Colonic involvement in Fabry's disease

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Summary: The case of a 54 year old man with Fabry's disease and extensive jejunal and colonic diverticulosis causing colonic stricture is presented. Histological examination of the resected colon revealed evidence of ceramide trihexose deposition in the myenteric nerve plexus. Colonic involvement in Fabry's disease has not been reported before.

Introduction

Fabry-Anderson's disease is a rare X-linked inherited disorder resulting from a deficiency of alpha galactosidase-A, an enzyme which metabolizes ceramide trihexose. This enzyme defect produces a multisystem disease characterized clinically by the presence of angiokeratoma corporis diffusum (the typical skin rash) and accumulation of ceramide trihexose which may lead to renal, cardiac, ocular and nervous system involvement.

Intestinal manifestations are not prominent although episodic diarrhoea has been described.¹ We report a case of Fabry's disease presenting with abdominal pain and found to be associated with a colonic stricture. Histological examination revealed extensive glycolipid deposition.

Case report

A 54 year old Caucasian male known to have Fabry's disease for 20 years was admitted for investigation of intestinal symptoms. He had suffered episodes of diarrhoea associated with abdominal cramps since childhood and these were usually accompanied by fever and arthralgia. These symptoms had been investigated at the age of 29 and a barium meal, barium enema and colonoscopy had all been normal. He re-presented with a 7-month history of colicky abdominal pain, and distension with the passage of occasional streaks of blood and mucus per rectum.

There was no other significant past medical history and he was taking no regular medication. In his immediate family a brother and a nephew were known to have Fabry's disease.

On examination, multiple angiokeratomas were present over his legs, forearms and lower abdomen. A systolic murmur was heard in the aortic area but the rest of the cardiovascular examination was normal. Abdominal examination revealed a mass 4 cm × 3 cm in the left iliac fossa which was firm and tender. Rectal examination was normal.

Investigations included a normal full blood count and blood biochemistry apart from an increased serum creatinine of 118 μmol/l (normal range 60–110 μmol/l). An echocardiogram demonstrated concentric hypertrophy but no intrinsic valvular lesion. A barium enema was performed which revealed a stricture of the sigmoid colon. A colonoscopy was performed which was limited due to the significant narrowing of the colonic lumen. No mucosal abnormality was seen at the stricture.

The patient underwent a laparotomy and a pelvic mass was found associated with the distal sigmoid colon. There was evidence of chronic diverticular disease and further examination revealed extensive diverticulosis of the jejunum. The ileum and proximal colon were normal. The inflammatory mass and sigmoid colon were removed, which was technically difficult due to the friable nature of the surrounding tissues. A colostomy was fashioned and the patient made an uneventful recovery.

Macroscopic examination of the resected sigmoid colon revealed extensive diverticular disease with muscle hypertrophy and pericolic abscess formation with surrounding fibrosis. Two benign polyps were also identified. Histological examination demonstrated glycolipid deposition in the interstitial muscle, the muscle of vessel walls, the intramural ganglion cells (Figure 1) and in the sinus macrophages of lymph nodes. Electron microscopy was also performed (Figure 2) which demonstrated laminated electron dense inclusions beneath the sarcolemma and within the cytoplasm of the muscle fibres.

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Figure 1 Ganglion cells of Auerbach's plexus showing glycogen in the cytoplasm. Periodic acid Schiff $\times 600$.

Figure 2 Electron micrograph of a smooth muscle cell in the colonic muscularis propria showing laminated inclusions of glycolipid and a membranous whorl. Uranyl acetate and lead citrate $\times 17500$.

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Discussion

Intestinal manifestations of Fabry's disease appear to be uncommon. Of the cases described in the literature the predominant gastrointestinal symptom is episodic diarrhoea with crampy abdominal pain.^{1–3} It is thought that these symptoms are due to accumulation of ceramide trihexose in the myenteric nerve plexus throughout the gut⁴ with consequent disordered motility. Dysmotility may produce areas of high intraluminal pressure allowing the formation of diverticulae. This has previously been reported in the jejunum of a patient with Fabry's disease.⁵ Diarrhoea predominates due to intestinal stasis and bacterial overgrowth. Our patient had extensive diverticulosis involving the jejunum and sigmoid colon and in view of this widespread involvement, disordered motility due to ceramide trihexose deposition is a more likely explanation for the pathological findings rather than the association of idiopathic jejunal with separate colonic diverticulosis.

Large bowel involvement has been suspected in some patients with Fabry's disease because of the loss of haustral markings on barium studies^{1,6} but there has been no histological demonstration of ceramide trihexose deposition in the colon, until this case. We believe this is the first case of Fabry's disease with large bowel stricture and diverticulae formation as a possible consequence of glycolipid deposition.

The prevalence of such abnormalities may be considerably underestimated and barium studies should be considered in patients with Fabry's disease presenting with gastrointestinal symptoms.

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