Abdominal tuberculosis: a retrospective review of cases presenting to a UK district hospital

J.P. MAMO¹, S.O. BRIJ¹ and D.A. ENOCH²

From the ¹Department of Medicine and ²Clinical Microbiology & Public Health Laboratory, Peterborough City Hospital, Peterborough and Stamford Hospitals NHS Foundation Trust, Peterborough PE3 9GZ, UK.

Address correspondence to D.A. Enoch, Clinical Microbiology and Public Health Laboratory, Peterborough City Hospital, Peterborough and Stamford Hospitals NHS Foundation Trust, Peterborough PE3 9GZ, UK. email: david.enoch@pbh-tr.nhs.uk

Summary

Introduction: Peterborough has one of the highest rates of tuberculosis in the East of England; ~40% of TB treated locally is extra-pulmonary.

Aim and methods: All adults diagnosed with abdominal tuberculosis (ATB) between January 2008 and September 2011 in Peterborough Hospitals were retrospectively evaluated with regard to their clinical history, investigation, management and outcomes.

Results: In total, 17 patients diagnosed with ATB were reviewed. All the patients were from (or descended from) high-risk ethnic groups. Four had co-existing pulmonary TB. Intestinal and peritoneal TB were the most common findings. The most common clinical manifestations included abdominal pain (71%), weight loss (59%), diarrhoea (47%) and pyrexia (41%). Fifteen patients had samples sent for microbiological investigation; 1 (6%) was smear positive and 9 (53%) were culture positive. Two (12%) were isoniazid resistant. No rifampicin resistance was detected. Anti-tuberculous therapy was given for 6–12 months. In total, 16 (94%) patients completed the treatment; 1 patient died prior to regime completion (crude mortality: 6%). There was one reported case of pyrazinamide intolerance and two episodes of isoniazid intolerance.

Discussion: ATB is a diagnostic challenge, especially in absence of lung involvement. It mimics other diseases and clinical presentation is usually non-specific, which may lead to diagnostic delay and development of complications. Extreme vigilance should be used when dealing with unexplained abdominal symptoms to ensure timely diagnosis of ATB. Early diagnosis with early anti-tuberculous therapy and surgical treatment are essential to ensure as positive an outcome as possible.

Introduction

Prior to the pasteurization of milk, abdominal tuberculosis (ATB) was not uncommon in the UK. However, recent surveillance from UK centres with high incidences of tuberculosis (TB) have found that ATB is relatively common in migrant populations.¹,² They concluded that ATB was a great mimic and that early surgical intervention assisted in the diagnosis.

Peterborough has one of the highest rates of TB in the East of England: the incidence of active TB in 2010 was 28.0 per 100 000 population compared with 6.3 per 100 000 population in the East of England and 15.1 per 100 000 population in England overall.³ Approximately 40% of TB treated in Peterborough is extra-pulmonary, the most common sites being cervical, supraclavicular or submandibular lymph nodal disease. This pattern of TB disease is seen predominantly in the Asian community. However, we recently noted an increase in cases of ATB; none were reported between 2000 and 2005.
We sought to review the epidemiology, management and outcome of all cases of ATB diagnosed in our population.

Methods

Setting

Peterborough and Stamford Hospitals NHS Foundation Trust is a district hospital with 600 beds serving a population of ~450 000 people in Cambridgeshire, England.

Study design and patients

All adults aged 18 years and above diagnosed with ATB between January 2008 and September 2011 in Peterborough and Stamford Hospitals NHS Foundation Trust were retrospectively evaluated with regard to their presentation history, related medical history, investigation, management and outcomes.

Variables

Demographic data (age, sex and ethnic background) and clinical information, including medical history, symptoms and signs (including duration), mode of presentation, physical findings, laboratory, therapeutic methods and outcomes were reviewed from the medical and nursing notes and analysed.

Definitions

ATB was defined as infections of the gastrointestinal tract, peritoneum or intra-abdominal solid organs caused by *Mycobacterium tuberculosis*. Diagnosis of ATB was made based on the presenting clinic features and one of the following criteria: (i) positive culture of *M. tuberculosis* from abdominal organ tissue or peritoneal fluid; (ii) positive acid-fast bacilli (AFB) stain from biopsies and (iii) histopathological demonstration of TB.

Microbiology

Samples received in microbiology underwent a fluorescent auramine stain to detect AFB and were cultured using solid culture techniques [Löwenstein-Jensen medium (Media for Mycobacteria Ltd, Penarth, UK)] until June 2011, when a liquid culture technique (Bactec™ MGIT™, 960 system; Beckton & Dickinson, Oxford, UK) was introduced. This required an incubation time of 8 weeks for sputum testing and 12 weeks for tissue and pleural fluid testing. Identification and susceptibility testing was performed at the National Health Protection Agency (HPA) National Mycobacterium Reference Laboratory (MRL) throughout the study. Nucleic acid amplification tests (NAATs) were not routinely available during the study period, but could be arranged at the HPA MRL in London. Interferon-gamma release assays (IGRAs) were available for use throughout the study period at the discretion of the clinical team after discussion with microbiology.

Statistical analysis was conducted using SPSS v.16. A *t*-test was used to determine statistical significance for continuous data. Approval for the study was sought and obtained from the Trust audit committee and categorized as surveillance.

Results

Seventeen patients (nine male; 52.9%) were diagnosed with ATB in the study period. Their ages ranged from 23 to 74 years (mean of 40.7 years). All the patients were from (or descended from) high-risk ethnic groups as shown in Table 1. The median duration of stay in the UK prior to diagnosis of gastrointestinal TB was 9 years (range: 3–50 years). Two patients had been born in the UK.

With regard to infection sites; the peritoneum was the most frequently infected site (*n* = 5), followed by the ileo-caecal valve (*n* = 5), small intestine (*n* = 4), retroperitoneum (due to psoas abscess *n* = 3), colon (*n* = 2) and liver (*n* = 1) (Figure 1). Two patients had co-existing ileo-caecal valve and ileal disease and one patient had co-existing ileo-caecal and colonic disease. Three patients had ATB and pulmonary or pleural TB. Two of these patients had positive respiratory samples only (sputum and broncho-alveolar lavage) and one patient grew TB from peritoneal tissue but not from pleural fluid. Another patient had co-existent tuberculosis in the occipital region of the brain, two patients with psoas abscesses had vertebral involvement and one patient with ileal TB had submandibular lymph node involvement. The most common clinical manifestations were abdominal pain (70.6%), weight loss (58.8%), diarrhoea (47.1%), pyrexia (41.2%) and abdominal distension (35.3%) (Figure 2). Patients were symptomatic prior to presentation for between 2 weeks and 12 months (median: 3 months). Twelve (70.6%) presented to the emergency department (eight under surgery, four under the physicians), three were seen in gastroenterology outpatients and two in respiratory outpatients.

In total, 15 (88.2%) patients had a sample sent to microbiology. One patient (5.9%) was smear positive and 9 patients (52.9% of total; 60% of those with a sample submitted for culture) were culture
Table 1  Summary of patient presentation and management outcomes

<table>
<thead>
<tr>
<th></th>
<th>Age (years)/ gender</th>
<th>Origin (duration in UK)</th>
<th>Site of infection</th>
<th>Diagnostic methods</th>
<th>Diagnostic results</th>
<th>Underlying diseases</th>
<th>Clinical manifestations</th>
<th>Mode of presentation</th>
<th>Surgery</th>
<th>Medical therapy (duration in months)</th>
<th>Therapy outcomes and TB drug reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>43/M</td>
<td>Afro-Caribbean (since birth)</td>
<td>Mesentery and peritoneum</td>
<td>CT scan and laparotomy (including biopsies)</td>
<td>AFB smear negative. MTB culture positive. INH resistant.</td>
<td>Eczema, personality disorder, hepatitis B positive, IVDU</td>
<td>1, 2, 4, 6, 14, 18</td>
<td>ED surgical</td>
<td>Y</td>
<td>12</td>
<td>Completed</td>
</tr>
<tr>
<td>2</td>
<td>26/F</td>
<td>Pakistan (since 1990)</td>
<td>Ileocaecal and pulmonary and left cortical tuberculoma</td>
<td>CT scan and colonic biopsies</td>
<td>AFB smear positive. MTB culture positive. Sensitive MTB.</td>
<td>Previous TB</td>
<td>2, 4, 5, 11, 12, 14, 16, 17, 18</td>
<td>Respiratory OPD</td>
<td>Y</td>
<td>10</td>
<td>Completed</td>
</tr>
<tr>
<td>3</td>
<td>74/M</td>
<td>Afghanistan (since 2001)</td>
<td>Ileum</td>
<td>Laparoscopy and peritoneal biopsies</td>
<td>AFB smear negative. Culture negative. Granulomatous inflammation on histology.</td>
<td>IHD, renal stones</td>
<td>1, 2, 7, 11, 14</td>
<td>ED surgical</td>
<td>Y</td>
<td>6</td>
<td>Completed</td>
</tr>
<tr>
<td>4</td>
<td>27/F</td>
<td>India (since 2004)</td>
<td>Colon</td>
<td>CT scan and colonic biopsies</td>
<td>AFB smear negative. MTB culture positive. Sensitive MTB.</td>
<td>Nil</td>
<td>1, 3, 4, 5, 6, 9, 12</td>
<td>Gastroenterology OPD</td>
<td>N</td>
<td>6</td>
<td>Completed</td>
</tr>
<tr>
<td>5</td>
<td>47/F</td>
<td>Afro-Caribbean (since birth)</td>
<td>Peritoneum and pleura</td>
<td>Laparoscopy and pleural fluid</td>
<td>AFB smear negative. PCR negative. MTB culture positive. Sensitive MTB.</td>
<td>Abdominoplasty, pleomorphic adenoma, erythema nodosum, acne vulgaris, asthma, depression</td>
<td>1, 2, 4, 5</td>
<td>ED medical</td>
<td>N</td>
<td>9</td>
<td>Completed pyrazinamide intolerance</td>
</tr>
<tr>
<td>6</td>
<td>39/M</td>
<td>Pakistan (since 1996)</td>
<td>Peritoneum</td>
<td>Peritoneal fluid</td>
<td>AFB smear negative. MTB culture positive. Sensitive MTB.</td>
<td>Epilepsy</td>
<td>1, 5, 6, 11, 12</td>
<td>ED medical</td>
<td>N</td>
<td>12</td>
<td>Completedisoniazid intolerance (drug-induced hepatitis)</td>
</tr>
<tr>
<td>7</td>
<td>46/M</td>
<td>Morocco (since 2004)</td>
<td>Peritoneum</td>
<td>Laparoscopy and lymph node biopsies</td>
<td>AFB smear negative. PCR negative. MTB culture negative. Granulomatous inflammation on histology (AFB smear negative).</td>
<td>Previous laparotomy, stoma insertion</td>
<td>1, 2, 3, 4, 5, 6, 8, 11, 12</td>
<td>ED medical</td>
<td>N</td>
<td>12</td>
<td>Died</td>
</tr>
<tr>
<td>8</td>
<td>47/F</td>
<td>Pakistan (since 2003)</td>
<td>Psoas abscess</td>
<td>CT-guided aspiration</td>
<td>AFB smear negative. PCR negative. MTB culture negative. Granulomatous inflammation on histology (AFB)</td>
<td>DM</td>
<td>1, 5, 7</td>
<td>ED surgical</td>
<td>N</td>
<td>6</td>
<td>Completed</td>
</tr>
</tbody>
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(continued)
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<thead>
<tr>
<th>Age  (years)/gender</th>
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<tr>
<td>9 25/F</td>
<td>Pakistan (since 1987)</td>
<td>Jejunum and submandibular lymph node</td>
<td>Lymph node biopsy</td>
<td>AFB smear negative, MTB culture positive, INH and streptomycin resistant.</td>
<td>CD, previous TB, VDD 6, 8, 10, 18</td>
<td>Gastroenterology OPD</td>
<td>N</td>
<td>12</td>
<td>Completed</td>
<td></td>
</tr>
<tr>
<td>10 40/M</td>
<td>Lithuania (since 2005)</td>
<td>Ileocaecum and pulmonary</td>
<td>Lymph node biopsy and bronchial washings</td>
<td>AFB smear positive. MTB culture positive. Sensitive MTB.</td>
<td>Small bowel resection 1, 2, 6</td>
<td>ED surgical</td>
<td>Y</td>
<td>12</td>
<td>Completed Drug-induced hepatitis</td>
<td></td>
</tr>
<tr>
<td>11 40/F</td>
<td>Portugal (since 2008)</td>
<td>Peritoneum</td>
<td></td>
<td>AFB smear negative. MTB culture positive. Sensitive MTB.</td>
<td>VDD</td>
<td>ED surgical</td>
<td>Y</td>
<td>6</td>
<td>Completed</td>
<td></td>
</tr>
<tr>
<td>12 28/M</td>
<td>Bangladesh (since 2003)</td>
<td>Ileocaecum and colon</td>
<td>Colonoscopy (including biopsies)</td>
<td>AFB smear negative. Culture negative. Granulomatous inflammation on histology.</td>
<td>VDD, asthma 4, 6</td>
<td>ED surgical</td>
<td>N</td>
<td>6</td>
<td>Completed</td>
<td></td>
</tr>
<tr>
<td>13 36/F</td>
<td>Pakistan (duration unknown)</td>
<td>Bilateral psoas abscesses and thoracic vertebral lesions</td>
<td>CT scan (including biopsies)</td>
<td>AFB smear negative. MTB culture positive. Sensitive MTB.</td>
<td>VDD, anaemia 5, 13, 19</td>
<td>ED medical</td>
<td>N</td>
<td>6</td>
<td>Completed</td>
<td></td>
</tr>
<tr>
<td>14 31/M</td>
<td>India (since 2008)</td>
<td>Vertebræ, with co-existing psoas abscess</td>
<td>CT/MRI scan (including biopsies)</td>
<td>AFB smear negative. Granulomatous inflammation on histology (AFB smear negative). BCG reactive.</td>
<td>VDD</td>
<td>Respiratory OPD</td>
<td>N</td>
<td>9</td>
<td>Completed</td>
<td></td>
</tr>
<tr>
<td>15 23/F</td>
<td>Lithuania (since 2007)</td>
<td>Ileocaecum and appendix</td>
<td>Laparoscopy (including biopsies)</td>
<td>No sample to microbiology. Cavitating granulomas. Granulomatous inflammation on histology (AFB smear negative).</td>
<td>Nil</td>
<td>ED surgical</td>
<td>Y</td>
<td>6</td>
<td>Completed</td>
<td></td>
</tr>
<tr>
<td>16 68/M</td>
<td>Iran (since 1961)</td>
<td>Abdominal lymph nodes and liver abscess</td>
<td>CT scan and laparoscopy (including biopsies)</td>
<td>AFB smear negative. Culture negative. Granulomatous inflammation on histology (AFB smear negative). IGRA reactive. DM</td>
<td></td>
<td>ED surgical</td>
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Two isolates (11.8%) were isoniazid resistant and one (5.9%) was resistant to streptomycin. No rifampicin resistance was detected. All three patients who were tested by NAAT had a negative result but had suggestive histology (all were smear negative and two were culture negative). Treatment was nevertheless continued due to the clinical picture in all cases. Thirteen patients (76.5%) had an HIV test result documented in the notes, all of which were negative. None of the five patients with peritoneal disease had biochemistry performed on the isolate (for protein or glucose). IGRA testing was performed on two patients. One patient had a negative IGRA result but histology was highly suggestive, whereas another patient had two IGRA tests (initially negative before becoming positive). Histology was again highly suggestive. Both patients responded well to treatment.

Co-morbidities were identified in all but two patients and included vitamin D deficiency \((n=5)\), skin diseases \((n=4)\), previous TB infection or contact \((n=3)\), psychiatric illness \((n=3)\), asthma \((n=2)\), diabetes mellitus \((n=2)\), Crohn’s disease \((n=2)\), ischaemic heart disease \((n=1)\), renal calculi \((n=1)\), epilepsy \((n=1)\), and anaemia \((n=1)\). None of the patients in this series had malignancy or chronic renal failure and no patients were taking immunosuppressive therapy.

All patients received anti-tuberculous therapy (ATT) for a minimum of 6 months (range: 6–12 months; Table 1). A 6-month regime was given as minimum and the full regime was given wherever possible except in the situations where a particular drug was contra-indicated or a drug reaction was noted. Six patients (35.3%) also underwent surgical resection. Treatment was commenced in all patients with 16 (94.1%) patients completing treatment; one patient died prior to regime completion (crude mortality: 5.9%). There was one reported case of pyrazinamide intolerance and two episodes of isoniazid intolerance (acute hepatitis), which required adjustment of duration of treatment as per the National Guidelines.

No rifampicin resistance was detected. All three patients who were tested by NAAT had a negative result but two were culture negative. Treatment was nevertheless continued due to the clinical picture in all cases. Thirteen patients (76.5%) had an HIV test result documented in the notes, all of which were negative. None of the five patients with peritoneal disease had biochemistry performed on the isolate (for protein or glucose). IGRA testing was performed on two patients. One patient had a negative IGRA result but histology was highly suggestive. Both patients responded well to treatment.

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<tr>
<td>17 51/M</td>
<td>Iran (since 1971)</td>
<td>Small intestine and ileocaecum</td>
<td>Colonoscopy (including AFB smear negative. Culture negative. Chronic inflammation on histology atypical for Crohn’s disease. First IGRA negative. Second IGRA positive.)</td>
<td>CD</td>
<td>1, 4, 6, 15</td>
<td>Gastroenterology</td>
<td>OPD</td>
<td>N</td>
<td>6</td>
<td>Completed</td>
</tr>
</tbody>
</table>

F, female; M, male; MTB, *M. tuberculosis*; Anti-TB, anti-tuberculous; DM, diabetes mellitus; VDD, vitamin D deficient; CD, Crohn’s disease; IC, ileo-caecal; CT, computed tomography; MRI, magnetic resonance imaging; IHD, ischaemic heart disease; PCR, polymerase chain reaction; IVDU, intravenous drug user; OPD, outpatient department; ED, emergency department

Institute for Health and Clinical Excellence (NICE) guidelines.

About 15 patients (88.2%) who completed therapy had erythrocyte sedimentation rates (ESRs) and haemoglobin levels available prior to and after treatment. Mean pre-treatment ESR levels of 39.1 mm/h reduced significantly to a mean of 12.6 mm/h post-treatment ($P=0.0018$). There was a corresponding rise in the mean haemoglobin level from pre-treatment levels of 101.7 g/l to post-treatment levels of 135.6 g/l ($P=0.0001$) (Figure 3).
Discussion

The term ‘abdominal TB’ emphasizes the involvement of any or multiple parts of the gastrointestinal system. Case series of ATB are infrequently described from the UK but our experience is supported by a number of these studies. The majority of patients in these series were from high-risk ethnic groups, all of our cases were from these groups, reflecting Peterborough’s diverse ethnic make-up, with a large population of people from Pakistan and India and a rising population from Eastern Europe. Patients had been residing in the UK for a significant time prior to diagnosis for most patients (3–50 years), which is longer than previously reported (mean of 7 years; range: 2 months to 20 years). We did not record travel to endemic countries or contact with other people from endemic countries since arrival in the UK. Approximately one-third of patients had extra-intestinal disease, most frequently pulmonary. The site of infection most frequently observed was peritoneal in one study but ileal in others.

ATB is a diagnostic challenge, especially in the absence of lung involvement. It tends to mimic other diseases that affect the gastrointestinal tract including Crohn’s disease, tumours and other infectious diseases. Indeed, two of our patients with ATB also had Crohn’s disease. The clinical presentation of ATB is usually non-specific and therefore often results in diagnostic delay and hence the development of complications. ATB took an average of 3 months to be considered in our study, which is similar to another UK study. Abdominal pain, fever and weight loss were the most common manifestations in all series. Diagnosis proved troublesome in many cases. Anaemia and raised inflammatory markers were found in >90% of cases in some studies and frequent in others.

Diagnosis often requires some form of surgical intervention to obtain tissue samples for microbial and histological examination. In fact, all patients included in this study required some form of invasive intervention to be able to diagnose TB. Despite this, a sample was not sent to microbiology for two patients. Laparoscopy was the most effective investigation in one study, yielding a diagnosis in 23 (92%) of 25 patients.

We found the smear for AFB to be extremely insensitive, with only one (5.9%) being positive. This compares with 2 of 14 (14.3%) patients in one study. Nucleic acid amplification tests were also insensitive and did not aid the initial management. All three patients had suggestive histology and one patient was subsequently culture positive. Nucleic acid amplification tests were positive in only 1 of 14 (7.1%) samples in another study. Indeed, UK guidelines suggest the diagnosis of non-pulmonary TB should still be considered even if rapid tests are negative. This follows a meta-analysis involving 212 studies that suggested NAATs were less sensitive for non-pulmonary disease. They were, however, thought to be specific. IGRAs were performed on two patients. The role of IGRA testing for diagnosing active TB remains unknown. NICE concluded that IGRA tests may have a role in ruling out infection with M. tuberculosis. The Health Protection Agency subsequently suggested that IGRA tests are only considered in supporting the primary diagnosis of active TB when it has not been possible to confirm the diagnosis by culture and when strong support for the diagnosis is lacking from radiological and histopathological tests.

Treatment should not be delayed while awaiting culture when ATB is suspected clinically. A study of 60 patients with ATB found that 26 of 31 patients who died of ATB did so within 6 weeks of diagnosis; only eight of the patients with advanced disease died after the treatment commenced.

Peritoneal fluid, when sent for cytological examination, typically reveals a lymphocytic exudate, peritoneal fluid examination was not requested for the five patients who subsequently were diagnosed with peritoneal TB (four by culture, one by histology).

The recommended treatment for ATB is conventional anti-TB therapy for a minimum of 6 months. Surgical intervention was required in six of our patients to aid in the diagnosis. One of these patients required surgical intervention due to acute complications of adhesions and obstruction.

In conclusion, extreme vigilance should be used when dealing with patients complaining of unexplained abdominal symptoms as this may assist in the timely diagnosis of ATB. Early diagnosis with early anti-tuberculous therapy and surgical treatment, where required, are essential to ensure as positive an outcome as possible.

Learning points

- A high index of suspicion is required at all times. ATB often presents insidiously but should be considered in any patient who presents with abdominal pain, fever and weight loss and especially when another cause is not immediately apparent.
- It is important to ascertain whether patients were born in a country where TB is endemic. TB often presents within 10 years of migration. It is estimated that one-third of the world population are infected with TB and therefore ATB disease may be caused by re-activation of latent TB. However, re-infection from
other family members and following foreign travel should always be considered.

- Appropriate samples must be sent to microbiology for AFB and mycobacterial culture. Biochemical and cytological analysis of peritoneal fluid can suggest a diagnosis of TB that may later be confirmed by mycobacterial culture.

- Microscopy for AFB of ascitic fluid and pus is often negative (i.e. it has a low sensitivity). Direct visualization and biopsy of the lesion at colonoscopy or laparoscopy/laparotomy yields the best results. NAAT and culture can be misleading, as the sensitivity is not 100%. The clinical picture is crucial.

- A multi-disciplinary approach involving the local TB lead (Respiratory or Infectious Diseases Physician), the Clinical Microbiology laboratory and Surgical colleagues is essential. Therapy is prolonged and close review essential as complications with ATT (e.g. hepatitis, malabsorption and drug interactions) are not infrequent.

- None of the patients tested in this series was co-infected with HIV. However, HIV must always be considered. The annual incidence of TB in HIV infection is 10%.11

- We found IGRAs to be unhelpful in making a diagnosis of active TB and potentially misleading.

Conflict of interest: None declared.

References