INTRODUCTION

Abdominal tuberculosis is an extrapulmonary Mycobacterium tuberculosis infection, which is a rare clinical condition in nonendemic countries. We present a case series of three patients diagnosed and treated with abdominal tuberculosis in a tertiary hospital in Germany. Unspecific signs and symptoms were linked to a delayed diagnosis and treatment.

Abdominal tuberculosis (ATB) is an extrapulmonary infection caused by Mycobacterium tuberculosis potentially affecting the gastrointestinal (GI) tract, peritoneal cavity, abdominal lymphatic system, and/or solid visceral organs. The peritoneum and ileocecal region are the most common sites of this infection. Accounting for nearly 2% of all tuberculosis cases worldwide, ATB constitutes a significant issue for health-care providers, particularly in impoverished countries of the world. Yet, due to its nonspecific signs and presentations, ATB remains often overlooked or misdiagnosed, particularly in developed countries, such as the UK or Germany. The most common clinical manifestations are abdominal pain, unintended weight loss, diarrhea, and pyrexia. When involving the peritoneum, ATB presents more often with abdominal distension and ascites.

Several paths of intestinal pathogen transmission have been described so far. It is estimated that 15–20% of patients with ATB suffer from a concomitant active pulmonary infection. Those patients may ingest their sputum, and therefore,
a high bacterial load can be transferred to their GI tract. Hematogenous and/or lymphatic transmission to distant organs and/or local spread through directly adjacent tissues is also possible. Finally, a primary GI infection due to the ingestion of contaminated dairy products, in particular unpasteurized cows’ milk, may occur.5

The diagnostic workup, by clinical suspicion, should be based on radiologic and endoscopic findings.6,7 Histological examination of clinical samples and tissues, as well as serological and molecular tests have been implemented to confirm diagnosis.1 Thus, positive cultures facilitate antibiotic sensitivity testing. However, their most significant disadvantage is the delayed initiation of the treatment as final results may take up to eight weeks to be released. Several studies indicated that patients with extrapulmonary tuberculosis, compared to those with an isolated pulmonary disease, tend to have a worse prognosis, highlighting the need for early and accurate diagnosis in this setting.7,8 Complications may be severe, ranging from formation of fistulas and strictures to intestinal perforation and bleeding.9

We report three cases of abdominal tuberculosis being diagnosed in a tertiary hospital in Germany in the last 5 years. Our intention is to demonstrate crucial clinical signs and diagnostic findings, leading to an early diagnosis of this potentially life-threatening condition.

2 | CASE PRESENTATION

2.1 | Case 1. Pleural, retroperitoneal, and colonic tuberculosis

A 20-year-old male patient, an immigrant from Eritrea, was admitted to our department with a history of nausea, vomiting, watery diarrhea, and intermittent fever. The patient was extremely cachectic, with a body mass index (BMI) of 13. No previous medical history was known. During his physical examination, abdominal tenderness in all four quadrants was present. His biochemical tests showed increased inflammatory serum biomarkers, such as C-reactive protein (CRP) (233 mg/L, norm: <10 mg/L) and lactate dehydrogenase (LDH) (549 U/L, norm: <280 U/L). An abdominal ultrasonography confirmed the presence of ascites in all dependent recesses of the peritoneal cavity. A diagnostic puncture revealed peritonitis as the ascitic total cell count was 6712*1000/UL (norm: <1.000*1000/UL). An abdominal ultrasonography confirmed the presence of ascites in all dependent recesses of the peritoneal cavity. A diagnostic puncture revealed peritonitis as the ascitic total cell count was 6712*1000/UL (norm: <1.000*1000/UL). Immunohistochemical examination of the ascitic fluid showed leukocytosis, with predominantly T lymphocytes and macrophages, without evidence of malignant cells or bacterial pathogens. The Ziehl-Neelsen acid-fast stain of ascites was negative for mycobacteria.

A computed tomography (CT scan) of the chest and abdomen demonstrated ascites, mesenteric edema, and enlarged lymph nodes located in the retroperitoneal and mesenteric space. Bilateral ground-glass opacities of the lung were interpreted as atypical pulmonary infiltrates, and unilateral pleural effusion could be seen at the right side.

An upper and lower GI endoscopies were performed. Whereas the upper GI endoscopy was uneventful, mucosal erythema and three lesions of patchy wall thickening were observed in colonoscopy, one located in the rectosigmoid region and the other two in the sigmoid colon (Figure 1). Endosonographic examination of the lesions revealed an inhomogeneous pattern, containing areas of increased and decreased opacity. The aforementioned CT scan showed no correlation with the colonic lesions. As neither endosonography nor a second lower GI endoscopy could establish a clear submucosal or submural infiltration of the lesions, no biopsy was performed.

Stool samples were tested for bacterial and viral pathogens, without result. Finally, the serological analysis showed an elevated titer against Schistosoma mansoni (PHA 1:2560, norm: 1:<80; Schistosoma mansoni IgG EIA-positive,) as well as evidence of Schistosoma mansoni antigen. Once the diagnosis was confirmed, treatment with praziquantel 40-60mg/kg/day was initiated.

A month later, the patient was readmitted because of persistent abdominal pain and lethargy. Treatment of the Schistosoma mansoni infection did not result in a resolution of his clinical symptoms. Ascites was still present, and a diagnostic puncture was uneventful. Because of the persistent right pleural effusion, we decided to perform a video-assisted thoracic surgery (VATS) in order to obtain pleural biopsies, in which growth of M. tuberculosis could be shown. We, therefore, concluded that the patient suffered from pleural, retroperitoneal, and colonic tuberculosis. A six-month targeted treatment with rifampicin (six-month treatment), isoniazid (six-month treatment), pyrazinamide (two-month treatment), and ethambutol (two-month treatment) was
introduced, according to the current guideline,10 and resulted to a rapid clinical improvement and resolution of the patient's symptoms.

2.2 | Case 2. Peritoneal tuberculosis

A 73-year-old man from a rural region in the south of Turkey was admitted to our hospital with an increased waistline, loss of appetite, and intermittent abdominal pain. He further noticed progressive lethargy over the past few years. His past medical history included early-stage dementia, type 2 diabetes mellitus, and Parkinson's disease. During the physical examination, his abdomen appeared tender with resonant notes of gaseous distension of the bowel and loud peristaltic sound, indicating a possible bowel obstruction.

Gastroscopy and colonoscopy showed no signs of obstruction, and the patient's clinical signs gradually improved within his four-week hospital stay. Blood tests revealed moderately elevated CRP (53 mg/L, norm: <5 mg/L) and increased blood sedimentation rate (BSR) (34 mm/1h, norm: <20 mm/1h), and normocytic normochromic anemia (hemoglobin 11.8 g/dl, norm: 13.5–17.5 g/dl). Abdominal ultrasonography revealed perihepatic and perisplenic ascites, as well as ascites in the Douglas pouch. The diagnostic ascitic tap showed a predominantly lymphocytic exudate with a total cell count of 1294*1000/Ul (norm: <1.000*1000/UI). There was no evidence of malignant cells, and the polymerase chain reaction (PCR) for tuberculosis was negative.

A CT scan of the chest and abdomen showed enlarged mediastinal and retrocrural lymph nodes, areas of decreased opacity in the spleen, and high-density ascites. In order to exclude an underlying bowel perforation, a diagnostic laparoscopy was performed. Multiple nodules of the abdominal wall and major omentum were macroscopically visible. Biopsies were taken, and the histopathology revealed necrotizing/caseating epithelioid granulomas and multinucleated giant cells (Figures 2A,B), which is a pathognomonic finding of mycobacterial infections.1 PCR testing of the excised tissue could not confirm the presence of \textit{M. tuberculosis}. Subsequently, a test to confirm a latent \textit{M. tuberculosis} infection (Quantiferon test®) revealed a positive result.11 After two months under a quadruple tuberculostatic therapy with rifampicin, isoniazid, pyrazinamide, and ethambutol, the patient presented clinically improved with receding ascites.

2.3 | Case 3. Pulmonary, intestinal, retroperitoneal, and peritoneal tuberculosis

A 21-year-old male patient from Somalia presented with a three-month history of abdominal pain, nausea, vomiting, and weight loss. His medical history included posttraumatic stress disorder and drug abuse. Blood tests on admission showed no abnormalities. An underlying infection with human immunodeficiency virus (HIV) was excluded. One year later, the patient presented again reporting an intensification of similar symptoms. Physical examination showed a cachectic (BMI 13) nutritional state with slight epigastric pain on palpation, and abdominal ultrasonography revealed small amounts of ascites but no other abnormalities.

Because of the increased inflammatory markers (CRP 155 mg/L) and presence of elevated serum lactate (3.9 mmol/L, norm: 0.5–1 mmol/L), an emergency CT scan of the chest and abdomen was performed, in order to exclude a hollow-organ perforation. Ascites and multiple abscesses, located in the right pelvic crest, the nuchal region, and the muscle erector spinae, were detected. In particular, CT images showed a retroperitoneal formation compatible with tubercular subsidence abscess, which was CT morphologically mimicking a tumor (Figure 3A,B). In addition, several cavernous...
lesions, adjacent to the bronchial system, and pneumonia and empyema of the right pleura indicated a bilateral lung involvement (Figure 3c). Fine-needle biopsy of the abscess at the right pelvic crest revealed a necrotic process, with no evidence of causative pathogens. Further, a diagnostic puncture of the ascites provided no evidence of *M. tuberculosis* in the PCR. The diagnosis of *Mycobacterium tuberculosis* infection (TB) was made after sputum cultures were stained positive, and the patient went on a targeted course with rifampicin, isoniazid, ethambutol, and pirithamide. His clinical state improved dramatically within few weeks.

3 | DISCUSSION

Our article highlights the complexity in obtaining diagnostic proof of extrapulmonary tuberculosis in clinical routine. According to our case series, the time between symptomatic disease and treatment initiation was estimated about a mean of 200 days. Often, symptoms precede for a long time before admission and may lead to severe deterioration of general health and nutritional state. Socioeconomic factors and access to health-care facilities may influence the clinical course, and therefore, an early and accurate diagnosis in this setting remains crucial.7,8

The main demographic characteristics of this group may be helpful. Former studies have postulated that young age (<44 years) may be a strong predictive factor in diagnosing ATB.12 Our case series supports this notion as two of three patients were in their early twenties when admitted to our hospital (Table 1). All three patients came from a region with underdeveloped medical infrastructure. This is compatible with previous studies, where the immigration background from a country with high tuberculosis burden is considered to be a risk factor for the development of ATB.1,3 An interesting point in our series is that all patients were HIV-negative, which is a very uncommon observation in this group because a positive HIV status has been proved to be significantly associated with extrapulmonary tuberculosis.8

All three patients were admitted to the hospital with abdominal pain, ascites, and lethargy; two of three cases 1 and 3 had loss of appetite and ensuing weight loss, nausea, and vomiting, and only one case (case 1) had watery diarrhea and intermittent fever (Table 2). This is in

![Figure 3](A) Computed tomography of abdomen, showing a retroperitoneal tubercular subsidence abscess (arrow). (B) Computed tomography (coronary axis), showing the retroperitoneal tubercular subsidence abscess (arrow). (C) Computed tomography of the chest showing a left sided cavernous lesion, as well as pneumonia and empyema on the right side (7.9 cm × 3.2 cm × 9.3 cm)

| TABLE 1 | Demographic data and medical history of the presented cases |
|----------|----------------------|
| **Sex**   | Case 1 | Case 2 | Case 3 |
| Age (years) | 20 | 73 | 21 |
| Country of origin | Eritrea | Turkey | Somalia |
| Immunocompromised | No | No | No |
| Medical history of pulmonary tuberculosis | No | No | No |
| Family history of tuberculosis | No | No | No |
concordance with investigators studying common clini-
cal presentations in ATB,\textsuperscript{1} whereas other literature re-
sources describe a different spectrum of clinical features,
such as weakness, abdominal mass, abdominal distension,
and night sweats.\textsuperscript{13} Several laboratory markers, such as
serum albumin <26 g/L (norm: 35–55 g/L) and platelets
>340 × 10^9/L (norm: 150 × 10^9/L–450 × 10^9/L) have been
proposed to be useful in prediction models of ATB but still
have a very poor sensitivity.\textsuperscript{14} These parameters were all
normal in our patients, and none of them complained about
night sweats.

Abdominal ultrasonography revealed ascites in all cases.
Multiple diagnostic punctures, during the clinical course,
confirmed inflammatory ascitic fluid with predominant T
lymphocytes. No evidence of \textit{M. tuberculosis} was found mi-
croscopically, culturally, or even in the PCR. This comes to
support former results, where the conventional microbiologic
examination was not sensitive enough to confirm the diagno-
sis of tuberculous peritonitis.\textsuperscript{15}

Several studies emphasize the importance of CT imag-
ing as a diagnostic tool in ATB.\textsuperscript{6,7} The CT findings of our
cases are summarized in Table 2. However, features such as
intranal and extranal abscesses, fistula, mesenteric
thickening, “white bowl” sign, and hypoechoic edema of
Kerckring’s folds with mesenteric thrombosis were absent
in our series, and only merely enlarged mesenteric lymph
nodes, as detected in cases 1 and 2, were matching the fea-
tures described by Barreiros et al.\textsuperscript{16}

Histopathology is still the diagnostic gold standard in
ATB.\textsuperscript{17} However, obtaining a suitable material often proves
to be difficult in clinical practice. Our case series vividly
demonstrates that rigorous diagnostic workup is necessary.
Most interestingly, material from extra-abdominal sites,
such as pleural biopsies (case 1) and sputum samples (case
3), have been proven to be useful in order to confirm the
diagnosis.

\section*{4 | CONCLUSION}

ATB is a rare diagnosis in countries such as Germany and
uncommon in patients without an underlying immuno-
suppression. This case series aims to increase the awareness
of health-care practitioners regarding this clinical entity.
Diagnosis and treatment is often delayed, due to unspecific
symptoms during a prolonged clinical course. Therefore,
ATB should be included in the differential diagnosis by un-
specific abdominal complaints, especially in patients with
immigration background from a high-TB prevalence region.
Multiple and repetitive biopsies from extrapulmonary sites
are often needed to make the final diagnosis, whereas the
ascitic tap provides no evidence of the disease in most of
the cases. The early identification of this condition is cru-
ial in order to prevent clinical deterioration and ensuing
complications.

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\section*{CONFLICT OF INTEREST}

The authors declare that they have no competing interests
pertaining to this article.
AUTHOR CONTRIBUTIONS
MB collected data, drafted the initial manuscript, and revised the manuscript; MP reviewed and revised the manuscript and served as corresponding author; HW, AW, and SL collected clinical data and served as primary care physicians; and FS coordinated and supervised data collection and critically reviewed the manuscript for important intellectual content. All authors approved the final version of the manuscript as submitted.

ETHICAL APPROVAL AND INFORMED PATIENT CONSENT
A case report is intended to develop information to be shared for educational purposes and does not meet the definition of “original research.” Written informed consent for publication of any identifying information was obtained from each patient.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available in the supplementary material of this article.

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