Intestinal lymphangiectasia associated with recurrence of histiocytosis X

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ABSTRACT

Intestinal lymphangiectasia may occur as a primary congenital disorder or a secondary disorder. Secondary lymphangiectasia could be associated with diseases such as abdominal carcinoma, retroperitoneal fibrosis or chronic pancreatitis. This is the first reported case of intestinal lymphangiectasia associated with recurrent histiocytosis X. This case report illustrates the need for more prospective, well-designed studies to determine the natural history and outcome of intestinal lymphangiectasia in the duodenum. Hopefully, these studies will also help clinicians identify which group of patients with intestinal lymphangiectasia in the duodenum is more likely to have a secondary cause.

Keywords: histiocytosis X, intestinal lymphangiectasia, secondary cause

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INTRODUCTION

Intestinal lymphangiectasia is characterised by the obstruction of lymph drainage from the small intestine and the dilatation of lacteals and other intestinal lymphatics.[1,2] Intestinal lymphangiectasia may occur as a primary congenital disorder; it may also be secondary to a disease that blocks the intestinal lymph drainage. Secondary lymphangiectasia may occur due to extensive abdominal or retroperitoneal carcinoma or lymphoma, retroperitoneal fibrosis, chronic pancreatitis, mesenteric tuberculosis, Crohn's disease, Whipple's disease, autoimmune disease or in chronic pericarditis.[1,2] We present a case of intestinal lymphangiectasia associated with recurrence of histiocytosis X.

CASE REPORT

In 2003, a 32-year-old Chinese man was diagnosed with histiocytosis X involving the pituitary gland. Computed tomography (CT) of the thorax and abdomen showed no evidence of metastases. Bone imaging was also unremarkable. In the same year, the patient's histiocytosis X was treated with endoscopic transseptal pituitary resection followed by radiotherapy. Since then, magnetic resonance (MR) imaging of the pituitary gland for reassessment of the disease had been performed annually until 2008. No evidence of recurrence was detected on follow-up MR imaging.

The patient presented in early 2010 with an acute onset of pain in the left side of the chest wall. Physical examination on presentation was unremarkable. Investigation was also unremarkable, with normal complete blood picture, erythrocyte sedimentation rate, C-reactive protein and liver and renal biochemistry. Serial cardiac enzymes, troponin T, electrocardiogram, echocardiogram and chest radiograph were all normal. Since the persistent severe chest pain was not relieved by analgesia, upper endoscopy was performed, which revealed diffuse prominent villi with whitish discoloured tips in the first and second part of the duodenum. This lesion extended beyond the second part of the duodenum. Multiple biopsies taken from the first and second part of the duodenum showed minimally inflamed duodenal mucosa, with scattered dilated lymphatic channels that were consistent with intestinal lymphangiectasia (Figs. 1 & 2).

Capsule endoscopy was performed to evaluate the extent of the lymphangiectasia, which was seen to extend to the mid-small bowel. Workup for malabsorption in the patient showed no abnormality in serum albumin, globulin, immunoglobulin or cholesterol. His body mass index was 35.5 kg/m^2. In view of the lack of evidence for malabsorption, stool for α1-antitrypsin was not collected, especially since he did not have diarrhoea. In view of his previous history of histiocytosis X and the extent of the lymphangiectasia, he was investigated for secondary cause of intestinal lymphangiectasia. His autoimmune markers were all negative, and complement 3, complement 4, immunoglobulin A, immunoglobulin G and immunoglobulin M were all within normal limits. The mid-stream urine for routine microscopy was also normal, with no evidence of microscopic haematuria or proteinuria. Colonoscopy did not reveal any evidence of inflammatory bowel disease.

Positron emission tomography-computed tomography (PET-CT) of the whole body was subsequently performed. PET-CT showed an abnormal bone uptake on the left side of the fifth thoracic (T5) spine, with a corresponding lytic lesion on CT. Another

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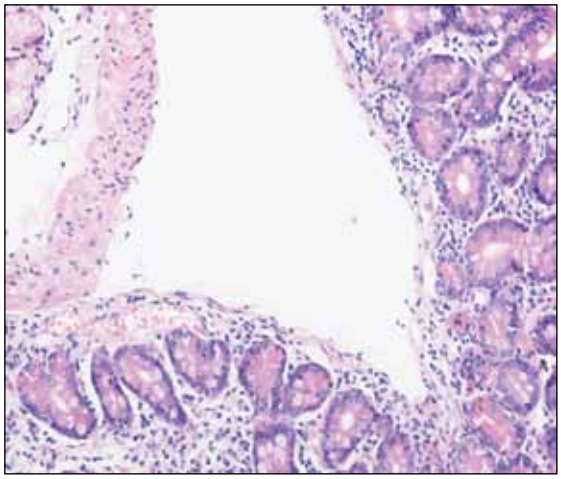

Fig. 1 Photomicrograph of the duodenal biopsy shows dilated lymphatic channels.

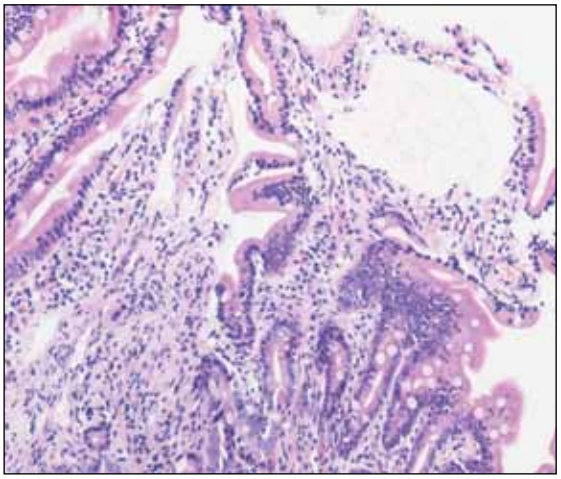

Fig. 2 Photomicrograph of the duodenal biopsy shows minimally inflamed duodenal mucosa and dilated lymphaic channels, which are compatible with intestinal lymphangiectasia.

focus of increased uptake was detected at the right femoral shaft without any corresponding lytic lesion on CT. The 18-fludeoxyglucose (18-FDG) glycolysis in the left side of the T5 and right femoral shaft had standardised uptake values (SUVmax) of 10.1 and 9.6, respectively, which were suggestive of malignancy. No other abnormal tissue intensity was detected on PET-CT of the whole body. The lytic lesion on the left side of the T5 spine was identified as the cause of the patient's left chest wall pain.

The patient was confirmed to have recurrent histiocytosis X after an examination of trephine biopsy for Langerhans cell histiocytosis involvement and immunohistochemistry of trephine biopsy for CD1a and CD207 monoclonal antibodies. He then underwent chemotherapy and radiotherapy for the recurrent histiocytosis X. Unfortunately, the disease failed to respond to treatment. The patient developed lytic lesions in the left iliac bone and the first and fifth lumbar spines. In view of the uncontrolled disease, upper endoscopy to assess the status of his intestinal lymphangiectasia was not repeated.

DISCUSSION

Classical intestinal lymphangiectasia is associated with impaired absorption of chylomicrons and fat-soluble vitamins. The re-entry of intestinal lymphocytes into the peripheral circulation may also be impeded, resulting in an increased amount of intestinal lymph leaking into the intestinal lumen. This can induce protein-losing enteropathy, steatorrhoea and lymphopenia.[3]

Femppel et al were the first to report the occurrence of transient intestinal lymphangiectasia in the duodenum of healthy volunteers after nasogastric olive oil infusion.[4] Since then, there have been other reports describing endoscopic evidence of intestinal lymphangiectasia in the duodenum of patients without any clinical evidence of malabsorption.[5,6] Most recently, Kim et al retrospectively found that 3.2% of their patients undergoing upper endoscopy for health examination had endoscopic intestinal lymphangiectasia in the duodenum.[2] Furthermore, in their prospective series, they found that 8.9% of the patients had histologically proven intestinal lymphangiectasia in the duodenum. Of greater significance is the fact that none of the subjects in the two series had any clinical or biochemical evidence of malabsorption.[2] Although none of their patients had evidence of malabsorption, 60% of the 35 cases in their retrospective series had "associated diseases". Only two of these patients with so-called associated diseases had diseases that have been classically identified with intestinal lymphangiectasia; one had systemic lupus erythematosus while the other had chronic pancreatitis.[2]

To the best of my knowledge, this is the first reported case of intestinal lymphangiectasia associated with recurrent histiocytosis X. Although incidental findings of intestinal lymphangiectasia in the duodenum have been reported, the clinical significance is uncertain. Studies have reported the benign nature of these lesions.[3,5,6] However, reports have also described gastrointestinal bleeding that was attributed to intestinal lymphangiectasia in the duodenum.[1,7-10] This bleeding either resulted in mortality or was so severe that surgical excision was required to control it.[7,8,10]

The reason why our patient developed intestinal lymphangiectasia associated with recurrence of histiocytosis X in the thoracic spine is uncertain. Since

an upper endoscopy done in 2006 had not revealed any evidence of intestinal lymphangiectasia, it could not be attributed to the previous radiotherapy done in 2003. One can hypothesise that the metastatic lesion in the thoracic spine may have resulted in an increased pressure in the thoracic lymphatic ducts, leading to an obstruction in the efferent flow of chyle from the intestine. This, in turn, may have caused raised lymphatic pressure, resulting in the formation of intestinal lymphangiectasia.

This case report illustrates the need for more prospective, well-designed studies to determine the natural history and outcome of intestinal lymphangiectasia in the duodenum. Hopefully, such studies will also help clinicians identify which group of patients with intestinal lymphangiectasia in the duodenum is more likely to have secondary causes. In conclusion, this is the first reported case of intestinal lymphangiectasia in the duodenum associated with recurrence of histiocytosis X. Clinicians should be cautious before considering all intestinal lymphangiectasia in the duodenum to be benign. Until more studies on the natural history and outcome of intestinal lymphangiectasia in the duodenum are available, clinicians would have to rely on their clinical experience and skills when deciding which group of patients is more likely to have a secondary cause for the lymphangiectasia and thus warrant further investigation.

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