

Protein-Losing Enteropathy Resolved by *Helicobacter pylori* Eradication

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ABSTRACT

Protein-losing enteropathy (PLGE) is an uncommon condition with a multifactorial origin, that is characterized by excessive loss of serum proteins into the gastrointestinal tract, resulting in hypoproteinaemia and oedema.

The authors present the case of a 24-year-old man admitted to hospital for a 2-month history of lower extremity oedema and diarrhoea with a secretory pattern. Blood analysis revealed hypoalbuminaemia and iron deficiency anaemia. Liver disease and severe proteinuria were excluded as possible aetiologies. Upper gastrointestinal endoscopy revealed signs of chronic *Helicobacter pylori* gastritis. After completion of *H. pylori* eradication, the patient had complete resolution of clinical and laboratory abnormalities.

The results suggest the need to consider less frequent aetiologies for peripheral oedema and hypoproteinaemia, such as PLGE, especially those caused by prevalent bacterial agents like *H. pylori*.

KEYWORDS

Protein losing-enteropathy, oedema, hypoalbuminaemia, *Helicobacter pylori*

LEARNING POINTS

- Protein-losing enteropathy may be related to *Helicobacter pylori* infection.
- Protein-losing enteropathy and its associated symptoms may be resolved by *H. pylori* eradication.

INTRODUCTION

Protein-losing enteropathy (PLGE) is an uncommon condition characterized by an excessive loss of serum proteins into the gastrointestinal tract, resulting in hypoproteinaemia and generalized oedema. It should be considered when other causes of hypoproteinaemia (malnutrition, liver disease, severe proteinuria) have been excluded^[1]. It is secondary to a variety of diseases, including bacterial and viral infections.

CASE DESCRIPTION

A 24-year-old Caucasian man was admitted to hospital for investigation of a 2-month history of bilateral lower limb and testicular swelling and diarrhoea with a secretory pattern. He had a history of pulmonary embolism and type 1 diabetes, and was chronically medicated with insulin and rivaroxaban. Furosemide had recently been added to control oedema, with no response.

Physical examination confirmed marked oedema of the lower limbs with Godet's sign and of the scrotum (Fig. 1). No physical signs of pleural effusion or ascites were detected.

Laboratory investigations identified iron deficiency anaemia and severe hypoproteinaemia with concomitant hypoalbuminaemia. Urine analysis was negative for proteinuria. A 24-hour urine sample was also collected and confirmed the absence of proteinuria. An electrocardiogram showed sinus rhythm and normal tracing. Chest radiography was unremarkable. Cardiac disease was ruled out by transthoracic echocardiography.

Liver disease was also considered and an abdominal ultrasound was performed with evidence of slight hepatomegaly but with no signs of cirrhosis or portal hypertension. Chronic viral hepatitis (hepatitis C and B) and other causes of chronic liver disease were also excluded, namely Wilson's disease, haemochromatosis, alpha 1 antitrypsin deficiency, primary biliary cirrhosis and autoimmune hepatitis. Other viral diseases were also considered and eventually ruled out by serological studies (CMV, EBV and HIV 1/2).

In light of the clinical history and laboratory findings, after exclusion of other causes of hypoproteinaemia and oedema, PLGE was the most likely diagnosis. To investigate this hypothesis, the patient underwent upper gastrointestinal endoscopy (Fig. 2) that ultimately revealed large and hyperaemic mucosal folds confined to the gastric antrum. Histological analysis showed signs of chronic gastritis of the antrum associated with *Helicobacter pylori* infection.



Figure 1. Patient's marked oedema of the lower limbs with Godet's sign



Figure 2. Endoscopic image from the gastric antrum revealing large and hyperaemic mucosal folds confined to the gastric antrum

Stool was also collected for parasitological and bacterial analysis, which was negative.

Based on these results, treatment with esomeprazole, amoxicillin and clarithromycin to eradicate *H. pylori* infection was instituted. Clinical improvement was noted with rapid resolution of diarrhoea and progressive improvement and eventual resolution of oedema a few weeks later. Anaemia and hypoproteinaemia also spontaneously resolved after treatment.

The final diagnosis of PLGE secondary to *H. pylori* gastritis was established.

DISCUSSION

The hallmark of PLGE is protein leakage from the gastrointestinal tract, leading to peripheral oedema and rarely to progressive dyspnoea or painless abdominal distention due to symptomatic pleural effusions or ascites^[2].

This protein leakage can occur via one of three possible mechanisms: increased capillary permeability (caused by autoimmune diseases, eosinophilic gastroenteropathy, giant hypertrophic and lymphocytic gastritis, and bacterial and parasitic infections)^[2,3]; increased lymphatic pressure (caused by lymphatic obstruction, congenital abnormalities of the lymphatic system or other disorders that result in increased lymphatic pressure); and breakdown of the mucosal barrier, such as mucosal erosion or ulcers, allowing free passage of interstitial protein into the intestine^[3].

Among the bacterial causes, an association has been recognized since the early 1990s between PLGE and *H. pylori* infection, but with few cases reported^[3,4]. Endoscopic findings of PLGE with *H. pylori* infection mainly consist of Ménétrier's disease, diffuse varioliform gastritis, or rarely cap polyposis^[3,4]. Ménétrier's disease has been previously reported to be associated with *H. pylori* infection. One of the first retrospective studies describing the connection between *H. pylori* and Ménétrier's disease showed an association between hypertrophic gastropathy and *H. pylori* infection in more than 90% of cases^[5]. Other previous reports have showed that the eradication of *H. pylori* completely resolved PLGE in Ménétrier's disease, and also in cases of hypertrophic lymphocytic gastritis or erosive gastritis associated with *H. pylori* infection^[3,4,6].

The mechanisms by which *H. pylori* infection causes PLGE are not completely understood^[6], but in Ménétrier's disease, the presence of giant folds and wider tight junctions between cells may lead to increased permeability and protein-rich exudates in the stomach [7]. A recent report showed PLGE due to *H. pylori* infection without giant rugal folds, erosion or polyposis^[3], suggesting a defect in the epithelial tight junction caused by *H. pylori* infection in the intestine polyposis^[3,4].

In our case, oedema and hypoproteinaemia started to resolve a few weeks after the institution of the eradication protocol, strongly suggesting a link between the infection and symptoms. Also, despite the endoscopic findings of large and hyperaemic mucosal folds, they were not related to classic Ménétrier's disease, but instead to chronic gastritis secondary to *H. pylori* infection.

Some studies show a relationship between chronic *H. pylori* gastritis and changes in tight junctions associated with the expression and high production of hepatocyte growth factor^[8]. These induced tight junction changes could lead to protein loss and consequent oedema (by hypoalbuminemia), and even be responsible for reduced iron absorption and iron deficiency anaemia (present in our patient).

The present case emphasizes the need to consider less frequent aetiologies for peripheral oedema and hypoproteinaemia, such as PLGE, especially those caused by prevalent bacterial agents in the general population, like *H. pylori*. This close association also suggests that *H. pylori* eradication is warranted in patients with PLGE accompanied by *H. pylori* infection.

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