

Thrombotic thrombocytopenic purpura mimicking acute small bowel Crohn's disease

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Abstract

A 39 year old woman presented with a short history of bloody diarrhoea. She subsequently developed microangiopathic haemolysis, platelet consumption, and renal impairment. Initial investigations suggested underlying Crohn's disease of the terminal ileum complicated by sepsis and disseminated intravascular coagulation. However, after resection of a perforated caecum and terminal ileum, the diagnosis of thrombotic thrombocytopenic purpura was made. There was weak serological evidence of yersinia infection, this may have caused the early localisation of the lesions to the terminal ileum. This is believed to be the first report of thrombotic thrombocytopenic purpura affecting the small bowel alone at presentation.

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Gastrointestinal ischaemia, like many other diseases, may mimic inflammatory bowel disease at presentation. Microvascular occlusion in the haemolytic-uraemic syndrome may cause acute colitis,^{1,2} and in paroxysmal nocturnal haemoglobinuria small bowel ischaemia has been described.³ We report a patient with thrombotic thrombocytopenic purpura who presented with small bowel involvement that was clinically indistinguishable from Crohn's disease.

Case report

A 39 year old white woman was admitted to hospital with a presumptive diagnosis of severe

infective or inflammatory colitis following one week of bloody diarrhoea, colicky abdominal pain, vomiting, and fever. There was no other history of note and she was not taking oral contraceptives or any other medication. Initial investigations showed a leukocytosis ($27.3 \times 10^9/l$), a normal haemoglobin concentration (14.7 g/dl) and platelet count ($262 \times 10^9/l$), and hypoalbuminaemia (31 g/l). Other investigations including stool cultures were normal. She was rehydrated intravenously and, because of her toxic state, intravenous cefuroxime, metronidazole, hydrocortisone (100 mg four times daily) were begun.

Four days later the fever and diarrhoea continued and she became uncharacteristically agitated. Her urine output fell to 400 ml per 24 hours despite adequate rehydration, and there were increases in plasma urea (19.7 mmol/l) and creatinine ($220 \text{ } \mu\text{mol/l}$). This was associated with microscopic haematuria, a fall in haemoglobin (8.3 g/dl) and platelet count ($39 \times 10^9/l$), and an increasing leukocytosis ($45 \times 10^9/l$). The blood film showed crenated red cells, burr cells, schistocytes, and nucleated red cells. Concomitantly, there was prolongation of the prothrombin time (20.2 seconds, control 15.5) and thrombin time (21.5 seconds, control 13.7) and the titre of D-dimer fragments of fibrin (XDPs) was raised ($500\text{--}1000 \text{ ng/ml}$). A picture consistent with microangiopathic haemolysis and disseminated intravascular coagulation. Marrow aspirate and trephine showed plentiful normal megakaryocytes and reactive features. Abdominal radiographs showed dilated small bowel loops and multiple fluid levels on an erect film. After a change in antibiotic therapy and the administration of fresh frozen plasma there was a dramatic clinical improvement with a return of renal function and the blood count to normal. The blood, film, however, continued to show fragmented red cells.

A small bowel meal showed an oedematous stricture of the terminal ileum strongly suggestive of Crohn's disease (Fig 1). No other source of sepsis was detected by abdominal ultrasound or computed tomography.

On day 22 after hospital admission she was well, taking a reducing course of oral prednisolone only, and ready for discharge. However, 24 hours later she became acutely ill with clinical features of intestinal perforation and thrombocytopenia (89×10^9). At laparotomy the terminal ileum and caecum were inflamed with multiple perforations necessitating hemicolectomy and resection of the terminal ileum.

Histology of sections from the resected bowel showed mucosal ulceration with occlusion of submucosal arterioles by recent and organising thrombi (Fig 2). There was no vasculitis or

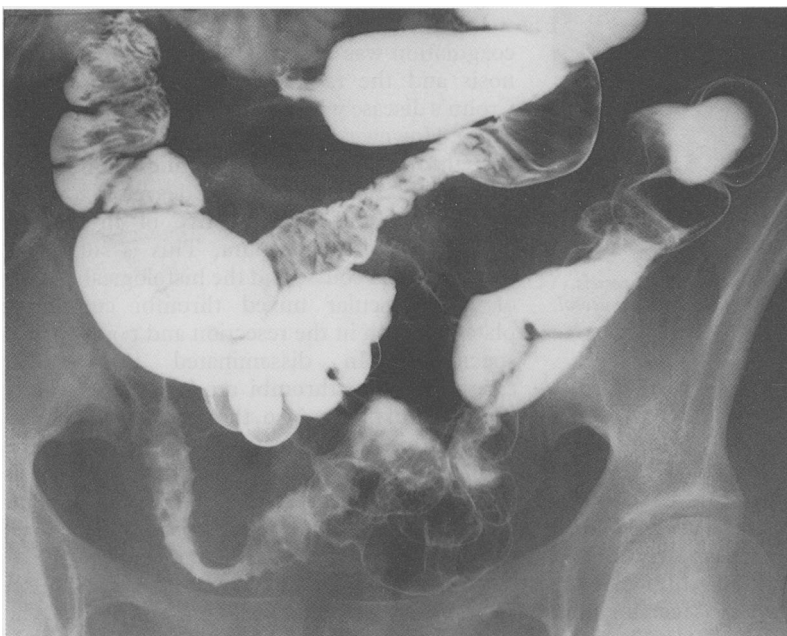


Figure 1: Small bowel barium meal showing oedema of the terminal ileum.

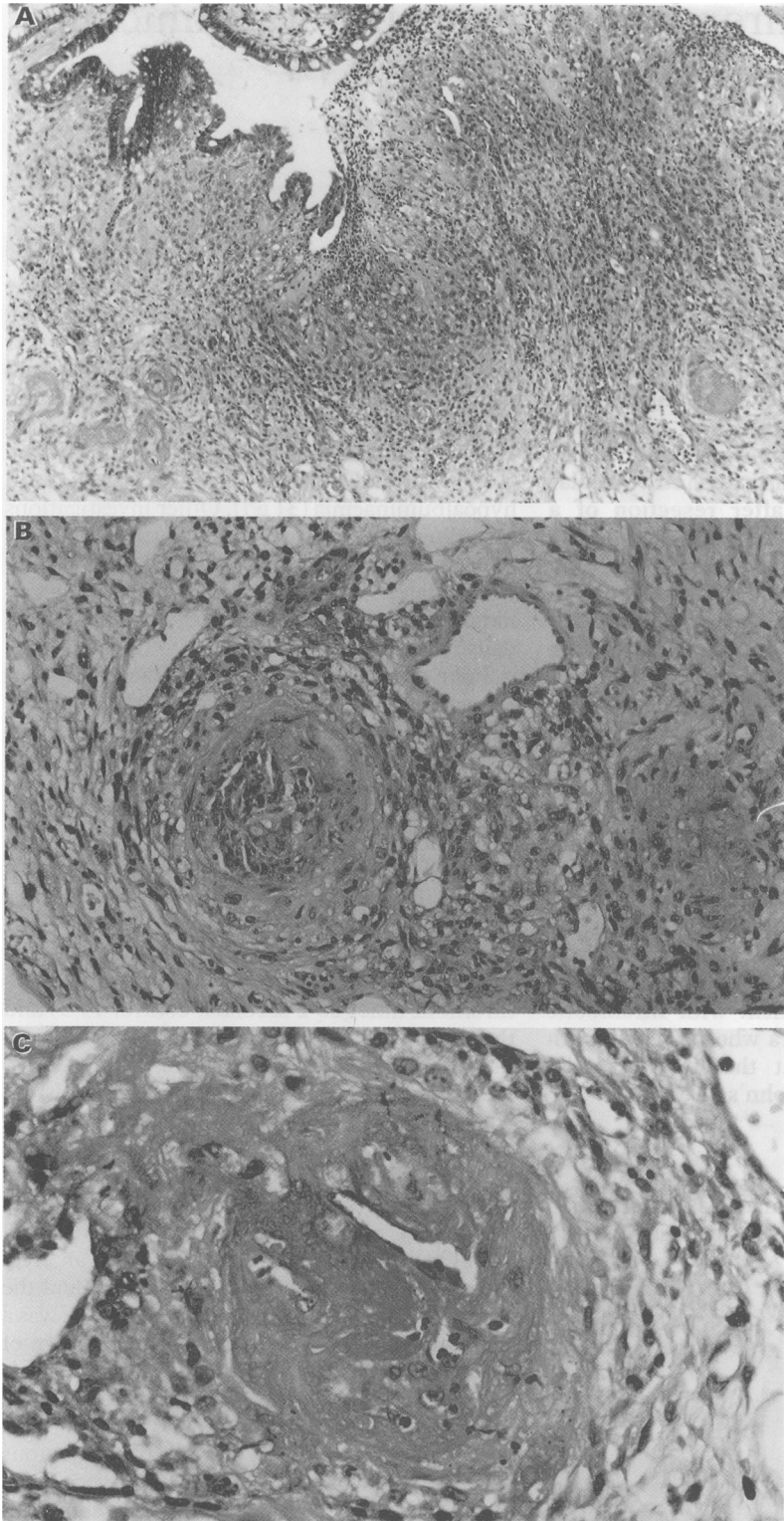


Figure 2: (A) Ischaemic ulceration of the caecum with thrombosed submucosal blood vessels. (Haematoxylin and eosin, original magnification $\times 75$.) (B) Mixed thrombus in a submucosal artery of the terminal ileum. (Haematoxyline and eosin, original magnification $\times 300$.) (C) Organised thrombus in a submucosal arteriole of the caecum. (Haematoxylin and eosin, original magnification $\times 600$.)

histological features of Crohn's disease. The mesenteric blood vessels were normal.

After operation she became confused, drowsy, and feverish, followed by several grand mal convulsions. Her renal function deteriorated again and the blood count and film showed microangiopathic haemolysis (haemoglobin 8.0 g/dl), platelet consumption ($30 \times 10^9/l$), and a leukocytosis. There was an associated mild

coagulation disturbance, slightly raised XDPs and raised bilirubin ($41 \mu\text{mol/l}$). A diagnosis of thrombotic thrombocytopenic purpura was made and treatment with daily plasmapheresis was begun (3 l exchanges with 2 l of fresh frozen plasma and 1 l of normal saline) in addition to intravenous steroids and antibiotics. As there was no clinical improvement after one week, despite a partial recovery in platelet count, she was also given two doses of vincristine (2 mg) one week apart. On day 21 after operation she developed respiratory distress syndrome that required ventilation. Despite intensive treatment, cerebral oedema and renal failure ensued. She died four weeks after surgery.

At necropsy, apart from the complicating respiratory distress syndrome, there were further multiple discrete ischaemic areas in the small and large bowel, enlarged pale kidneys with identical microangiopathy, and cerebral oedema. None of the thrombi were of the type seen in disseminated intravascular coagulation (see Discussion); some were fresh while others were in different stages of organisation. On retrospective assessment, the changes were most severe in the resected ileum and caecum. Serology from one week after admission showed raised *Yersinia enterocolitica* 0:9 antibody titres of 1:320, consistent with recent infection (result received after the patient's death).

Discussion

Thrombotic thrombocytopenic purpura is a rare, acute condition of undetermined aetiology. It is characterised by a pentad of features first described by Amorisi.⁴ These consist of fever, bleeding or purpura – generally with thrombocytopenia, microangiopathic haemolytic anaemia, neurological manifestations, and renal disease, as demonstrated by this patient. Routine coagulation tests are usually normal, although a minority of cases have a mild disturbance^{4,5} which may represent disseminated intravascular coagulation secondary to red cell fragmentation.^{6,7}

In this patient disseminated intravascular coagulation was our initial haematological diagnosis and the radiological findings led us to Crohn's disease with an abscess as the underlying cause. However, the disproportionate severity of the thrombocytopenia and microangiopathic haemolysis compared with the degree of coagulation disturbance is suggestive of thrombotic thrombocytopenic purpura. This is supported by the clinical course and the histological finding of microvascular mixed thrombi containing platelets, both in the resection and post mortem specimens. In disseminated intravascular coagulation the thrombi are largely or wholly composed of fibrin. Also, the initial improvement seen in this patient may have been due to the fresh frozen plasma she was given, which is effective in treating some patients with thrombotic thrombocytopenic purpura when used alone.⁷

The alternative diagnosis is adult onset haemolytic uraemic syndrome in which the above described pentad of features of thrombotic thrombocytopenic purpura can be seen. The

major differences are that early multiorgan involvement and a fulminant course are features more of thrombotic thrombocytopenic purpura than haemolytic uraemic syndrome, however the histopathological findings of affected organs are identical.⁵ Indeed, there may be some overlap between the two conditions. Neurological manifestations, when seen, tend to occur late in the course of haemolytic uraemic syndrome. In this patient, although florid neurological features (drowsiness and fits) did not occur until 23 days after presentation, she was uncharacteristically agitated on day 4. At the time steroid induced psychosis was considered a possible cause, but her agitation resolved with clinical improvement in spite of continuing high dose steroid treatment. In retrospect, this was probably early cerebral involvement by thrombotic thrombocytopenic purpura. Finally, although colitis has been described in haemolytic uraemic syndrome,¹² presentation with small bowel ischaemia alone has not.

The isolation of certain bacteria and viruses in cases of thrombotic thrombocytopenic purpura has led to the suggestion that an infective aetiology may be important⁷ and there is evidence that exacerbations of recurrent thrombotic thrombocytopenic purpura are linked to episodes of infection.^{8,9} Moreover, in haemolytic uraemic syndrome there are strong links with gastrointestinal infections such as verocytotoxin producing *E coli*¹⁰ and *shigella*¹¹ Therefore, yersinia infection may have precipitated thrombotic thrombocytopenic purpura and linked the pathological process to the terminal ileum in this case. Against this, the histology of resected ileum showed microvascular occlusive disease identical to that in the post mortem kidneys, typical of thrombotic thrombocytopenic purpura, and with no specific features to suggest recent infection. The normal platelet count at presentation might favour the initial diagnosis of yersinia infection, but this is recognised in thrombotic thrombocytopenic purpura.⁴

Evidence of gastrointestinal involvement in thrombotic thrombocytopenic purpura, as in the haemolytic-uraemic syndrome, is surprisingly common; up to 30% of patients having abdominal pain at presentation.⁵ This abdominal pain has been ascribed to pancreatitis secondary to occlu-

sion of pancreatic arterioles.¹² However, vascular occlusion of the colonic wall¹³ and massive gastro-oesophageal haemorrhage¹⁴ have also been reported.

We are not aware of any previous reports of bloody diarrhoea in association with abdominal pain occurring at the onset of thrombotic thrombocytopenic purpura and before any of the other clinical or laboratory features become manifest. Similarly, we have found no reports of thrombotic thrombocytopenic purpura or haemolytic uraemic syndrome presenting with discrete infarction of the terminal ileum and caecum clinically and radiologically indistinguishable from Crohn's disease. It is a reminder of the differential diagnosis of Crohn's disease of the terminal ileum.

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