CASE REPORT

Tuberculous intestinal perforation during anti-tuberculous treatment

Intestinal perforation is an uncommon but potentially fatal complication of intestinal tuberculosis. We report on a 63-year-old HIV-negative man who developed terminal ileal perforation approximately 3.5 months following initiation of anti-tuberculous treatment for pulmonary tuberculosis and a concomitant tuberculous perianal abscess. Clinical and radiological improvements were initially evident following commencement of anti-tuberculous treatment, and the paradoxical response phenomenon was suspected. The patient subsequently underwent surgical resection of the affected bowel segment with primary anastomosis, and made an uneventful recovery. Anti-tuberculous medication was continued for another 12 months, and after a further 12 months there was no evidence of recurrent tuberculosis. This case illustrates that tuberculous intestinal perforation can develop during chemotherapy for tuberculosis. Prompt diagnosis and appropriate surgical treatment are essential to avoid morbidity and mortality.

Introduction

The incidence of intestinal tuberculosis (TB) in western countries has increased along with an overall resurgence of TB. This resurgence is related to an increasing incidence of human immunodeficiency virus (HIV) infection, an ageing population, increased use of immunosuppressive drugs, and the emergence of multi-resistant strains of Mycobacterium tuberculosis. One of the most feared complications of intestinal TB is intestinal perforation: it occurs in 1 to 15% of patients. We describe a patient who developed acute tuberculous intestinal perforation while receiving anti-tuberculous treatment. The patient experienced an initial clinical improvement with anti-tuberculous therapy so the phenomenon known as the paradoxical response was suspected. Paradoxical deterioration during anti-tuberculous therapy refers to the clinical or radiological worsening of pre-existing tuberculous lesions or the development of new lesions not attributable to the normal course of disease in a patient who initially improves with anti-tuberculous therapy.

Case report

A 63-year-old Chinese man was admitted to United Christian Hospital in July 2003 with a history of fever, night sweats, weight loss, malaise, a productive cough, and a perianal discharge. He had no other gastrointestinal symptoms and physical examination of the abdomen was unremarkable. The patient had a history of a perforated peptic ulcer treated by patch repair 7 years ago, but no history of TB. Routine blood tests revealed mild anaemia (haemoglobin 121 g/L), lymphopenia (lymphocyte count, 0.4 x 10⁹ /L; reference range, 1.0-3.8 x 10⁹ /L), and hypoalbuminaemia (albumin, 20 g/L; reference range,
ranging from 1 to 15%. Perforations may be solitary or multiple, and usually occur in the distal ileum. As reported in previous studies, intestinal perforation may occur after anti-tuberculous treatment has commenced, and has been reported as occurring between 2 days and 4 months after the initiation of anti-tuberculous therapy. When perforation occurs shortly after the institution of anti-tuberculous therapy, it may merely be representing the natural progression of the disease. Alternatively, it has been suggested that a reduced inflammatory response as a result of anti-tuberculous treatment results in impaired ulcer healing and a reduced tendency to reinforcement by the mesentery. Some patients have had clear documentation of initial improvement with anti-tuberculous treatment before the occurrence of intestinal perforation, and such deterioration could be attributed to the paradoxical response phenomenon.

The pathogenesis of paradoxical deterioration during effective anti-tuberculous therapy is not fully understood. Possible mechanisms include a strengthening of the host’s delayed hypersensitivity response, and an increased exposure to mycobacterial antigens released as bacilli are killed by effective chemotherapy. This phenomenon has been increasingly reported in HIV-positive patients being treated for TB, especially among those prescribed highly active anti-retroviral therapy. Paradoxical deterioration has also been reported to occur in up to 11.1% of HIV-negative patients during treatment for TB, and it is seen more frequently in patients with extra-pulmonary TB, and among those with low baseline lymphocyte counts. Nevertheless, an inadequate response to anti-tuberculous therapy as a result of drug resistance or poor drug compliance should be excluded before accepting such a diagnosis.

In a review of 122 episodes of paradoxical responses, the median time from commencement of anti-tuberculous treatment to development of the paradoxical response was 60 days (range, 14–270 days). Our patient developed paradoxical deterioration with intestinal perforation approximately 3.5 months after initiation of anti-tuberculous therapy. Although anti-tuberculous therapy was interrupted for a short period, clinical and radiological improvement had been documented before the occurrence of intestinal perforation. Hence, a paradoxical response rather than treatment failure was suspected. Improvement in general health and nutritional status following effective treatment of TB may have contributed to recovery of the immune system in our patient. The rise in albumin levels and recovery of lymphocyte counts after anti-tuberculous therapy support this observation. An upsurge in lymphocyte counts is also common in patients during a paradoxical response. In addition, an exaggerated tuberculin skin reaction may be observed; the tuberculin test was not performed in our patient. The strain of \textit{M. tuberculosis} identified in our patient was sensitive to standard anti-tuberculous agents. Determination of resistance to pyrazinamide is not routinely performed as this is technically problematic. Nonetheless, resistance to pyrazinamide is not routinely performed as this is technically problematic.

Discussion

Free intestinal perforation is an uncommon but serious complication of intestinal TB: the reported incidence ranging from 1 to 15%. Perforations may be solitary or multiple, and usually occur in the distal ileum. As reported
Pyrazinamide is uncommon in the absence of resistance to other first-line drugs. Acid-fast bacilli were identified in the resected surgical specimen but these were probably non-viable organisms: a stain for AFB can remain positive in the affected tissues for up to 5 months despite effective anti-tuberculous treatment.

The treatment of choice for perforation in intestinal TB is resection of the affected bowel segment followed by an end-to-end anastomosis. Simple closure of the lesion is not recommended as it is associated with a high incidence of leakage and fistula formation. The mortality associated with tuberculous intestinal perforation is high with reported figures ranging from 25 to 100%. Factors linked to increased morbidity and mortality include delayed operation, presence of multiple perforations, primary closure of perforations, leakage from the operated area, and steroid treatment. Anti-tuberculous therapy should be started as soon as possible. A duration of 6 to 9 months is sufficient for immunocompetent patients treated with a regimen of four first-line drugs, namely isoniazid, rifampicin, ethambutol, and pyrazinamide. A longer period of therapy is necessary if one or more of these first-line drugs cannot be used because of intolerance or drug resistance. In situations when rifampicin cannot be used, as in the present case, isoniazid, ethambutol, and a fluoroquinolone should be given for a minimum of 12 to 18 months, supplemented by pyrazinamide for at least the initial 2 months.

This case highlights the need to maintain a high index of suspicion when treating patients who present with acute abdominal pain while receiving treatment for TB. Early recognition and timely surgical intervention are essential if excessive morbidity and mortality are to be avoided.

References