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CASE REPORT

A rare cause of failure to thrive in infancy

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Primary intestinal lymphangectasia (PIL), also known as Waldmann's disease, is a rare disorder characterized by an exudative enteropathy resulting from morphologic abnormalities of the intestinal lymphatics.

Moderate to severe oedema with pleural effusion, pericarditis, or chylous ascites is the main clinical manifestation but lymphoedema, abdominal pain, weight loss, moderate diarrhoea, vomiting, and fat-soluble vitamin deficiencies may also be present. Patients can also develop hypocalcaemia secondary to failure to absorb fat and fat-soluble vitamins.

We report a nine-month-old male infant with a four-week history of diarrhoea, vomiting, failure to thrive, peripheral oedema and tetany. Hypoalbuminaemia, hypocalcaemia, low vitamin D levels and lymphopaenia were found on initial investigations. A raised stool alpha-1-antitrypsin supported a diagnosis of a protein losing enteropathy. At gastroscopy typical 'cotton ball or frosted appearance' was visible particularly in the second (D2) and third part (D3) of the duodenum. Biopsies from D3 revealed dilated lymphatics suggestive of primary intestinal lymphangectasia. The infant was managed with a high protein, high MCT, low fat diet with improvement in his symptoms and growth pattern.

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Primary intestinal lymphangectasia (PIL) is a rare protein-losing gastroenteropathy caused by congenital malformation or obstruction of the intestinal lymphatic drainage.[1] The condition was first described by Waldmann in 1961. Factors causing elevated pressure of lymph drainage in the intestinal wall can lead to dilatation and even rupture of the lymphatic vessels which, in turn, result in the leakage of lymphatic fluid.[2,3] Leakage of lymph will result in hypoproteinaemia, lymphocytopenia and decreased serum levels of immunoglobulin.[4] The condition usually presents in the first two years of life. Up to 2013 less than 200 cases had been reported in children world-wide.[4]

CASE REPORT

9-month-old, male infant (non-consanguineous parents) presented to the paediatric emergency department with a three-week history of vomiting and a four-week history of diarrhoea. On admission he was found to be poorly perfused and dehydrated. Parents had reported poor urine output. Blood pressure was maintained but in view of the severe dehydration and marked hyponatraemia at presentation he was transferred to the paediatric intensive care unit for further management.

On examination the infant had periorbital oedema and lower limb pitting oedema. His abdomen was distended but there were no clinical signs of ascites. An initial ultrasound of the abdomen confirmed the absence of ascites but showed multiple, fluid filled, small intestinal loops with mural thickening due to oedema. Chest imaging did not reveal any evidence of pleural effusions. Urine analysis was negative for protein, serum albumin was 16 g/l (normal value, 32-52 g/l) with a low total protein of 29 g/l (66-87 g/l). Full blood count showed a normal haemoglobin, mild reactive thrombocytosis and significant lymphopaenia with a lymphocyte count of between 0.7 and 0.7 $x10^9$/l (1.16-3.33 $x10^9$/l). Initial elevation of INR was noted and this normalized following administration of vitamin K. Episodes of intermittent carpopedal spasm were attributed to a low calcium and vitamin D deficiency, and these stopped following replacement therapy.

Following rehydration and repeated albumin infusions the condition of the infant improved. A stool alpha-1-antitrypsin level was elevated at more than 2.25 (normal values <0.3mg/g). With the clinical presentation suggestive of a protein losing enteropathy, documented severe hypoproteinaemia and persistent lymphopaenia, a diagnosis of PIL was considered. Once the patient's condition improved, treatment with medium chain triglyceride (MCT) based Milk, MCT oil and a fat free diet were started. Once the patient's stabilised, an upper gastrointestinal endoscopy was performed. During endoscopy, the oesophagus and stomach appeared normal. There were typical 'cotton wool exudative lesions' or 'frost like' lesions on the duodenal mucosa, more prominent in the second (D2) and third (D3) part of the duodenum (Figure 1). Histological examination showed no abnormalities in the oesophagus, stomach and D1 and D2 Biopsies from D3 which showed dilated lymphatic vessels (Figure 2) were also highlighted on D2-40 immunohistochemistry. These changes were consistent with a diagnosis of PIL. The infant was subsequently discharged on an MCT based milk ('Monogen Nutricia'), fat free diet and vitamin and mineral supplementation. Regular review up to three

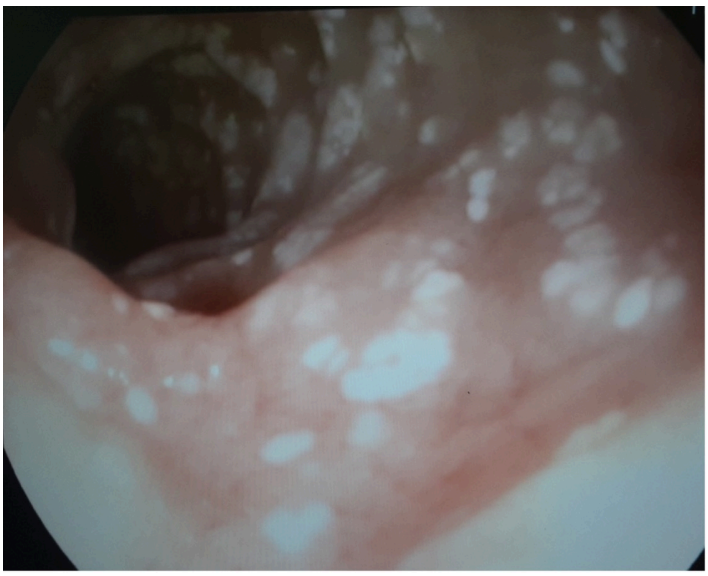

Figure 1 'cotton wool exudative lesions' visible in the duodenum

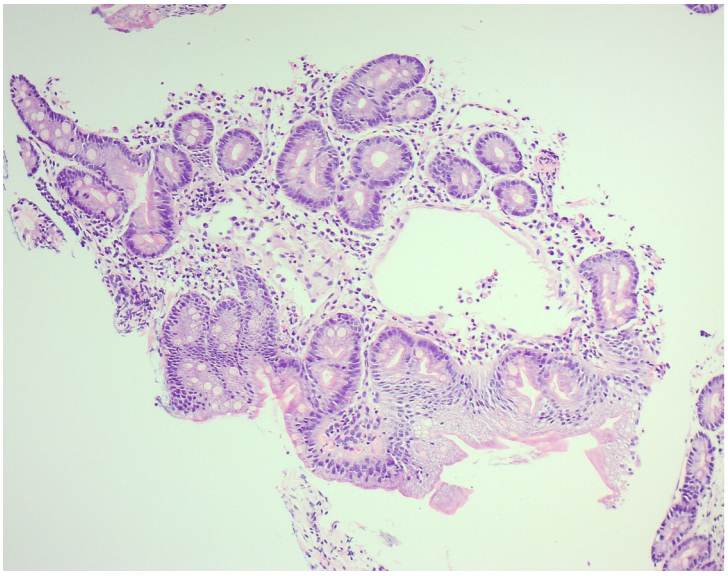

Figure 2 Haematoxylin and Eosin stain of the duodenal biopsy showing a markedly dilated lymphatic within the mucosa. Magnification x100

months post presentation showed a marked improvement in dry weight gain, improvement in abdominal distension, cessation of vomiting and diarrhoea, resolution of tetany and marked improvement in biochemical analysis.

DISCUSSION

PIL is a rare disease characterized by protein-losing enteropathy (PLE).[1] Clinical symptoms are induced by the excessive loss of lymphatic contents including protein, fat, and lymphocytes, resulting in hypoproteinaemia and oedema..[1,5] It is generally diagnosed before the age of three years, and affects boys and girls in equal proportions. The prevalence of the disease is unknown. Patients with PIL often present with oedema, lymphoedema, diarrhoea, ascites that may be complicated by fatigue, abdominal pain, nausea, vomiting, weight loss, inability to gain weight, iron deficiency anaemia and obstructive ileus. Other major features are lymphopenia, hypoalbuminemia, and hypogammaglobulinemia due to lymph leakage from the ruptured lymph vessels.[1,5]

The diagnosis should be considered when young children present with a PLE. An elevated alpha-1-antitrypsin level is highly suggestive of a PLE, and this should warrant further investigation. Secondary intestinal lymphangiectasia can be caused by cardiac causes such as constrictive pericarditis, haematological causes such as lymphoma and other rare causes would include Budd Chiari syndrome, sarcoidosis and scleroderma.[6] Histological confirmation is required but recurrent endoscopies are frequently required to establish a diagnosis. The typical 'snow frost or cotton ball' exudates are not always evident, and biopsies are more likely to show the typical lymphatic dilatation from more distal parts of the small intestine. These are not easily accessible on traditional upper oesophagogastroscopy and may require double balloon interventions.[4,7] Capsule endoscopy provides complete examination of small bowel mucosa thus can evaluate the extent of lymphangiectasia. However, the disadvantage of capsular endoscopy is the inability to obtain biopsies.

Management in the acute stage of presentation may require repeated albumin infusions, management of vitamin D and calcium deficiency resulting in tetany and nutritional support. Immunoglobulin deficiency or concurrent infection due to hypo-gammaglobulinemia may need to be addressed in the acute setting. A high protein, fat free diet and MCT based formula together with vitamin supplementation are required in long term. On occasions, a period of total parenteral nutrition might be required if enteral feeding results in worsening of symptoms. The presence of chylous ascites suggests a more severe form of the disease and is of importance in deciding the management steps in this condition.[8] In refractory cases, the management is guided by the extent of the intestinal lymphangiectasia (IL). MRI lymphangiogram can be used to distinguish between segmental IL or more extensive disease. In the case of segmental IL surgical resection of the area.[9] might be considered in children not improving on the conventional diet. In more extensive disease pharmacological treatment that has been tried with anecdotal evidence of success includes propranolol treatment in infants and use of interleukin inhibitors (tacrolimus or sirolimus) in older children.[10,11] Other therapeutic options described in the literature include octreotide and tranexamic acid but data on these treatments are limited.[8]

CONCLUSION

IL should be suspected when there is a clinical picture of chronic diarrhoea and protein-losing enteropathy accompanied with oedema at any level, as well as hypoalbuminemia, hypocalcaemia, lymphopenia, hypogammaglobulinemia, and hypercholesterolemia. All children presenting with IL should undergo an upper gastrointestinal series with bowel transit time and endoscopy with biopsies taken at the level of the duodenum. Treatment includes diet and the periodic administration of albumin and gamma globulin.

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