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<u>Attrition</u>
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Sex as a biological variable
not detected.
Subject Demographics
Age: not detected.
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not detected.
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Antibodies	Yes (indicate where provided: page no/section/legend)	n/a
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catalogue number and RRID, if available	Please add identifiers for all resources where possible	

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Design		
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By Leila Laamara

Access Microbiology Peritoneal Tuberculosis: An Underestimated Diagnosis --Manuscript Draft--



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Peritoneal Tuberculosis: An Underestimated Diagnosis

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Abstract

Tuberculosis 13 an infectious disease that most often affects the lungs, it is of human-to-human transmission caused by *Mycobacterium tuberculosis*, and is still a major public health problem worldwide. It spreads through the air when infected people cough, sneeze or spit.

In Morocco, a total of 29,327 cases were notified and put on treatment in 2021, as part of the National Tuberculosis Control Program (PNLAT). Peritoneal tuberculosis is an extra-pulmonary form of the disease that usually manifests itself as an ascitic syndrome, with or without fever, in a context of altered general condition, often in endemic areas.

We report a case of peritoneal tuberculosis in a young female patient aged 18, who had presented for 10 days with a progressive increase in abdominal volume associated with vomiting and diarrhea.

Due to the exudative and lymphocytic nature of the ascites fluid, a molecular biology PCR GeneXpert® MTB/RIF test for Mycobacterium tuberculosis complex was carried out and found to be positive, leading to the diagnosis of peritoneal tuberculosis.

The diagnosis of peritoneal tuberculosis is not always easy, as the clinical signs are often insidious and unspecific. The most common are weight loss, fever and abdominal pain. Peritoneal tuberculosis should therefore be suspected in the presence of any chronic febrile abdominal pain syndrome.

Diagnosis must be based on clinical and radiological evidence, but confirmation must be bacteriological and/or histological. Bacterial culture remains the gold standard.

Technological progress, 4 rticularly in molecular biology, has provided clinicians with new tools of diagnosing tuberculosis. The Xpert/MTB/Rif or GeneXpert® test, approved for use by the WHO in December 2010, has increased sensitivity and, shortened the time taken to confirm tuberculosis. GeneXpert® has also made it possible to detect resistance to Rifampicin which is a problem of growing concern

Our case demonstrated the vital role of molecular biology in the rapid diagnosis of extra-pulmonary tuberculosis.

In an endemic area, any unusual presentation of abdominal enlargement should raise suspicion of peritoneal tuberculosis to ensure timely therapeutic intervention. The management of peritoneal tuberculosis is multidisciplinary and requires coordination between physicians, bacteriologists and surgeons.

Key words: Peritoneal tuberculosis, peritonitis, GeneXpert® MTB/RIF

Data Summary

No data was generated during this research or is required for the work to be reproduced.

Introduction

Tuberculosis is defined as a contagious microbial disease caused by an infection with *Mycobacterium tuberculosis*, also known as Koch's bacillus (BK). [1]

It is currently on the increase in developing countries due to population growth and the acquired immunodeficiency syndrome (AIDS) pandemic. Abdominal tuberculosis ranks fourth after pulmonary, lymph node and osteoarticular tuberculosis. This abdominal tuberculosis is characterized by clinical and declinical diversity. [2]

According to the World Health Organization (WHO), the incidence of tuberculosis was 10.6 million in 2021 and 11s still responsible for 1.6 million deaths in 2021.

Globally, tuberculosis is the thirteenth leading cause of death and the second leading cause of death due 3 an infectious disease, behind COVID-19 [3].

In Morocco, a total of 29,327 cases, have been notified and put on treatment in 2021, as part of the National Tuberculosis Control Program (PNLAT). [4]

Extrapulmonary tuberculosis is an infectious disease caused by Koch's bacillus that is located outside the lung parenchyma.

Peritoneal tuberculosis is an extra-pulmonary form of the disease, usually manifesting as a febrile or non-febrile ascitic syndrome in a context of altered general condition, often in endemic areas.

We report a case of peritoneal tuberculosis in a young female patient aged 18, who had been presenting with a progressive increase in abdominal volume associated with vomiting and diarrhea.

Case Presentation

The patient was 18 years old with no particular medical history admitted to the emergency department with acute diarrhea.

The history of the disease began 10 days before admission with a progressive increase in abdominal volume associated with vomiting and diarrhea. All of this evolved in a context of asthenia with an untified fever.

The patient had no personal or family history of tuberculosis.

Clinical examination on admission revealed a conscious patient in moderately maintained general condition, hemodynamically stable, pale skin and mucous membranes, and diffuse abdominal tenderness on palpation.

The initial laboratory tests on admission showed a microcytic hypochromic anemia of 11.2 g/dL, hyperleukocytosis of 12,600/mL, with predominantly composed of PNN, thrombocytosis of 493 14 0/mL, C-reactive protein (CRP) of 222.5 mg/l and a prothrombin (TP) level of 48%. However, the liver function tests were normal.

An abdominal CT scan showed abundant partitioned ascites associated with peritoneal thickening and diffuse mesenteric infiltration.

An exploratory puncture of the ascites fluid was performed, with a biochemical and bacteriological test. The ascites fluid was cloudy/turbid, the color was yellow with a leucocyte count of 350/mm3 predominantly composed of lymphocytes (73%), and red cells count of 1700/mm3. The aerobic bacterial culture remained sterile.

The biochemical test of the ascites fluid showed a protein level of 64g/l.

 Due to the exudative and lymphocytic nature of the ascites fluid, a molecular biology PCR GeneXpert® MTB/RIF test for *Mycobacterium tuberculosis* complex was performed and came back positive.

A sputum test of *Mycobacterium tuberculosis* was used in the diagnosis of pulmonary tuberculosis using 3 samples, was negative.

The diagnosis of peritoneal tuberculosis was posed and the patient was put on anti-tuberculosis treatment according to our national protocol based on Isoniazid, Rifampicin, Pyrazinamide and Ethambutol.

Discussion

Peritoneal 10 erculosis is the most common abdominal form. It most frequently affects young women. Peritoneal tuberculosis is the fourth most common form of extra-pulmonary tuberculosis, particularly in Africa. [5] It is the leading etiology of ascites in developing countries.

Peritoneal tuberculosis is often caused by a rupture of a mesenteric lymph node, but can also occur through intestinal or genital contamination [6].

Diagnosis of peritoneal tuberculosis is not always easy because clinical signs are often insidious and unspecific. [7] The most common clinical signs are weight loss, fever and abdominal pain. Peritoneal tuberculosis should therefore be suspected in the presence of any chronic febrile abdominal pain syndrome. [8]

Biological abnormalities in ascites fluid guide the diagnosis, but are not specific. An exudative, lymphocytic fluid associated with a biological inflammatory syndrome of elevated erythrocyte sedimentation rate and inflammatory proteins, as well as anemia, are often associated with the symptomatology.

The Interferon-gamma release assays (QuantiFERON® or ELISpot TB®) is often useful for extra pulmonary tuberculosis in immunocompetent patients. Their specificity is 97% when the level exceeds 112 g/ml. [9]

The detection of Koch's bacillus in ascites fluid is rarely positive through direct examination. Its sensitivity varies between 0% to 6%. Bacterial culture on a specific medium has a better sensitivity with a positivity rate up to 85% of cases, but it requires, with traditional methods, delays of 4 to 8 weeks, which delays diagnosis and can burden the prognosis. [10]

Measuring of lactate dehydrogenase (LDH) in ascites fluid can make an important diagnostic contribution. It is a sensitive test for levels above 90 IU/l, but its low specificity (14%) limits the interest of its use in routine practice. [10]

Measurement of adenosine deaminase activity in ascites fluid has a good diagnostic value when the level is greater than or equal to 30 IU/l (sensitivity between 83% and 100% and specificity between 92% and 100%). This is a non-invasive, low-cost test that could be an alternative to invasive diagnostic tests [11].

Modern diagnostic methods, such as measuring adenosine deaminase activity and interferon gamma, are crucial but are not available everywhere in tuberculosis-endemic areas.

Technological progress, especially in molecular biology, has provided clinicians with new diagnostic tools for tuberculosis, including the Xpert/MTB/ Rif or GeneXpert® test, approved for use since December 2010 by the WHO, which has increased sensitivity and shortened the time needed to confirm tuberculosis in just two hours [12]. GeneXpert has also enabled the detection of Rifampin resistance, which is becoming an increasingly worrying problem, particularly in a situation where culture is not routinely available. However, classic tests such as microscopic examination after Ziehl-Nielsen staining,

160 bacterial culture on solid and liquid nail and radiology remain the reference approach and should 161 remain essential in the management of patients suspected of having tuberculosis. [12] 162 163 In a prospective study conducted between October 2009 and October 2011, Clemente et al analyzed 164 1,630 extra-pulmonary samples using conventional techniques (direct examination after Ziehl-Nielsen 165 staining, followed by bacterial culture on solid and liquid media) and Xpert MTB/RIF. Of the 72 166 samples ultimately positive for M. tuberculosis (including 15 pleural fluids, 13 urines, 9 lymph node 167 biopsies and 4 CSF), only 9 (12.5%) were positive on direct examination, while 53 (73.6%) were 168 positive with Xpert MTB/RIF. [13] 169 170 In another study conducted by Browne 1 et al, who also carried out a meta-analysis on the diagnostic 9 rformance of Xpert MTB/RIF in extra-pulmonary tuberculosis. According to this study, the 171 172 performance of Xpert MTB/RIF, compared to the result of bacterial culture as the reference technique, 173 was 43% for puncture fluids (pleura, ascites, CSF, etc.). [14] 174 175 In Peritoneal tuberculosis, the differential diagnosis must be made with other causes of ascites, including 176 inflammatory causes and also peritoneal carcinosis. 177 The treatment of Peritoneal tuberculosis consists of two components: emergency surgical treatment of 178 179 the peritonitis and anti-bacterial treatment. 180 181 Conclusion 182 183 Peritoneal tuberculosis is still common in our country, and is poorly described in the literature. 184 In an endemic context, any unusual presentation of increased abdominal volume should raise suspicions 185 186 of peritoneal tuberculosis in order to ensure timely therapeutic intervention 187 188 The introduction of new tools, such as molecular biology tools has made a major contribution to the 189 diagnosis of pulmonary and extra-pulmonary tuberculosis. 190 191 The management of peritoneal tuberculosis is multidisciplinary, requiring coordination between 192 clinicians, bacteriologists and surgeons. 193 **Funding Statement** 194 This research received no specific grant from any funding agency in the public, commercial, or not-for-195 profit sectors. **Author contributions** 196 197 L.L. contributed to the initial drafting of the manuscript, while B.E, B.Y, M.A and C.M. revised it. E.L.M. 198 provided final approval for the version to be published. 199 Conflicts of interest: 200 201 The authors declare that there are no conflicts of interest.

Written informed consent was obtained from the patient to publish this report in accordance with the

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