Case report

Extramedullary haemopoiesis in the small bowel

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SUMMARY A patient with myelofibrosis developed repeated gastrointestinal haemorrhage from the small intestine, which was found to be infiltrated with extramedullary haemopoiesis. Nineteen months later he presented with subacute intestinal obstruction; radiology and laparotomy documented progressive infiltration of the small bowel. Histological examination of the resected terminal ileum showed patchy mucosal ulceration, with underlying submucosal and serosal extramedullary haemopoiesis.

We describe a patient with extramedullary haemopoiesis involving the small intestine, who presented initially with rectal bleeding and later developed small bowel obstruction.

Case report

A 43 year old man presented in 1977 with a history of recurrent oral ulceration. He was found to have uncomplicated aphthous ulceration, but a peripheral blood film showed a number of nucleated red blood cells with marked anisocytosis, poikilocytosis, and spherocytosis. His haemoglobin was 11.9 g/dl. A trephine bone biopsy revealed appearances consistent with early myelofibrosis. He remained asymptomatic until March 1979 when he developed spontaneous bruising over both ankles and occasional episodes of epistaxis. In May 1979 he underwent an elective splenectomy to relieve severe thrombocytopaenia. In August 1980 and January 1981 the patient reported two episodes of brisk bleeding *per rectum* which settled spontaneously; a barium enema was normal.

In December 1981 he presented with further bleeding *per rectum*. His haemoglobin was 10.9 g/dl, WBC $12.1 \times 10^9/l$ and platelets $270 \times 10^9/l$. Upper gastrointestinal endoscopy and colonoscopy within

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Fig. 1 Barium follow-through in July 1982, showing displacement of ileal loops, with narrowing of the terminal ileum, caused by extramedullary haemopoiesis.

12 hours of the haemorrhage failed to identify a source of bleeding. A barium small bowel follow-through revealed a dilated distal small bowel with thickening and infiltration of the terminal ileum. At laparotomy the terminal ileum was noted to be thickened with patches of inflammation. The mesenteric lymph nodes were large and fleshy, and the peritoneum was thickened. Biopsies taken from the terminal ileum, peritoneum, and mesenteric lymph nodes all revealed histological appearances consistent with extramedullary haemopoiesis. He was started on a low residue diet, to avoid bolus obstruction. One month later he suffered a further episode of rectal bleeding; his Hb fell to 9.1 g/dl and he was transfused two units of packed cells.

In June 1982 he developed further intermittent cramping lower abdominal pain. In July 1982 he was admitted with severe lower abdominal pain and vomiting: a plain radiograph of the abdomen showed several air fluid levels in the right iliac fossa. A barium follow through showed separation of the distal ileal loops by adjacent masses, and the terminal ileum was narrowed at its junction with the caecum (Fig. 1). At laparotomy the surgeon

(AAML), who had operated seven months earlier, noted more extensive thickening of the small intestinal wall. He resected the most severely affected bowel, leaving macroscopic disease in the jejunum and the proximal ileum. The resected specimen comprised 60 cm of the terminal ileum and the proximal 3 cm of the caecum. Nine areas of mucosal ulceration were identified in the terminal ileum, ranging from 0.5 to 1.0 cm in maximum diameter. The mesentery was normal but the mesenteric lymph nodes were slightly enlarged.

Histological sections from the ulcerated areas (Fig. 2) showed well demarcated mucosal ulcers of variable depth with acute inflammatory exudate and slough overlying granulation and fibrous tissue. The intervening non-ulcerated mucosa had a normal villous architecture. Subjacent to the ulcers were areas showing striking evidence of extramedullary haemopoiesis (see inset, Fig. 2) with large atypical megakaryocytes, groups of normoblasts and immature myeloid precursors. Similar extramedullary haemopoiesis was present focally in the serosa and the perinodal fat, but the lymph nodes showed reactive follicular hyperplasia only. There

Fig. 2 Photomicrograph showing ileal mucosal ulceration with megakaryocytes, normoblasts and myeloid precursors (see inset) present in the ulcer base.

was no evidence of vascular occlusion in any of the sections.

After the ileocaecal resection, the patient had a stormy postoperative period with several severe wound and skin infections.

The patient suffered no further episode of gastrointestinal haemorrhage until April 1983 when he was admitted to another hospital having passed 'a large quantity' of fresh blood *per rectum*. When reviewed in outpatients in September 1983 he mentioned that he had suffered two further episodes of rectal bleeding during the preceding three weeks but he did not seek medical advice. Investigations revealed a haemoglobin of 8.1 g/dl, WBC $8.5 \times 10^9/l$ with 60% myeloblasts, platelets $82 \times 10^9/l$. He had transformed to acute myeloblastic leukaemia. The patient refused aggressive chemotherapy; he was given transfusions of blood and platelets as supportive measures. He died at home in February 1984. An autopsy was not performed.

Discussion

Extramedullary erythropoiesis occurs in conditions accompanied by increased numbers of circulating myeloid progenitor cells¹⁻². The commonest sites of extramedullary haemopoiesis are the spleen, liver, kidneys and the adrenal glands. Other organs are occasionally involved, however, these include the posterior mediastinum, the pericardium, skin, joints, and the epidural space.³⁻⁵ The haemopoietic mass can cause symptoms resulting from compression of adjacent structures. For example, progressive paraplegia may develop when extramedullary haemopoiesis occurs in the epidural space.⁵

A search of the medical literature failed to reveal any report of extramedullary haemopoiesis occurring within the wall of the small intestine. This absence is surprising as lymphoid tissue is present in abundance throughout the small intestine, particularly in the terminal ileum. The pathogenesis of this patient's mucosal ulceration seen in the resected ileum is unclear; it is possible that pressure from submucosal extramedullary haemopoiesis caused localised ischaemic ulceration. There was no histological evidence of Crohn's disease, tuberculosis or a primary lymphoma. In addition there was no evidence of a vasculitis, or features of an ulcerative enteritis.⁶

Gastrointestinal haemorrhage caused by ruptured oesophageal varices, although uncommon in patients with myelofibrosis, has been reported by several authors.⁷⁻¹¹ It is aggravated by the presence of either a low platelet count or platelet dysfunction. Portal hypertension is due to two main mechanisms: firstly, an increased blood flow through the mass-

ively enlarged spleen; secondly, functional intrahepatic obstruction caused by extramedullary haemopoiesis or periportal fibrosis in the liver. This patient did not have portal hypertension, as assessed by oesophagoscopy or laparotomy.

In a series of 138 patients with myelofibrosis, over a five year period, 12 patients died from acute myeloid leukaemia, six died from gastrointestinal haemorrhage (three of whom had ulcerative lesions of the duodenal mucosa) and seven died from infections.¹² This patient died from acute myeloid leukaemia, having survived not only subacute intestinal obstruction and gastrointestinal haemorrhages due to infiltration of the small bowel wall by extramedullary haemopoiesis, but also severe postoperative sepsis.

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