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Brief Report**Peritoneal tuberculosis in two young immigrants with fever of unknown origin**S.G.S. Vreden ^a, B.J. Brenninkmeijer ^b and J.W.M. van der Meer ^a^a *Department of Medicine, University Hospital St. Radboud, Nijmegen, Netherlands;* ^b *Department of Medicine, St. Joseph Hospital, Veghel, Netherlands*

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Two patients with long-standing fever and weight loss underwent extensive diagnostic procedures before peritoneal tuberculosis was diagnosed by explorative laparotomy. By that time they had developed signs of intestinal obstruction. Both recovered after treatment, but one developed serious neurological complications, which could not be explained. Peritoneal tuberculosis is a manifestation of tuberculosis that is often difficult to diagnose. It should be borne in mind when diagnosing patients with fever of unknown origin, especially if they are originally from countries with a high prevalence of tuberculosis. *Neth J Med* 1992;41:218–221.

Key words: Tuberculosis; Peritonitis; Paresis; Fever of unknown origin

Introduction

Nowadays, peritoneal tuberculosis (Ptbc) is rarely encountered in western countries. Most cases concern immigrants from regions in which tuberculosis is endemic. The lack of pathognomonic symptoms or signs often causes a delay in establishing the diagnosis, even if diagnostic procedures are aimed at tuberculosis. Here we report two patients in whom the diagnosis was made 3 and 8 weeks, respectively, after admission.

Case 1

A 23-yr-old male of Turkish descent, was admitted to hospital because of fever and abdominal discomfort, which had already lasted for about

5 weeks. There were frequent bouts of profuse sweating, at night as well as during the day. The pain was located in the right lower abdominal quadrant, continuous and related to movement and coughing. Although not frequent, his stools had been loose, with no blood or mucus. He had lost more than 12 kg of body weight. The medical history so far had been unremarkable. The patient grew up in Turkey, but had lived in The Netherlands for several years. His last visit to Turkey was 18 months before.

On examination the patient was not very ill. The temperature was 39.5°C, the pulse rate 100 bpm, and the blood pressure 108/54 mmHg. There was no lymphadenopathy. On percussion of the thorax we found the lower border of the right lung about 3 cm higher compared to the left, but both lungs were clear. A Grade 1 systolic murmur was heard along the upper left sternal border. The bowel sounds were normal. The abdomen was tense and somewhat protuberant, but soft. Liver and spleen were not palpable and there was no shifting dullness. Rectal examina-

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tion revealed no mass or tenderness. Neurological examination was negative. The ESR was 126 mm/h, haemoglobin 6.1 mmol/l, WBC $13.8 \times 10^9/l$ with 82% neutrophils, 11% lymphocytes and 7% monocytes. The urine gave 5–20 monomorphic erythrocytes per high power field, sporadic leucocytes and no cell casts. The BUN was 2.1 mmol/l, the serum protein 70 g/l (the albumin 30.6 and gamma-globulin 12 g/l). The ALAT was 91 U/l, ASAT 68 U/l, LDH 320 U/l, CK 18 U/l. A differential diagnosis was made, which included tuberculosis, salmonellosis, abdominal abscess, leishmaniasis, malignant lymphoma and familial mediterranean fever. Cultures of blood, urine and stools remained negative. Serological tests for several microbial pathogens, including HIV were negative. An X-ray of the thorax was normal, except for an elevated right hemidiaphragm, which on fluoroscopy proved not to be paralysed. Because a subdiaphragmatic mass was suspected, an ultrasound study of the abdomen was performed: no subdiaphragmatic mass or fluid could be detected; there was a trace of ascites in Morrison's pouch; the intestinal wall of ileum and sigmoid and also the mesenterium were somewhat extended. An ^{111}In -labelled leucocyte scan did not reveal abscesses or focal inflammation. The tuberculin skin test, performed twice, was negative, as was the skin test with candida antigen. Varidase antigen, however, elicited an erythema of 15 mm. Microscopic examination of biopsy specimens of the bone marrow and the duodenal mucosa was unremarkable; in a liver biopsy, aspecific intralobular and portal infiltrates containing lymphocytes, histiocytes and polymorphonuclear cells were observed. During the 3-week period in which the patient had been observed and all investigations had been performed, his condition worsened; he lost another 8 kg. When he developed signs of intestinal obstruction, we decided to perform an explorative laparotomy. This revealed massive infiltration of the small intestine and numerous granulomas on the peritoneal and mesenterial surface. In a biopsy, acid-fast bacilli could be demonstrated, which on culture proved to be *Mycobacterium tuberculosis*, sensitive to all usual tuberculostatic drugs. Therapy was started with

ethambutol 900 mg and rifampicin 600 mg, both once daily, administered i.v. Isoniazid 300 mg once daily was only started 4 days later, when the patient could take oral therapy. Pyridoxine 50 mg b.i.d. was added to prevent neurotoxicity from isoniazid. The patient recovered slowly on this regimen and he gained weight. On the day that isoniazid was initiated, he complained of pain and muscle weakness in both upper legs; this had started a few days prior to surgery. On physical examination there was marked atrophy of both quadriceps and also paresis of the iliopsoas, adductor and abductor, gastrocnemius and tibialis anterior muscles. Knee and achilles tendon reflexes were absent and there was hypaesthesia on the medial side of both upper legs. An EMG revealed mass denervation of all muscles innervated by the lumbar plexus. CSF examination and myelography were negative. A computed tomography of the abdomen revealed no lymphadenopathy or abscesses in the psoas region; the lower thoracic and lumbar vertebrae were not affected. Since the paresis developed on the same day as the initiation of isoniazid therapy, the drug could not be responsible for this complication. Although there was some improvement in subsequent weeks, the patient remained seriously handicapped.

A second EMG performed 5 months later was still consistent with bilateral impairment of the lumbar plexus. Ethambutol was withdrawn after three months of treatment and isoniazid, rifampicin and pyridoxine were continued for nine months.

Case 2

A 26-yr-old Somalian refugee was admitted to hospital because of fever and diarrhoea. He also had anorexia, nausea, and epigastric pain. He had been living in The Netherlands for 11 months. The medical history so far had been unremarkable. On examination the patient was found to be moderately ill and his nutritional condition was poor. The temperature was 40°C. The pulse rate was 100 bpm and the blood pressure 120/70 mmHg. The lungs were clear and there were no heart murmurs. The abdomen was supple, spleen

and liver were not enlarged. Rectal examination revealed no mass or tenderness. The urine was unremarkable. The ESR was 125 mm/h, Hb 7.4 mmol/l, WBC $7.1 \times 10^9/l$, with 15% rods, 58% neutrophils and 21% lymphocytes. Minerals, BUN and transaminases were normal. Albumin 20.1 g/l. A differential diagnosis was made, which included AIDS, tuberculosis, salmonellosis, an abscess, malignant lymphoma and familial Mediterranean fever. Parasitological and bacteriological examination of the stools was negative. Serological assays for several microbial pathogens, including HIV were negative, as were blood cultures. Repeated chest X-rays were normal. A tuberculin skin test was positive, with an induration of 20 mm in diameter. Microscopic examination of biopsy specimens of the skin, the jejunal and rectal mucosa and bone marrow showed no abnormalities, as was the case with ultrasound and computed tomography of the abdomen. A barium-enema examination revealed a normal appearance of the small and large intestines. A total body ^{67}Ga scan did not show areas of focally increased uptake. During a period of 8 weeks in which the patient had been observed and all investigations were performed, his condition worsened; this was demonstrated by an additional weight loss from 44 to 38 kg. A therapeutic trial with colchicine, as treatment of suspected familial Mediterranean fever was not effective. Shortly thereafter the patient started complaining of abdominal pain. Because of progressive signs of peritoneal irritation and sub-ileus, it was decided to perform an explorative laparotomy, 61 days after admission. There was a diffuse peritonitis with multiple granulomas and adhesions of the intestines. Histology showed a necrotizing inflammation with granulomas, indicative of tuberculosis. Smears did not reveal acid-fast bacilli, but later cultures of the granulomatous material were positive for *Mycobacterium tuberculosis*, sensitive to all usual tuberculostatic drugs. Therapy with isoniazid 200 mg, rifampicin 450 mg and pyrazinamide 750 mg (all once daily) was started, together with parenteral nutrition. The temperature decreased slowly and the patient recovered completely. Pyrazinamide was discontinued 3 months after initiation of the therapy, the other drugs after 9 months.

Discussion

In both patients fever and weight loss were the most prominent clinical features on admission. Despite these nonspecific signs, an infection was suspected in these young people and because of their origin from Turkey and Somalia, respectively, tuberculosis ranked high in the differential diagnosis. The tuberculin skin test was negative in one of the patients, but this may reflect anergy and does not exclude active tuberculosis, especially in severely ill patients. Bone marrow cultures and liver biopsy (in case 1) were negative, despite the relatively high yield of these methods in patients with tuberculosis [1,2]. In both patients an explorative laparotomy was necessary to establish the diagnosis.

It is debatable whether ethambutol or pyrazinamide should be the third component in initial therapy. Ethambutol is far less active and is mostly used to prevent emergence of isoniazid resistant strains. However pyrazinamide is ineffective against *M. bovis*, which in developing countries may still play an important part in tuberculosis, especially if the infection may have been alimentary.

Paraparesis is a well-known complication of tuberculous spondylitis or paravertebral abscess [3–6]. In patient 1 none of these conditions could be demonstrated. Lifeso and colleagues described a series of 107 patients with spinal tuberculosis [5]. In 5 of these patients neurological impairment was caused by extradural or intradural involvement of the spinal canal with tuberculomas or arachnoiditis. This was not detected by myelography or computed tomographic scans, but only after laminectomy [5]. Thus, in retrospect such a complication may have occurred in our patient.

Peritonitis is an uncommon manifestation of tuberculosis. It accounts for 0.1 to 1% of all reported cases [7–9], and its exact incidence in The Netherlands is unknown. In a Dutch series of 85 patients with tuberculosis, collected in a university hospital, Smelt et al. reported one case with peritoneal disease [10]. The clinical symptoms and signs of Ptbc are nonspecific. Most patients have abdominal pain, fever and weight loss. Especially when there are no extraperitoneal localisations of tuberculosis, it takes a long time

before the diagnosis is made. In several series of patients with Ptbc, ascites could be established on physical examination in 16 to 80% [11-17]. Acid fast bacilli, however, could only be demonstrated in 11 to 50% of ascitic fluids. In these series, the percentage of patients in whom the diagnosis was made after laparoscopy or laparotomy varies from 5 to 40% and 40 to 97%, respectively. Although laparoscopy has been performed successfully in many cases, it bears a certain risk when intestinal adhesions are present. Recently, two studies have been published concerning the diagnostic value of adenosine deaminase activity in ascites and in the serum of patients with Ptbc [18,19]. Both articles report high specificity and sensitivity of this test for Ptbc. Several serodiagnostic tests for establishing active tuberculosis have been developed, with varying sensitivity and specificity [20-23]. However, these tests are still not available for routine use in the diagnosis of tuberculosis.

It is assumed that Ptbc represents a reactivation of tuberculosis, rather than primary infection [13,24]. The finding that Ptbc in Europe is mostly seen in patients from foreign countries, where there is a high prevalence of tuberculosis, supports this theory [12,13,17].

Ptbc remains a condition which is often only diagnosed after the elimination of a variety of other conditions. The diagnosis should be considered in young adults, with persistent fever and wasting, with or without abdominal symptoms, especially when they are originally from areas where tuberculosis is endemic. Until the value of adenosine deaminase activity or specific antibody assays has been established, the diagnosis of Ptbc remains highly dependent on invasive diagnostic procedures, such as laparoscopy and laparotomy. Normal chest X-rays and negative tuberculin skin tests are insufficient to exclude tuberculosis in patients with fever of unknown origin.

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