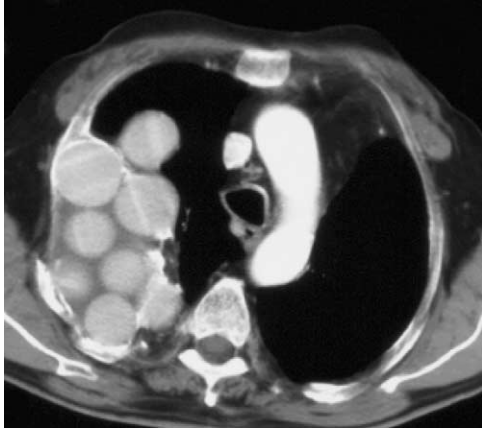


Fig. 28. Treatment of TB: CT shows the presence of right-sided Lucite ball plombage.

8. Radiographic screening

The screening of TB with chest plain films aims to identify individuals with active disease [9]. Radiological screening has higher efficacy than sputum examination for detecting pulmonary TB, especially when the disease is clinically inapparent; chest plain films are recommended as effective screening devices for pulmonary TB in populations in which the prevalence of the disease is high [85]. Some authors advocate performing chest films in all HIV-positive contacts of persons with positive skin tests as well as in patients selected to undergo chemoprophylaxis to rule out active TB [72].

A normal chest plain film has a high negative predictive value for the presence of active disease. Whereas the rate of false positive cases approaches 1% in immunocompetent individuals [47,68], this frequency increases to 7–15% in HIV-infected patients [76,77].

Temporal evolution allows radiographic distinction between active and inactive disease. An absence of new radiographic findings over a period of 4–6 months is a reliable indicator of inactive disease [13,43].

9. Conclusions

The chest plain film is the mainstay in the radiological evaluation of suspected or proven pulmonary TB. CT is useful in the clarification of certain confusing findings and some typical features should suggest the diagnosis; CT may also be helpful in the determination of disease activity.

Primary TB is increasingly seen in the adult population. It generally manifests as a parenchymal consolidation, which can affect any lobe. Associated hilar and/or mediastinal adenopathy is more frequent in children than in adults. Lymphadenopathy alone is unusual.

Postprimary disease is characterized by parenchymal infiltrates in the upper lung, generally in association with cavitation. Cavitory disease is associated with several complica-

tions (endobronchial spread, haematogenous dissemination, pseudoaneurysm formation). Lymphadenopathy is rare.

Pleural involvement is more frequent in primary TB. Exudative pleural effusions are large and unilateral. Miliary TB is also more often found in association with primary than with postprimary disease.

However, the radiological presentation of TB is changing, with fading of the classical distinction between primary and postprimary disease. Atypical patterns are more frequent, especially in elderly and immunocompromised patients. In these groups, there is a lower prevalence of consolidation, cavitation and postprimary pattern and a higher prevalence of lymphadenopathy and miliary disease in comparison with immunocompetent subjects.

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