

Extrapulmonary Tuberculosis: Tomographic manifestations and associated complications

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Abstract

Tuberculosis (TB) is a re-emerging disease and an important cause of mortality. It manifests in two forms: pulmonary, which affects only the lungs, and extrapulmonary, which is defined as bacteriologically confirmed or clinically diagnosed infection by *Mycobacterium tuberculosis* that involves organs other than the lungs, being the pleural one of the most common. Extrapulmonary tuberculosis is usually the result of hematogenous dissemination of pulmonary infection and, therefore, indicates long-standing disease. The diagnosis of these forms of presentation represents a challenge due to the varied clinical manifestations, which requires a high index of suspicion, and early identification is essential to establish adequate treatment in these patients, since this presentation represents greater morbidity than the pulmonary form.

Keywords: Tuberculosis; Tomography; Extrapulmonary; Diagnosis

1. Introduction

According to the World Health Organization (WHO) classification, based on the anatomical location of tuberculosis (TB), extra-pulmonary tuberculosis (EPTB) is defined as infection by *Mycobacterium tuberculosis* bacteriologically confirmed or clinically diagnosed that involves organs other than the lungs; although pulmonary TB is the most frequent form of presentation, both in adults and children, extra-pulmonary TB (EPTB) presents greater morbidity and mortality. These forms of presentation include pleural, lymph node, central nervous system, bone, and less frequently cutaneous, genitourinary and peritoneal TB; thus, the most frequent extra-pulmonary presentation is pleural TB.

Tuberculosis (TB) is a re-emerging disease and a major cause of mortality. In 2018, 1.5 million people died from this disease worldwide [1].

PEDT is usually the result of hematogenous dissemination of pulmonary infection and, therefore, indicates long-standing disease, and may be a marker of immunosuppression. The diagnosis of these forms of presentation represents a challenge due to the varied clinical manifestations, which requires a high index of suspicion. These paucibacillary

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forms require the application of systematized diagnostic strategies to avoid delay in the initiation of treatment and reduce morbidity and mortality [2]. Extra pulmonary forms correspond to 20% of non-HIV-infected patients, increasing up to 50% in HIV-infected patients. Other risk factors for the occurrence of extra pulmonary forms of the disease include neoplasms, mainly lymphomas, and treatment with corticosteroids or anti-TNF agents [3].

There are factors that condition the body's immune response to infection in the case of a deficiency of the host's defenses, such as malnutrition, weight loss, alcoholism, DM, chronic renal insufficiency with hemodialysis, immunosuppression, AIDS and others, increase the risk of acquiring the disease. Once the microorganism invades the intestine, the most active inflammation occurs in the submucosa and serosa, which causes thickening due to edema, cellular infiltration, lymphatic hyperplasia, granuloma formation and finally, fibrosis [4]. The clinical presentation does not have pathognomonic signs or symptoms, the main symptom of abdominal tuberculosis is chronic pain, which makes diagnosis very difficult in some occasions, especially when it is not suspected. There may be chronic abdominal pain, the most common symptom in these patients referred by 80 to 90 %, hemorrhage and obstruction, the latter being the most frequent (20-60 %), fever between 35 and 50 %, constitutional syndrome of chronic or subacute evolution, weight loss occurs in two thirds of the cases, night sweats, diarrhea and vomiting 20 %, asthenia and hyporexia [5]. Early identification is essential to institute adequate treatment in these patients, which follows the guidelines for pulmonary tuberculosis with a two-month regimen consisting of four drugs (rifampicin, isoniazid, pyrazinamide and ethambutol), followed by a four-month therapy with two drugs (rifampicin and isoniazid). The duration of treatment is extended in tuberculous meningitis to one year and in skeletal dissemination to six to nine months. Corticosteroids are recommended in cerebral and pericardial tuberculosis. The duration of treatment is extended in tuberculous meningitis to one year and in skeletal dissemination up to six to nine months. Corticosteroids are recommended in cerebral and pericardial tuberculosis [6].

2. Material and methods

For the realization of this article a bibliographic search was performed in various databases such as Elsevier, Scielo, Medline, pubmed, ScienceDirect and Ovid, selecting original articles, case reports and literature reviews from 2015 to 2020, but older bibliographies 1995- 2007 were used due to their weight and information necessary for the realization of this work, in Spanish and English language using MeSH terms: tuberculosis, diagnosis, extrapulmonary and using the Boolean operators: and/ or. Including all documents dealing with extrapulmonary tuberculosis: tomographic manifestations and associated complications and related information, the data found were between 10-15 records, thus using 12 articles for this document.

3. Results

Taking into account that Tuberculosis (TB) is an infectious-contagious pathology of high morbimortality in the world, being the second cause of death by infectious matter and is considered a pathology of high relevance at public health level. It is caused by a highly virulent and contagious bacterium called *mycobacterium tuberculosis*. In a study published in the Argentine journal of radiology, an iconographic essay was made about the extrapulmonary tomographic manifestations of TB and some of its associated complications[5].

A review of the main imaging findings by CT (Computed Tomography) in extrapulmonary TB, reported in the literature, is presented. We grouped the different compromises as follows:

3.1. Nodal involvement

It is one of the most common locations of extrapulmonary TB, the cervical or supraclavicular presentation is the most commonly affected lymph node group. Tuberculous cervical adenitis or scrofulosis occurs (Fig. 1) [6].

In CT, lymph nodes are seen with peripheral thickening and central hypodense attenuation. These images are very suggestive of a lymph node TB, but it is not pathognomonic, so differential diagnoses such as metastasis, lymphoma and inflammatory pathologies must be taken into consideration (Fig. 2) [6].

The cervical lymph node presentation or scrofulosis can have several complications, among them the compromise of the neck vessels, due to the contiguity of them in relation to the lymph node groups, being able to present thrombophlebitis of the main vessels (Fig. 3) [6].

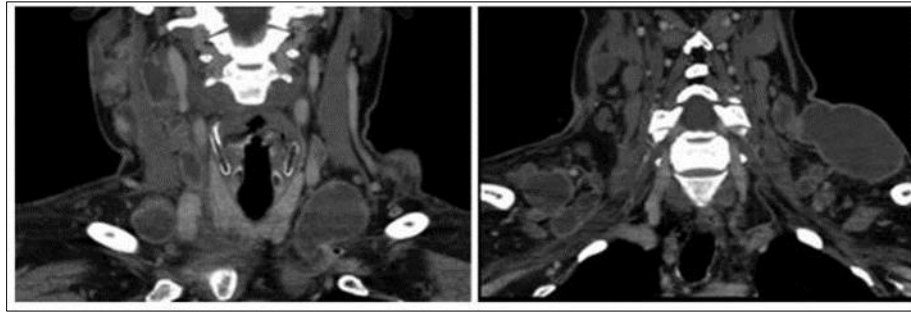


Figure 1 Man with non-painful swelling in the neck, with fever, diaphoresis and weight loss. Computed tomography (CT) of the cervical region showed multiple lymph node involvement with peripheral enhancement and central hypodense attenuation. A diagnosis of tuberculous cervical adenitis or scrofulosis was made.

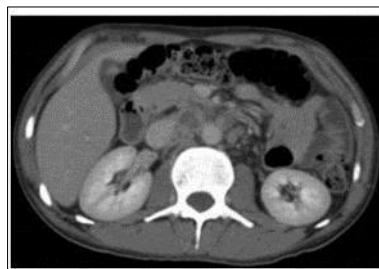


Figure 2 A man with a history of human immunodeficiency virus (HIV) and miliary tuberculosis (TB) underwent CT scan of the abdomen due to abdominal pain. Multiple peripancreatic adenopathies with peripheral enhancement and hypodense center, suggestive by clinical context and image of extrapulmonary TB

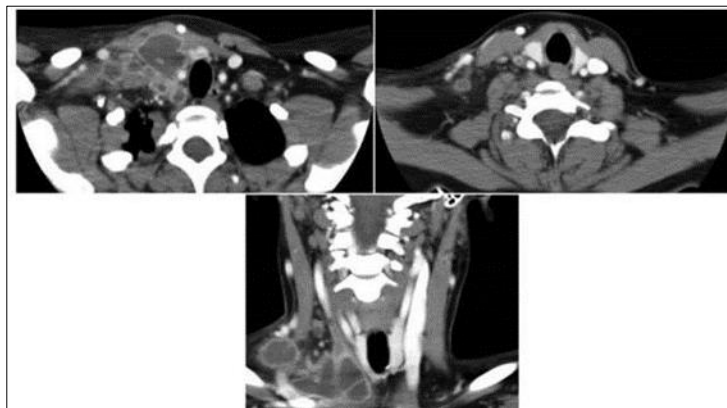


Figure 3 Woman with weight loss, cervical pain and fever. During the physical examination, she presented palpable supraclavicular lymphadenopathies. A CT scan of the neck was performed, highlighting in the right supraclavicular and ipsilateral parathyroid region a conglomerate of abscessed lymphadenopathies of necrotic aspect, measuring up to 7 cm in greatest diameter. A thrombus was identified in the right internal jugular vein.

3.2. Urogenital involvement

Genitourinary presentation is one of the main sites in patients with extrapulmonary TB. It mainly affects the kidney by hematogenous dissemination from the lungs.

The earliest alteration is seen at the level of the calyces with "moth-eaten" erosions. This finding is followed by papillary necrosis. Renal failure and dilatation of the pyelocaliceal system can be observed (Fig. 4) [7].

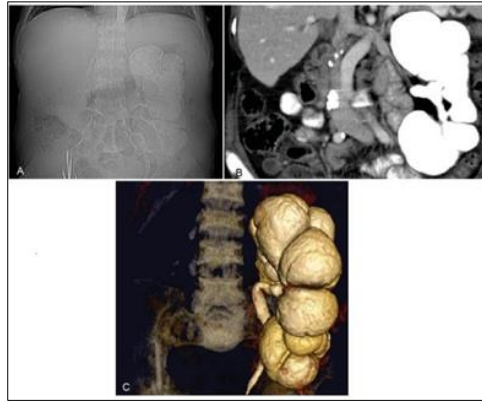


Figure 4 A 44-year-old woman with a history of pulmonary, pleural and genitourinary TB, right nephrectomized, chronic kidney disease on hemodialysis, consulted for abdominal pain and secondary hypertensive crisis. (a and b) CT was performed, which showed a marked dilatation of the calyceal system with cortical or corticomedullary caseous destruction and renal parenchyma. (c) A 3D CT reconstruction was performed highlighting with greater emphasis the mentioned dilatations. In the urine examination *Mycobacterium tuberculosis* bacilli were isolated.

3.3. Osteoarticular involvement: Tuberculous spondylitis

Involvement of the spine, also known as Pott's disease, is the most common site of extrapulmonary TB in osteoarticular presentations, accounting for up to 50% of cases of bonetuberculosis [7].

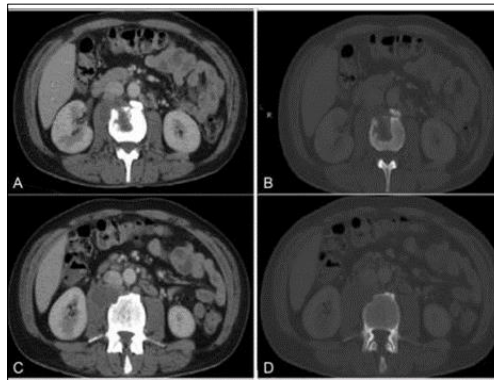


Figure 5 Male patient, 36 years old, with a history of HIV, consulted for bilateral testicular pain and enlargement of approximately 2 months of evolution, CT of the abdomen and pelvis was requested due to suspicion of testicular tumor. (a, b, c and d) Hypodense lesion in relation to the psoas muscle, with peripheral enhancement of its borders, which appears to come from a well-defined osteolytic lesion affecting the anterior border of the vertebral body of L2-L3. (e and f) Coronal reformatting shows involvement of the intervertebral disc with decreased L2-L3 disc space. (g and h) Predominantly nodular center lobular images, some of them with branching in a tree-shoot pattern, characteristic of TBC.

It is characteristic to observe the predominantly anterior involvement of the vertebral body, a very useful finding to make a differential diagnosis with metastatic disease [7]. Infection of paravertebral structures may be found, which involve the psoas major muscle, sometimes resulting in abscesses of the psoas major muscle (Fig. 5). CT and magnetic resonance imaging (MRI) are the images of choice to demonstrate small foci of bone infection and the extent of the disease [8].

Miliary involvement Miliary TB affects in a range of 1% to 7% of patients with all forms of TB presentation. It is usually seen in patients of extreme age and immunocompromised, the chest radiograph may initially be normal, where only signs of hyperinflation are seen, the most characteristic findings are micronodules of 2 to 3 mm (Fig. 6), with a predominance of up to 85% in the lower lobes [8].

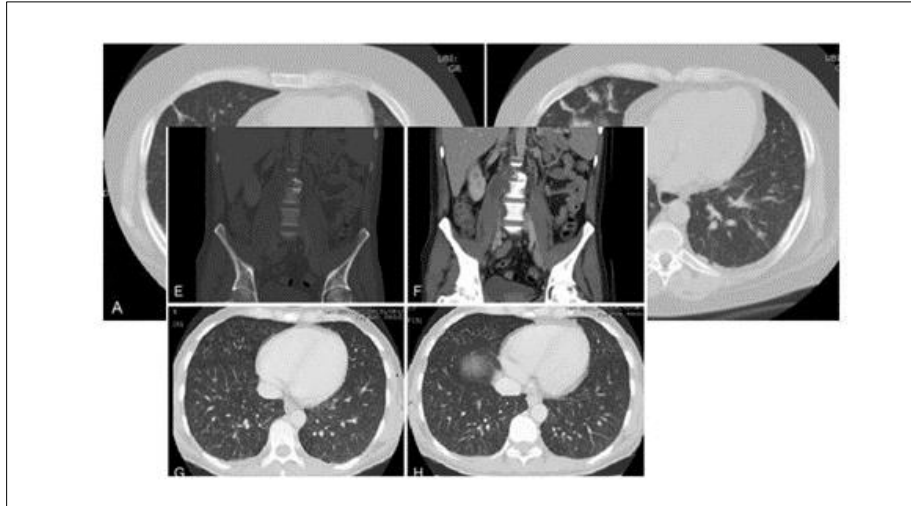


Figure 6 A woman with a history of systemic lupus erythematosus in treatment with immunosuppressants, hospitalized for suspected pneumonia. A chest CT scan was performed showing: (a and b) multiple micronodules of diffuse distribution in lung parenchyma. Some bilateral nodules with poorly defined borders were also visualized. Some hyperdense linear images of cicatricial aspect were visualized (arrow), mainly involving the pulmonary bases in their peripheral portions.

3.4. Abdominal involvement (intestinal and splenic TBC)

In patients with abdominal TB, ileocecal involvement is present in 80% to 90% of patients [14]. In CT, half of the patients with gastrointestinal tuberculosis show circumferential thickening of the cecum and terminal ileum, enlargement of the ileocecal valve, and mesenteric lymphadenopathy (Fig. 7) [8]. Findings such as asymmetry of the ileocecal valve, thickening of the medial wall of the cecum, exophytic extension and immersion of the terminal ileum, associated with multiple lymphadenopathies are more suggestive of tuberculosis.

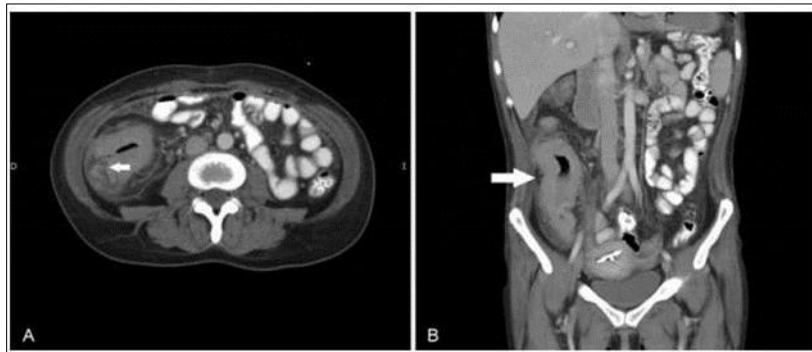


Figure 7 40-year-old woman hospitalized for suspected intestinal TB, CT scan was requested, which showed: (a) severe diffuse and concentric parietal thickening of the distal ileum, which does not significantly stenosed the lumen and involves the ileocecal valve (arrow). There is increased density of the adjacent mesenteric and pericecal fat with small low density adenopathies of the ileocolic chain measuring up to 8 mm in diameter. (b) The intestinal wall reaches a thickness of 13 mm and homogeneous contrast enhancement.

Splenic involvement of TB usually manifests in patients with miliary TB and may present as micronodules or macronodules at the level of the spleen or liver. In CT, multiple hypodense micronodules of diffuse distribution of 1 to 3 cm in diameter are identified (Figs. 8 and 9), the macronodular form or tuberculoma is rare [8].

In a study initially performed at the Military Zone Hospital, Zapopan, Jalisco; with studies performed at the Regional and Medical Specialties Hospital in Guadalajara, Jalisco, in the respective Radiology and Imaging Departments in 6 patients in which five (83%) were female and one (17%) male. The age ranges fluctuated between 17 and 61 years of age, with three cases in the second stage of life (two at 17 and one at 19 years of age); one at 27 and one over 42 years of age. The reason for consultation was abdominal pain in four (66%) and in one of them with severe malnutrition; one

(17%) was for abdominal mass and one (17%) for ascites under study, in their physiological puerperium. All cases underwent abdominopelvic CT: with oral and intravenous contrast in one of the cases, with rectal and intravenous contrast in one more and the remaining four only with intravenous contrast. All six cases represented new cases of TB. With the exception of the patient with severe malnutrition, no associated diseases were found that aggravated the development of the clinical picture. The imaging findings allowed us to point out and suggest the diagnostic possibility of TB in five cases, three of them with suggestive parietal intestinal thickening, and two with ascites and mesenteric lymphadenopathy; In one of the cases peritoneal carcinomatosis was identified with probability of ovarian primary and in retrospective the histopathological result proved peritoneal tuberculous involvement, intra-abdominal calcifications in the root of the mesentery were identified in one of the cases, as well as hepatosplenomegaly and splenomegaly in two (33%). Although the identification of polyserositis in extrapulmonary TB has been reported, pericardial effusion, pleural effusion and ascites were identified in only two cases (33%) (Table 1) [9].

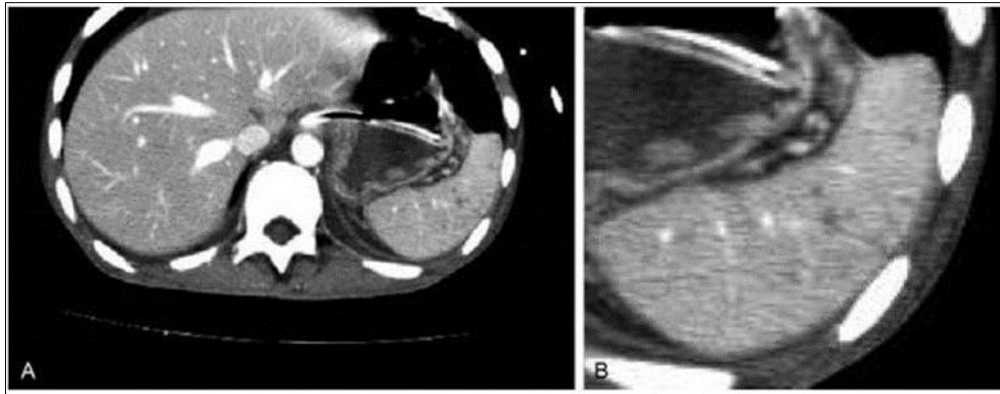


Figure 8 A 36-year-old man with a history of miliary TB. Multiple lymphadenopathies and febrile symptoms, CT of abdomen and pelvis was requested. (a) Hypodense multiple micronodular involvement in spleen of miliary character. (b) Enlargement of micronodules, the largest measuring 1 cm.

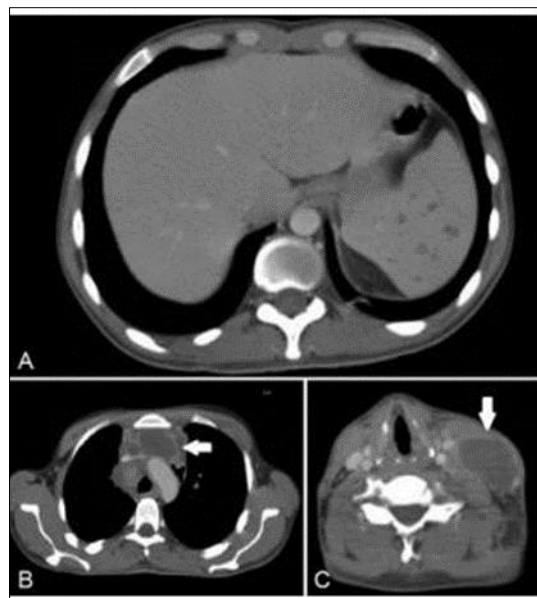


Figure 9 A 27-year-old man with HIV was studied for cervical tumor on physical examination. A CT scan was performed which showed: (a) multiple hypodense splenic images compatible with microabscesses of fluctuating diameters between 1 and 2 cm of diffuse distribution, (b) large conglomerates of peritracheal mediastinal, subcarinal and prevascular adenopathies were observed, reaching in the latter a maximum axial diameter of 8 cm (arrow) and (c) multiple cervical adenopathies in both jugular chains and in the left posterior cervical space. They presented hypodense center with peripheral enhancement with contrast medium. The largest one in the left posterior cervical space measured approximately 4.5 x 2.7 cm in its maximum transverse axes (arrow).

Table 1 Number of patients, sex, age, clinical presentation, and computed tomography findings

No. of patient	Sex	Age (years)	Presentation clinic	Tomographic findings, intravenous contrast enhanced MDCT studies in which demonstrated respectively
1	F	27	Pain abdominal, malnutrition	Intra-abdominal calcifications, heterogeneity of intra-abdominal fat, mesenteric; cecal mural thickening, with locoregional adenopathies, scant pericecal free fluid with SOI, sign of fecalization of intestinal intraluminal contents in sentinel loop of small bowel. Histopathology: intestinal and nodal TB.
2	M	17	Pain abdominal	Splenomegaly, heterogeneity of intra-abdominal fat, mesenteric; cecal and terminal ileum mural thickening, with intravenous postcontrast enhancement, with locoregional, pericecal adenopathies, scarce pericecal and pelvic free fluid with SOI, sign of fecalization of intestinal intraluminal content in sentinel loop of small intestine. Histopathology: intestinal and nodal TB.
3	F	19	Pain abdominal	Hepatosplenomegaly, heterogeneity of intra-abdominal fat, mesenteric; cecal and terminal ileum mural thickening, with postcontrast IV enhancement, with mesenteric locoregional adenopathies, intra-abdominal and pelvic free fluid with SOI, fecalization sign of intestinal intraluminal content in sentinel loop of the small intestine. Histopathology: intestinal and nodal TB.
4	F	42	Abdominal mass	Ascites, generalized peritoneal thickening with postcontrast enhancement, thickening of the intestinal wall and right adnexal mass. The possibility of peritoneal carcinomatosis secondary to ovarian primary was considered. Histopathology: peritoneal TB.
5	F	61	Pain abdominal	Bilateral pleural effusion, predominantly left, ascites and subdiaphragmatic nodes with intra-abdominal fat heterogeneity and reinforcement of the intestinal wall in small loops towards the pelvic hollow. Histopathology: peritoneal TB.
6	F	17	Ascites under study	Physiologic puerperium and ascites under study/polyserositis characterized by pericardial effusion, left pleural effusion, and ascites, this one of loculated appearance, with peritoneal enhancement without definition of nodular lesions in it and SOI with postcontrast intravenous enhancement of the intestinal wall. Exploratory laparotomy with severe right piosalpinx, ipsilateral acute oophoritis and severe acute peritonitis; multiple surgeries/BAAR (+) and Histopathology: peritoneal TB. Death due to disseminated TB

4. Discussion

The TBEP as an infectious disease of high mortality due to its high involvement with the immune system of each patient and more frequent in patients with diseases such as HIV, with variable extrapulmonary symptomatology and various forms of presentation including pleural, lymph node, central nervous system, bone tuberculosis, cutaneous tuberculosis, genitourinary and peritoneal less common, being the pleural form the most common extrapulmonary manifestation. In which the use of diagnostic aids such as computed axial tomography, especially with oral and intravenous contrast, at the abdominopelvic level in most cases according to studies, help greatly to determine the location of TBEP, the

associated complications such as suggestive parietal intestinal thickening, ascites, mesenteric adenopathies, intra-abdominal calcifications in the root of the mesentery, as well as hepatosplenomegaly and hepatosplenomegaly, as well as hepatosplenomegaly and splenomegaly, pericardial effusion, plural effusion, tuberculous affections at parietal level, where abdominal affections such as ascites, thickening of the peritoneum and lymph node alterations predominate in most cases, also allowing early treatment, thus reducing mortality in these patients, which is representatively high [10,11].

5. Conclusion

There are different types of manifestations of extrapulmonary tuberculosis, each one having its own characteristic manifestations and pathognomonic signs in imaging studies such as computed axial tomography, they also have complications depending on the extrapulmonary site that is affected, some complications being more serious than others; therefore, when extrapulmonary tuberculosis is suspected, the necessary tests should be performed in a timely manner, in order to establish an accurate treatment and avoid complications.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflicts of interest.

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