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LETTER TO THE EDITOR

Intestinal tuberculosis as a cause of gastrointestinal bleeding in a renal transplant recipient

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Tuberculosis (TB) is an important cause of mortality and morbidity in renal transplant recipients. Among the different sites of TB, intestinal involvement is extremely rare. The symptoms of intestinal TB are usually nonspecific which make an early diagnosis difficult.

A 64-year-old man with history of diabetes mellitus, hypertension and end-stage renal failure secondary to IgA nephropathy underwent first deceased kidney transplantation (CMV Donor−/Recipient+). He was given cyclosporine, azathioprine, and prednisolone as maintenance immunosuppressive therapy. Eight months later, he experienced an episode of Banff type 1A acute rejection. He was treated with pulse methylprednisolone and cyclosporine was switched to tacrolimus.

His renal function started to deteriorate 2 years post-transplant. Renal graft biopsy was done and the histology revealed changes of acute T-cell mediated rejection (i2t1) in a background of severe interstitial fibrosis and tubular atrophy. He was treated with another course of pulse methylprednisolone. Immunosuppressive regimen was not further escalated in view of severe chronic background changes.

One month later, he was diagnosed to have cytomegalovirus (CMV) antigenaemia (CMV pp65 antigen: 1 per 2×10^5 WBC) and was given a course of valganciclovir. The immunosuppressive regimen at that time included prednisolone 7.5 mg daily, azathioprine 75 mg daily and tacrolimus 6 mg daily [abbreviated AUC_{0-12}: 75 ng × h/ml (target AUC_{0-12}: 80–100 ng × h/ml)]. Moreover, he also complained of severe anaemic symptoms. His haemoglobin was 4.7 g/dl, mean cell volume 71.8 fl, reticulocyte count 1.7% and white blood count (WBC) 1.0×10^9/l. There was no epigastric pain, tarry stool or per rectal bleeding. In view of profound anaemia and leucopenia, azathioprine and valganciclovir were stopped. Subsequently he developed high fever and chest X-ray (CXR) showed right middle zone and right lower zone infiltration. Cefoperazone was started. Repeated CMV pp65 antigen remained positive (1 per 2×10^5 WBC) and valganciclovir was initiated again. However, his symptoms deteriorated despite treatment. Tacrolimus was stopped in view of further radiologic deterioration and subsequent confirmation of pulmonary TB (sputum smear positive for acid fast bacilli). Anti-tuberculosis treatment including isoniazid, rifampicin and pyrazinamide was initiated.

At this juncture, he had repeated episodes of fresh melaena with significant haemoglobin drop. No bleeding source could be identified by the oesophago-gastro-duodenoscopy. Colonoscopy failed because the luminal view was obscured by blood clots. Coeliac and mesenteric angiogram showed patchy and active contrast extravasation from the ileocolic artery, mainly located at proximal ascending colon and caecum (Fig. 1). In view of persistent gastrointestinal bleeding, colonoscopy was repeated which showed features of terminal ileitis with multiple ileal ulcers involving the ileocaecal (IC) valve. There were also features of colitis at caecum and proximal ascending colon with few shallow ulcers and erosions but there was no active bleeding from the ulcers. Third colonoscopy was performed 2 days later, which showed multiple patches of ulcerative mucosa in the terminal ileum, 5 cm from IC valve (Fig. 2a). There was a 3-cm clean base ulcer with small adherent clots in the caecum (Fig. 2b) and a 2-cm clean base ulcer in proximal transverse colon with friable ulcer edge.

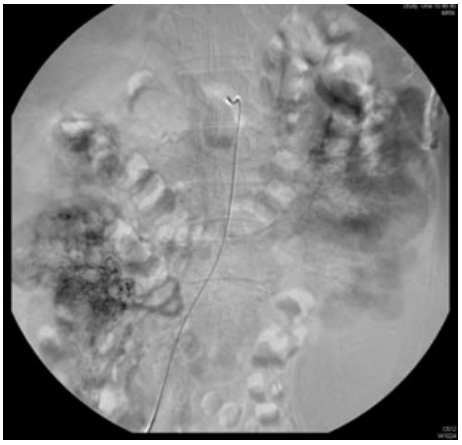

Figure 1 Coeliac and mesenteric angiogram showing patchy and active contrast extravasation from the ileocolic artery.

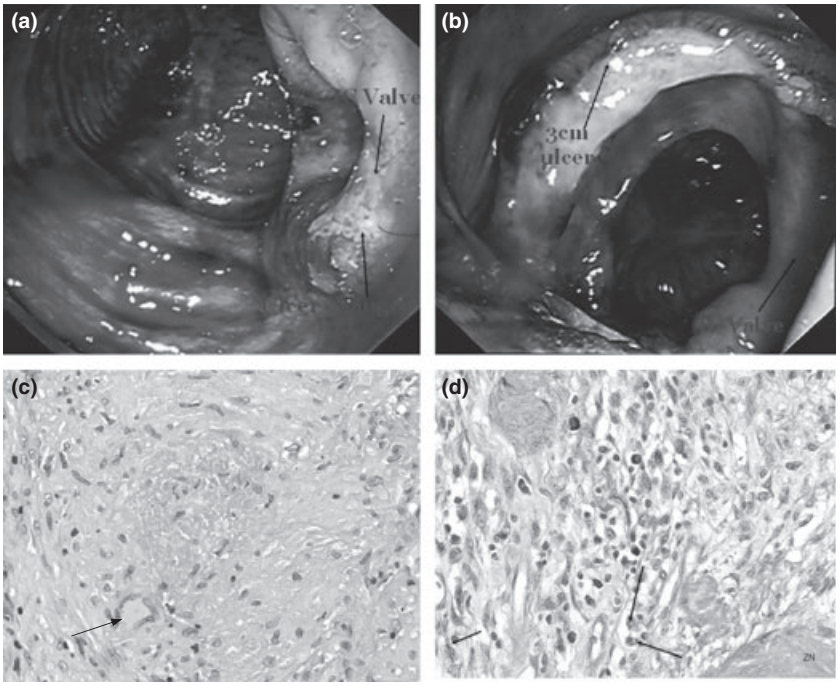

Figure 2 (a) Multiple patches of ulcerative mucosa in the terminal ileum, 5 cm from ileocaecal valve. (b) A 3-cm clean base ulcer with small adherent clots in the caecum. (c) Langhan's giant cell (arrow) in edge of a necrotizing granuloma (H&E stain). (d) Ziehl-Neelsen stain reveals acid fast bacilli (arrows).

However, fresh melaena still persisted and emergency laparotomy was arranged. There was a 1-cm perforated ileum (30 cm from IC valve) walled off by omentum. Finally, right hemicolectomy with double barrel stoma was done. Histology of the resected bowel revealed multiple granulomata in the ileal wall around the site of perforation and ulcerated regions (Fig. 2c). Moreover, necrotizing granuloma was also present in the regional lymph nodes. The colonic resection margin showed a few Langhans' giant cells and granuloma. Ziehl-Neelsen stain revealed the presence of acid fast bacilli in the granuloma (Fig. 2d), which was compatible with *Mycobacterium tuberculosis* infection.

There was no more gastrointestinal bleeding and his haemoglobin remained static. The white cell count normalized. CMV pp65 antigen became negative. The CXR was clear. His serum creatinine remained static at around 500 μmol/l. He was planned for completion of total 1-year anti-TB treatment.

Postrenal transplant TB can occur in different parts of the world. However, the prevalence varies widely, ranging from less than 1% in Western countries [1] to around 15% in India [2]. In Hong Kong, the prevalence is 5.2% [3]. In addition to the local epidemiological risk, other predisposing factors include hyperglycaemia, use of potent immunosuppressive agents such as tacrolimus alone or in combination with mycophenolate mofetil, use of long-term steroid, repeated episodes of acute rejection requiring high-dose steroid and use of antilymphocyte globulin [4,5].

Table 1 summarizes the clinical features of the postrenal transplant recipients with intestinal TB published in literature in recent years. The symptoms of intestinal TB are usually nonspecific [6]. It can also cause both upper and lower gastrointestinal haemorrhage [7]. Moreover, intestinal TB associated intestinal perforation was also common [8]. Colonoscopy is the most useful diagnostic test for intestinal TB. Histological findings of colonic biopsy include noncaseating granulomas, collection of loosely arranged epitheloid cells and chronic nonspecific inflammatory changes. The diagnosis of intestinal TB requires microbiological and culture confirmation. With the aid of polymerase chain reaction assays, a rapid diagnosis can be made. On the other hand, surgical exploration was reserved for those with diagnostic difficulty by endoscopic means or complications like perforation, intestinal obstruction and haemorrhage which failed to be controlled with medical treatment.

Mycobacterium tuberculosis (TB) infection after organ transplantation poses high mortality and the mortality was mostly related to co-existing infections and side effects of anti-TB treatment, mainly hepatic failure [6]. Furthermore, the mortality associated with intestinal perforation is high, ranging from 25% to 45.5% [8,9].

In summary, intestinal TB is potentially life-threatening. An early diagnosis is difficult because its presentations are usually nonspecific. Anaemia and gastrointestinal bleeding could be the only presenting signs and symptoms. Early surgical intervention is necessary when the gastrointestinal bleeding cannot be

Table 1. Summary of clinical features of intestinal tuberculosis in renal transplant recipients from 1995 to 2009.

Gender/Age	Presentation	Diagnosis	Outcome	Immunosuppressive agents	Acute rejection before diagnosis of TB	Reference
F/39	Abdominal pain, recurrent bloody diarrhoea	Histology and PCR of colonic biopsies	Survived	Not reported	Not reported	[10]
M/49	Severe anaemia with fresh melaena and rectal bleeding	Histology of resected bowel	Died	Cyclosporine, azathioprine, prednisolone	No	[7]
F/61	Fever, bloody diarrhoea, severe anaemia	Histology and PCR of colonic biopsies	Survived	Tacrolimus, MMF, prednisolone	Yes	[11]
F/26	Fever, abdominal pain, diarrhoea	Culture of colonic specimens	Survived	Not reported	Not reported	[12]
M/34	Anaemia, melaena	Histology of resected bowel and lymph node	Survived	Cyclosporine, azathioprine, prednisolone	No	[13]
M/57	Fever, massive upper gastro-intestinal bleed	Histology of resected stomach	Died	Cyclosporine, azathioprine, prednisolone	No	[14]
F/32	Fever, abdominal pain	Histology and culture of colonic specimens	Survived	OKT3, Cyclosporine, azathioprine, prednisolone	No	[15]

controlled by medical therapy or complication like bowel perforation was developed. A high index of suspicion in vulnerable patients is the key to timely diagnosis and allows early initiation of anti-TB treatment.

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