EXTRA-MUCOSPULMONARY TUBERCULOSIS

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Resumen

La tuberculosis (TBC) continúa siendo un importante problema de salud pública a nivel mundial y una causa significativa de enfermedad y muerte en muchos países. El incremento de la prevalencia en las últimas décadas se debe al aumento en el número de pacientes inmunocomprometidos, frecuentemente con afectación extra-pulmonar. Dado que puede comprometer cualquier parte del cuerpo humano, es una de las entidades a tener en cuenta entre los diagnósticos diferenciales, sea cual fuera el área afectada. Así, la diversidad de los hallazgos radiológicos de la TBC dificulta reconocer esta entidad y realizar su diagnóstico. El compromiso extra-pulmonar se presenta en el sistema músculo esquelético y el área más afectada es la columna vertebral. En el sistema nervioso central adquiere varias formas que incluyen meningitis, tuberculoma, absceses, cerebritis y miliary spread de mycobacterium tuberculosis. Ileocecal involvement is present in 80-90% of cases of gastroin-

Abstract

Tuberculosis (TB) remains a major public health problem worldwide and a significant cause of illness and death in many countries. The increasing prevalence in recent decades is due to the increase in the number of immunocompromised patients, often with extrapulmonary conditions. Since it can involve any part of the body, it is one of the entities to be considered in the differential diagnosis, whatever the affected area is. The diversity of radiological findings of TB makes it difficult to recognize this entity and provide a diagnosis. Extrapulmonary involvement occurs in the musculoskeletal system and the most affected area is the spine. In the central nervous system, it acquires several forms including meningitis, tuberculoma, abscesses, cerebritis and miliary spread of mycobacterium tuberculosis. Ileocecal involvement is present in 80-90% of cases of gastroin-
Extrapulmonary tuberculosis

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Introduction

Tuberculosis (TB) is generally associated with the involvement of the respiratory system; however, it can affect any organ. Its increasing prevalence is related to the increase in the number of immunocompromised patients and the resistance to pharmacologic treatment. These determining factors make TB an important entity that has to be taken into account in the diagnosis, especially in developing countries. This article presents the most frequent radiological findings of extrapulmonary TB.

Musculoskeletal system

TB of the musculoskeletal system represents up to 35% of cases of extrapulmonary tuberculosis. However, only 1-3% of all cases of TB show this type of involvement and less than 50% have evidence of concomitant active thoracic TB (1, 2). The most frequent forms of presentation are spondylitis, arthritis, and osteomyelitis. Bone conditions and joint destruction cause a severe morbidity. Vertebral involvement causes severe neurological consequences (2).

Spondylitis (Pott disease)

In the musculoskeletal system, the most affected site by TB is the spine, and the most affected levels are the lower dorsal region and the upper lumbar region. Generally, it involves more than one vertebral body, although isolated involvement of one vertebra can be observed. It is believed that the process is a result of homogeneous dissemination through venous plexus. The infection starts in the anterior part of the vertebral body adjacent to the inferior plates, followed by demineralization of the vertebral plate with a loss of image definition and extension towards the adjacent intervertebral disc. The alteration of the internal structure of the disk allows the dissemination towards the contiguous vertebral segment, resulting in the classical pattern of more than one vertebral body with intervertebral disc involvement (Figures 1a and 1b). The infection can also extend towards paravertebral tissue, creating muscle abscesses (Figures 1c and 1d), including the psoas muscle (Figure 2). A delay in treatment can cause vertebral collapse or anterior wedging of the vertebral body with formation of a hump. As a consequence of treatment, there can be ankylosis of the affected segment. The...
differential diagnosis includes metastatic disease, pyogenic infection, brucellosis, mycosis, and sarcoidosis. The main difference with metastasis lies in the lack of frequency with which TB involves posterior vertebral elements. In initial stages, it is difficult to differentiate the involvement of pyogenic infection due to TB and, therefore, it is essential to consider the clinical evolution of the patient to differentiate the conditions (3).

**Arthritis**
The tuberculous arthritis is a monoarthritis that progresses slowly and compromises the joints that support weight, such as the hip and knees. The dissemination is produced from a focal point of diaphyseal osteomyelitis that goes through the metaphysis and opens towards the joint. With less frequency, it disseminates hematogenously towards the synovial membrane. Radiological findings are unspecific and similar to other types of inflammatory or infectious arthritis with osteopenia, synovitis, soft tissue inflammation, marginal erosion mainly at the synovial insertion, partial destruction of the cartilage, and decreased articular space in later stages. In young patients, synovial compromise causes hyperemia and epiphyseal overgrowth. The progression of the infection can cause bone sequestration. The final result is fibrous ankylosis of the joint. The clinical presentation is insidious and causes pain, joint edemas and a decrease in the range of movement. Diagnosis is established due to clinical evolution, mild sclerosis compared to other entities, limited periosteal reaction and lack of alterations in the articular space in later stages. The differential diagnosis includes pyogenic and fungal infection.

**Osteomyelitis**
Extrapulmonary tuberculosis osteomyelitis often appears with local pain and can affect any bone, mainly the femur, the shinbone or the bones of hands and feet. Generally, it appears with osteolytic lesion and minimal sclerosis at the level of metaphysis (Figure 3). Also, it can cause bone destruction, bone sequestration and extension to soft tissues. The involvement of adjacent structures can lead to complications such as carpal tunnel syndrome, tenosynovitis and facial paralysis (5). Tuberculous osteomyelitis without associated arthritis is not frequent.

**Central Nervous System**
Around 5% of patients with TB have CNS compromise, although this prevalence increases in immunocompromised patients. Generally, dissemination occurs hematogenously and can manifest itself as a meningoencephalitis, communicating hydrocephalus, tuberculoma, tuberculous abscess or cerebritis (1).

**Meningoencephalitis**
Meningeal TB is the most common manifestation of the central nervous system. Its early diagnosis is essential due to the associated morbidity and mortality. Dissemination can be hematogenously or through direct extension of CSF. A typical finding is meningeal enhancement with intravenous contrast, more marked in basal cisterns, cerebral convexity and Sylvian fissures (Figure 4). The most frequent complication is communicating hydrocephalus and ischemic stroke due to vascular compression and occlusion of small puncturing vessels (6) (Figure 5). Radiological findings are unspecific and the differential diagnosis is done with other infectious agents, sarcoidosis and neoplastic involvement.

**Tuberculoma**
The most frequent lesion of the cerebral parenchyma is tuberculoma or tuberculous granuloma. It can be isolated or multiple and its most frequent location is frontal or parietal. They appear as nodules or rounded masses of variable density in CT with homogenous enhancement or ring enhancement after contrast administration (Figure 6). In some cases, there is a target sign due to the presence of a central calcification. The appearance in MRI depends on the level of central caseous necrosis showing a hyperintense center in case of liquid content. Perilesional edema is variable and generally less than the metastatic lesions. Tuberculomas can be associated with meningoencephalitis (7).

**Tuberculous abscess**
Tuberculous abscess are masses with a multiloculated liquid center, heterogeneous enhancement after contrast administration, severe edema and mass effect. The differential diagnosis includes other abscesses of infectious origin.
Abdominal tuberculosis

Gastrointestinal TB

Gastrointestinal compromise is rare and the ileocecal region is the most affected (80-90%). Typically, it is presented with concentric parietal thickening of the cecum wall, terminal ileum and ileocecal valve (Figure 7). It can cause a luminal stenosis with intestinal occlusion, dilation of loops and appear with regional mesenteric adenopathy. When the disease is advanced, there can be deformity, stenosis, shortening or retraction of the intestine. Differential diagnosis is made with adenocarcinoma, intestinal inflammatory diseases, amebiasis and Behçet’s disease (8).

Hepatosplenic TB

This form of presentation generally occurs in patients with disseminated disease and can adopt a micro- or macro-nodular pattern. The micro-nodular or miliary form is seen in patients with miliary lung TB. It appears with dispersed small nodules measuring less than 2 mm. They can be seen with MRI but they may not be seen with CT. Differential diagnosis is made with metastasis, mycosis or sarcoidosis (Figure 8). Macronodular form is rare and it is also called tuberculoma. It can be isolated or multiple, it measures from 1 to 3 cm, it is hypodense in CT, hypointense in T1 and hyperintense in T2. Enhancement is variable, but most frequently marginal. Differential diagnosis is made with metastasis, primary neoplasia or pyogenic abscesses (9).

Peritoneal TB

Frequently, peritoneal involvement is associated with other types of gastrointestinal tuberculosis. Dissemination can be hematogenously or direct. The most frequent form of presentation is with great amount of free liquid or loculated viscous fluid, omental and mesenteric multinodular thickening simulating a peritoneal carcinomatosis. There is also a fibrotic retractable form with mesenteric thickening and intestinal adhesions (10) (Figure 9).

Figure 1. Spondylitis due to TB.

Images of the cervical rachis. MRI in T1 (A) and STIR (B). CT with contrast (C and D). Hyperintense signal of bone marrow in C6, C7 and intervertebral disc in A and B (arrows). Large paravertebral collection (C) and lytic involvement of vertebral bodies (D) (arrows).
Figure 2. CT of lumbar spine. Osteolytic lesion due to TB (A) and small abscess of the left psoas muscle (B) (arrows).

Figure 3. Tuberculous osteomyelitis in CT. Metaphyseal lytic lesion in the medial end of the left collarbone (A) with a collection of fluid (B) (arrows).

Figure 4. Meningoencephalitis. Sagittal T1 with contrast (A) and FLAIR (B). There is meningeal enhancement and thickening in cerebral convexity (A) and right parietal edema (B) (arrows).
figure 5. skull CT without contrast.
Communicating hydrocephalus in patient with tuberculous meningitis.

figure 6. skull CT with contrast in two patients with tuberculoma (A and B).
Intraparenchymatous nodules with annular enhancement and scarce perilesional edema (arrows).

figure 7. abdominal CT with contrast in patient with ileocecal TB.
Concentric ileocecal parietal thickening and node with necrotic center in the root of the mesenterium (arrows).
Genitourinary system

Renal TB
Frequently, renal compromise is unilateral in 75% of patients in its initial presentation. It appears as a cortical caseous lesion with destruction of the tissue. Generally, it is self-limited. In other occasions, it evolves progressively adopting the following patterns:

1- Nodular form: It is similar to tuberculoma in other locations; however, it is rare (Figure 10).

2- Cavitary exudate/caseous form: It is the most frequent and it is characterized by caseous necrosis and a tendency to open towards the calyx or renal pelvis.

3- Mastic kidney: It represents the natural healing of renal TB. It is also called retractable fibro-caseous renal tuberculosis and corresponds to the destruction of the renal parenchyma after accumulation of caseous material due to ureter obstruction of inflammatory origin.

Radiological findings include erosion of calyces that is evident in excretory phase, hydronephrosis of irregular margins, filling defects due to caseous material, and cavitation of the renal parenchyma. In later stages, more than 50% of the cases present lobar calcifications, scars and retractions (11).

Ureteral TB
Dilation and irregular appearance of urothelium are the first signs of ureteral TBC. Ureteral dilation is caused mainly by an inflammation of the uretero-vesical union due to urethritis or tuberculous cystitis. In later stages there can be areas of stenosis, shortenings, filling defects or calcifications (11) (Figure 11).

Vesical TB
Tuberculous cystitis in initial stages does not present specific characteristics, although in later stages it can...
be small, irregular and calcified. Differential diagnosis is made with schistosomiasis, actinic changes or calcified carcinoma (11) (Figure 12).

**Female genital TB**
Female genital TB compromises the fallopian tubes in 94% of the cases and can disseminate towards peritoneum, endometrium, ovaries, cervix, and vagina. Patients have pelvic pain, present infertility and vaginal bleeding. Tubo-ovarian abscesses with intra- or extra-peritoneal extension are suggestive of tuberculosis (12).

**Male genital TB**
The most affected organ by TB is the prostate. Ultrasound shows hypoechoic areas with an irregular pattern that predominates in the peripheral region. Lesions are hypodense in CT, and they cannot be differentiated with pyogenic prostatic abscesses or neoplasia. To be able to do it, MRI is the most useful means due to its high contrast definition (12).

**Lymphatic system**
Adenopathy is a frequent form of presentation in extrapulmonary TB, especially at the cervical and supracervical level in pediatric patients. CT shows adenopathic conglomerates with hypodense center due to caseous necrosis and marginal enhancement with intravenous contrast injection (13) (Figure 13).

**Other rare forms of presentation**

**Adrenal TB**
Generally, TB compromise is bilateral and asymmetrical with diffuse enlargement of the glands, creating big heterogeneous masses that are difficult to differentiate from metastasis. After treatment, the glands are stunted and there is diffuse calcification of them (Figure 14).

**Mammary TB**
Is a rare condition. Even though findings are unspecific, it can be seen as a hypoechoic mass of abscesses in ultrasound with moving internal echoes and posterior acoustic enhancement. In MRI, these abscesses are hypointense in T1, hyperintense in T2 and have peripheral enhancement (2).

**Laryngeal TB**
Radiological findings of laryngeal TB are thickening of soft tissues with infiltration of pre-epiglottic and para-laryngeal fatty space, which is impossible to differentiate from other inflammatory or neoplastic processes, such as lymphoma (14) (Figure 15).

**Ocular TB**
It is an infrequent condition and can compromise any component of the orbit. Habitual forms are chronic anterior uveitis, choroiditis and sclerokeratitis. However, choroidal tuberculoma is the best documented form of presentation (15) (Figure 16).

**Cutaneous TB**
Cutaneous presentation is not frequent and it is generally associated with disseminated disease. Infection can occur due to direct inoculation, which is rare, or hematogenously. Radiologically, they are seen as subcutaneous lesions with soft tissue density of unspecific aspect (16) (Figure 17).

**Pancreatic TB**
It is an atypical condition by TB and can simulate a carcinoma, lymphoma, cystic neoplasia, pancreatitis or pseudocyst. It affects immunocompromised patients and has multiple hypodense areas with marginal enhancement in the pancreatic parenchyma, with a tendency to present central liquefaction (17) (Figure 18).
**Figure 10. Abdominal CT with contrast.**
Small hypodense subcortical nodules in both kidneys with alteration of the nephrogram in patient with disseminated hematogenous tuberculosis (arrow).

**Figure 11. Abdominal CT with contrast.**
Coronal (A), sagittal (B) and axial (C) view. Left ureteral dilation with stenosis areas in the uretero-vesical union of tuberculous origin (arrows).

**Figure 12. Abdominal CT with contrast.**
Consequence of tuberculous cystitis with retracted bladder (arrow).
Figure 13. CT of three patients with adenitis due to TB.
Cervical and supracervical location (A and B); necrosis mediastinal location (C); and retroperitoneal location (D) (arrows).

Figure 14. Abdominal CT.
A) Increase in the size of the left adrenal gland of tuberculous origin and B) adrenal calcifications due to TBC (arrows).
Figure 15. Neck CT with contrast (A and B).
Concentric laryngeal thickening with involvement of the pre-epiglottic space due to TB in a pediatric patient (arrows).

Figure 16. Orbits CT with contrast.
Posterior focal thickening of the left ocular membranes with protrusion towards the interior of the eyeball and enhancement with contrast in a patient with disseminated TB (arrows).
Figure 17. Patient with HIV and disseminated tuberculosis. Multiple cutaneous/subcutaneous lesions that are visible in CT (A and B) (arrows).

Figure 18. Abdominal CT without contrast (A), with contrast (B), oblique reconstruction (C) and late phase (D). HIV patient with disseminated TB and pancreatic involvement with two hypodense images, necrotic center and marginal enhancement (arrows).
Conclusion

Radiological characteristics of extrapulmonary TB can simulate multiple diseases. It is essential to suspect the condition with high certainty, especially in risk patients. Generally, microbiological culture and anatomic pathology of the lesion are indicated to reach a definite diagnosis.

Bibliography