

## CASE REPORT

# ISOLATED INTESTINAL TUBERCULOSIS ASSOCIATED WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION

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### ABSTRACT

**Introduction.** Tuberculosis is a common and treatable human immunodeficiency virus-related (HIV) disease. Intestinal tuberculosis is much more recurrent in immunocompromised patients and presents as a complication of pulmonary tuberculosis due to swallow of infected sputum, hematogenic dissemination or even ingestion of contaminated milk. There is a strong need for close collaboration between HIV programmes and tuberculosis programmes.

**Case presentation.** A 48-year-old male patient presented for a three month history of frequent bowel movements (3-4 stools per day, without blood or mucus), a weight loss of eight kilograms, infrequent dry cough, fatigue, esophageal candidiasis, anorexia, persistent low-grade fever and intermittent pain in the right lower abdominal quadrant. Abdominal X-Ray revealed a marked dilatation of the small intestine. High resolution axial computed tomography described thickening of the terminal ileum and medial caecal wall, with slightly enlarged low density nodes. Histopathological examination of the intestinal mucosa revealed granulomatous design and caseous necrosis. The positive diagnosis was primary extrapulmonary multidrug-resistant tuberculosis with HIV infection. He received an individualized and second line antituberculous treatment combined with

### RÉSUMÉ

**Tuberculose intestinale isolée associée au syndrome d'immunodéficience**

**Introduction.** La tuberculose est une maladie liée au virus de l'immunodéficience humaine courante et traitable. La tuberculose intestinale est beaucoup plus récurrente chez les patients immunodéprimés et se présente comme une complication de la tuberculose pulmonaire due à la déglutition des expectorations infectées, à la dissémination hématogène ou même à l'ingestion de lait contaminé. Il existe un fort besoin de collaboration étroite entre les programmes du virus de l'immunodéficience humaine et les programmes de lutte contre la tuberculose.

**Présentation de cas.** Patient de 48 ans, qui avait des antécédents de selles fréquentes pour une période de trois mois (3 à 4 selles par jour, sans sang ni mucus), une perte de poids de 8 kilogrammes, une toux sèche peu fréquente, de la fatigue, une candidose œsophagienne, une anorexie, fièvre persistante à bas degré et douleur intermittente dans le quadrant abdominal inférieur droit. La radiographie abdominale a révélé une dilatation marquée de l'intestin grêle. La tomodensitométrie axiale à haute résolution a révélé un épaississement de l'iléon terminal et de la paroi caecale médiale; nœuds de faible densité légèrement agrandis.

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antiretroviral therapy. Later on, he developed pneumonia with *Pneumocystis jirovecii*. The patient had a good clinical response to all therapies.

**Conclusions.** Physicians should be aware that intestinal tuberculosis must be considered in the differential diagnosis of patients with abdominal symptoms, especially in immunocompromised patients.

**Keywords:** human immunodeficiency virus, extrapulmonary tuberculosis, sign of Fleischner, pneumonia with *Pneumocystis jirovecii*.

## INTRODUCTION

Tuberculosis is a common and treatable human immunodeficiency virus (HIV)-related disease. A large group of patients with human immunodeficiency virus and pulmonary tuberculosis die from pulmonary complications despite receiving antituberculosis treatment (Table 1). There is a strong need for a close collaboration between HIV programmes and tuberculosis programmes.

New data suggest that starting antiretroviral therapy while still on tuberculosis treatment could improve outcomes, according to Camelia study<sup>1</sup>. At the same time, immune reconstitution inflammatory syndrome, which is frequently cited by specialists as a reason to delay starting antiretroviral therapy, was more common among people with early HIV treatment, but did not offset the survival benefit provided by earlier antiretroviral therapy.

Hardly seen in modern countries, intestinal tuberculosis affects mainly immunocompromised patients and immigrants<sup>2-5</sup>. The incidence of intestinal tuberculosis has been constantly increasing in the past twenty years but only a few cases with intestinal tuberculosis, with isolated colonic involvement, are reported<sup>6-9</sup>.

Most important, intestinal tuberculosis should enter into the differential diagnosis (Table 2), especially in the lack of an active pulmonary infection, because it may mimic other abdominal diseases, such as: tumors, other infectious and inflammatory processes like abscess, and even Crohn's disease<sup>8</sup>.

Intestinal tuberculosis is much more recurrent in immunocompromised patients<sup>10</sup> and presents as a

L'examen histopathologique de la muqueuse intestinale a révélé un dessin granulomateux et une nécrose caséuse. Le diagnostic positif était une tuberculose extrapulmonaire multirésistante primaire avec infection par le VIH. Il a reçu un traitement antituberculeux individualisé et de deuxième ligne combiné à un traitement antirétroviral. Plus tard, il a développé une pneumonie à *Pneumocystis Jirovecii*. Malgré les problèmes cliniques existants, le patient a eu une bonne réponse clinique à toutes les thérapies.

**Conclusions.** Il est très important pour les médecins de savoir que la tuberculose intestinale peut être considérée comme un diagnostic différentiel chez les patients aux symptômes intestinaux, surtout les patients immunocompromis.

**Mots-clés:** virus de l'immunodéficience humaine, tuberculose extrapulmonaire, signe de Fleischner, pneumonie à *pneumocystis jirovecii*.

complication of pulmonary tuberculosis, due to swallow of infected sputum, hematogenic dissemination or even ingestion of contaminated milk<sup>11</sup>.

## CASE PRESENTATION

A 48-year-old male patient, presented for three months history of infrequent bowel movements (three-four stools per day, without blood or mucus), a weight loss of eight kilograms, infrequent dry cough, fatigue, esophageal candidiasis, anorexia, persistent low grade fever and intermittent pain in the right lower abdominal quadrant.

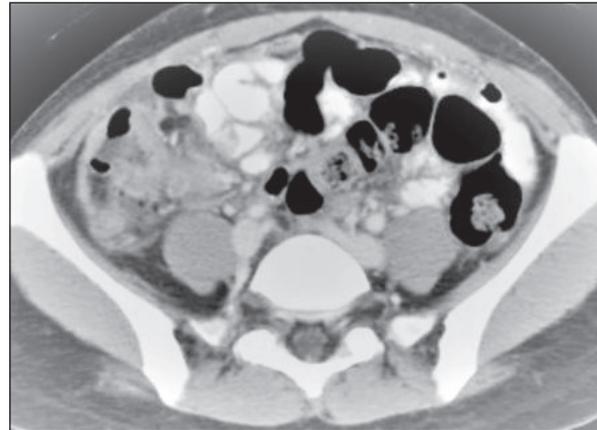
He was a widower, working in a street market. The patient had no history of tuberculosis. In childhood, he was vaccinated with Bacille Calmette-Guérin and there was no family history of any cancer. His medical history revealed intravenous drug use for the last three years, associated with alcohol drinking and cigarette smoking.

Physical examination showed slight abdominal tenderness, painful at palpation, mostly limited to the right lower quadrant. Laboratory tests revealed anemia with a decreased white blood cell count and increased C reactive protein levels. Chest X-Ray was normal. Stool samples were negative for infectious microorganisms. Urinalysis had normal values. Abdominal X-Ray revealed a marked dilatation of the small intestine (Figure 1).

High resolution axial computed tomography described thickening of the terminal ileum and medial caecal wall with slightly enlarged low density nodes (Figure 2).



**Figure 1.** Abdominal radiography revealed a marked dilatation of the small intestine



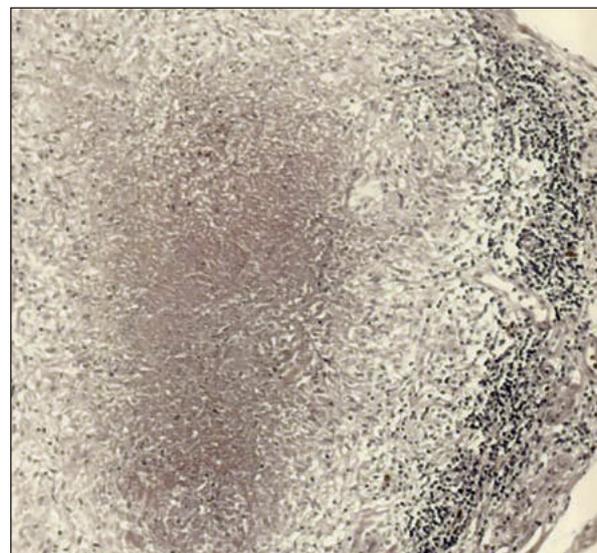
**Figure 2.** High resolution axial computed tomography revealed thickening of the terminal ileum and medial caecal wall with slightly enlarged low density nodes.



**Figure 3.** Bronchoalveolar lavage.

Barium follow through test was conducted and revealed the inverted umbrella sign of Fleischner. QuantiFeron-TB Gold negative. An apparently normal chest X-Ray is frequent in patients with intestinal tuberculosis, but does not exclude it. Both bronchoalveolar lavage (Figure 3) and gastric aspirate did not reveal acidfast bacilli.

The male patient was then referred to the Gastroenterology department, where colonoscopy was made. Biopsies from the tumoral lesion (Figure



**Figure 4.** Histopathological examination of the intestinal mucosa: optical microscope with oil immersion objective (1000 X magnification), carbol fuchsin as primary stain, described granulomatous design and caseous necrosis.

4) were evaluated and several tubercle bacilli were identified upon Ziehl Neelsen staining.

The detected *Mycobacterium tuberculosis* was resistant to isoniazid and rifampicin. Cultures were all negative. Because of the history of drug consumption and the clinical signs, an HIV test was performed, with a positive result. The positive diagnosis was extrapulmonary multidrug-resistant tuberculosis with HIV infection, sustained by histopathological examination of the intestinal mucosa and GeneXpert MTB/RIF. Because HIV test was positive, the patient was referred to a specialized infectious diseases center, where a cluster of differentiation four count of

**Table 1.** Pulmonary manifestations of HIV-infected patients depending on cluster of differentiation four count.

Any cluster of differentiation 4 count:	≤500 Cells/ μL	≤200 Cells/ μL	≤100 Cells/ μL	≤50 Cells/μL
1. Upper respiratory tract infection	1. Bacterial pneumonia	1. Pneumocystis pneumonia	1. Pulmonary Kaposi sarcoma	1. Disseminated Histoplasma capsulatum
2. Sinusitis	2. Pulmonary mycobacterial pneumonia	2. Cryptococcus neoformans pneumonia	2. Bacterial pneumonia	2. Disseminated Coccidioides immitis
3. Pharyngitis		3. Bacterial pneumonia	3. Toxoplasma pneumonitis	3. Cytomegalovirus pneumonitis
4. Acute bronchitis		4. Extrapulmonary tuberculosis		4. Disseminated Mycobacterium avium complex
5. Obstructive airway disease				5. Aspergillus infection
6. Bacterial pneumonia				
7. Tuberculosis				
8. Non Hodgkin lymphoma				
9. Pulmonary embolus				
10. Bronchogenic carcinoma				

**Table 2.** Differential diagnosis between tuberculosis and Crohn's disease (medical imaging)

	Tuberculosis	Crohn's disease
Chest radiography	Positive chest film (in 50% of cases)	Negative chest film
Barium appearance	Fleischner sign No creeping fat	Cobblestone mucosa Creeping fat
Computed tomography appearance	Omental and peritoneal thickening Enlarged low density nodes	Normal omentum and peritoneum Enlarged soft tissue density nodes

two-hundred cells per cubic millimeter was revealed, in urgent need of specialized treatment.

After prolonged attempts to persuade the patient and professional psychotherapy, he agreed to an individualized and second line antituberculous treatment combined with antiretroviral therapy. The effective dose using weight-based protocol consists in the use of: Pyrazinamide + Amikacin + Levofloxacin + Clofazimine + Linezolid + Rifabutin (300 milligrams twice-weekly) + Pyridoxine (50 milligrams daily)<sup>11</sup>.

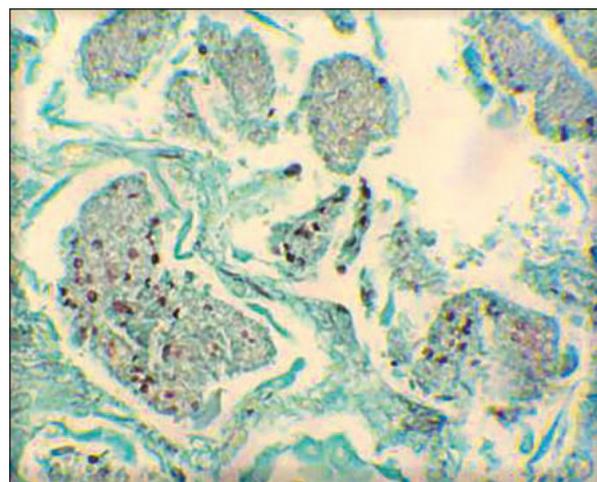
During the first month, because the patient was reluctant and began treatment later than normal, he developed pneumonia with *Pneumocystis jirovecii* (Figure 5), treated with trimethoprim-sulfamethoxazole and corticosteroids as adjunctive therapy.

We had to consider the existing clinical issues: toxicities and drug interactions, ability to adhere to two complex treatment schemes and laboratory abnormalities. Using this regimen, the patient did not experience clinically significant increases in rifabutin serum levels and had a good clinical response to therapy<sup>11</sup>.

The recommended duration of treatment scheme for multidrug resistant tuberculosis in HIV-seropositive patients is twenty-four months and posttreatment follow-up visits to monitor for tuberculosis relapse should be conducted every four months, for a total of twenty-four months<sup>11</sup>.

## DISCUSSION

Intestinal tuberculosis may be considered as a differential diagnosis in immunocompromised patients who present vague abdominal symptoms and relevant physical findings, especially in cases with centered pain and palpable mass in the right lower



**Figure 5.** Histopathological examination from lung biopsy: optical microscope, low power oil immersion objective (100 X magnification), Gomori methenamine silver stain, showed that the walls of the cysts are stained black and appear as folded spheres.

quadrant of the abdomen, in areas where tuberculosis is endemic (subregions of Eastern Europe).

*Mycobacterium tuberculosis* in HIV-positive patients is extremely difficult to treat. Adherence to treatment plays a significant role in the recovery and patients need constant professional psychological support. New treatments can prevent both symptoms and complications to evolve.

Together with lifestyle transformation and antiretroviral medications, most people with HIV infection can enjoy a lifetime similar to that of the general population. The integration of HIV and tuberculosis centers could serve as an important part in reducing and better managing the infected persons.

## CONCLUSIONS

The gastrointestinal tract is the sixth site of extrapulmonary tuberculosis<sup>12</sup>. Ileocecal site is the most frequently infected part of the gastrointestinal tract in around 85% of cases<sup>12</sup>. The gastric inclusion is sporadic, possibly due to the acidity and insufficiency of lymphoid tissue and the rapid crossing of its content to the small bowel<sup>13</sup>.

Abdominal pain is the most constant symptom, present in 90% of situations, but other symptoms may occur: diarrhea, vomit, fever, nausea, loss of weight, abdominal distension, poor absorption, weakness and even constipation<sup>14,15</sup>. Low digestive hemorrhage is rare<sup>16</sup>. The preferred diagnostic procedure is colonoscopy with biopsy.

Clinical, radiological and endoscopic images of intestinal tuberculosis are most likely to be mistaken as neoplasms. Surgery is used only in case of diagnostic contrariety and also the decisive treatment to prevent issues of disease progression, such as stenosis or fistulas<sup>17</sup>.

Regarding the histological diagnosis, the frequent findings in tuberculosis are the large granulomas with central caseation, which are confluent and multiple<sup>18</sup>, although the most reliable finding in biopsies is the evidence of *Mycobacterium tuberculosis*<sup>19</sup>. Different forms of cancer may have an endoscopic appearance of circumferential thickening, with fistulas formation and ulcers that mimic Crohn's disease<sup>20</sup>.

Worldwide, there was an estimation of nine million incident cases of tuberculosis in 2013, 13% co-infected with HIV<sup>21</sup>. There were an estimated one and a half million tuberculosis deaths (one million among HIV-negative people and half a million among HIV-positive people)<sup>21</sup>.

It is important that physicians should be aware of the necessity of testing the gastric aspirate<sup>22</sup>, Lowenstein-Jensen culture of biopsy tissue taken

during endoscopy, in the case Ziehl Neelsen doesn't demonstrate acid fast bacilli<sup>23</sup>. Enteroclysis followed by a barium enema may still be the best protocol for evaluation of intestinal tuberculosis<sup>24</sup>.

## Author contributions

*P. E. M. is responsible for the diagnostic procedures, clinical diagnosis, treatment decisions and also wrote the manuscript. The author has read and agreed to the published version of the manuscript.*

## Compliance with Ethics Requirements:

„The author declare no conflict of interest regarding this article“

„The author declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from the patient included in the study“

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