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An exotic cause of exudative enteropathy

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Conflict of interest: None declared

Patient: Male, 50
Final Diagnosis: Exudative enteropathy
Symptoms: Abdominal pain • diarrhea • fever • hyponatremia • lymphadenopathy • weight loss
Medication: —
Clinical Procedure: —
Specialty: —

Objective: Unusual clinical course
Background: Protein-losing enteropathy is a rare cause of hypoproteinemia. Erosive and non-erosive gastrointestinal diseases as well as vascular disorders that result in increased central venous pressure or mesenteric lymphatic obstruction may result in protein loss via the gastrointestinal tract.
Case Report: We present the case of a 50-year-old man with protein-losing enteropathy, who had profuse diarrhea, abdominal pain, lymphadenopathy, fever, and a weight loss of 10 kg in the preceding 2 months. Extensive work-up revealed infection with *Giardia lamblia*. We review clinical signs and symptoms, laboratory findings, and imaging studies, and discuss potential pitfalls in establishing the diagnosis.
Conclusions: To the best of our knowledge, this represents one of the few published cases of intestinal giardiasis as a cause of protein-losing enteropathy in an immunocompetent adult. The diagnosis of lambliasis should be based on a combination of stool cultures and serum serology, and in cases of high clinical suspicion, an endoscopy and biopsy of the upper GI tract is recommended.

MeSH Keywords: **Giardia Lamblia – pathogenicity • Protein-Losing Enteropathies – diagnosis • Protein-Losing Enteropathies – etiology • Protein-Losing Enteropathies – parasitology • Protein-Losing Enteropathies – therapy**

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Background

Hypoproteinemia is frequently caused by malnutrition, renal liver dysfunction, and rarely by protein-losing enteropathy. The characteristic finding in protein-losing enteropathy is a loss of serum proteins into the gastrointestinal (GI) tract, resulting in hypoproteinemia with subsequent low oncotic pressure, leading to edema, pleural effusions, ascites, and malnutrition [1]. Erosive and non-erosive GI diseases, as well as vascular disorders that result in increased central venous pressure or mesenteric lymphatic obstruction, can lead to protein loss via the GI tract [1]. Although not fully characterized, enteric infections can also damage the enteric mucosa and epithelial barrier function, thus leading to protein loss, especially in immunocompromised patients. Infective pathogens that have been associated with protein-losing enteropathy include bacteria such as *Salmonella*, *Shigella*, and *Clostridium difficile*, as well as viruses and parasites [2].

Case Report

A previously healthy 50-year-old Caucasian man presented with diarrhea and steatorrhea, diffuse abdominal pain, night chills, and a weight loss of 10 kg in the past 2 months. He also noted progressive swelling around his eyes and on his lower limbs. An external laboratory evaluation had revealed severe hypoproteinemia of 40 g/l (normal range: 66–83) and hypoalbuminemia of 26 g/l (normal range: 35–52).

At the time of his presentation at our institution, the patient had a temperature of 37.5°C and his vital signs were stable with a heart rate of 80 bpm and arterial blood pressure of 130/80 mm Hg. His body mass index was 24.7 kg/m², and clinical examination revealed distinct periorbital and lower extremity edema. There was no jaundice, and the liver and spleen were not enlarged. He did not report travelling abroad. Laboratory analysis confirmed severe hypoproteinemia and hypoalbuminemia. Furthermore, severe exocrine pancreatic insufficiency was documented by undetectable pancreatic elastase in the stool. The endocrine pancreatic function, complete blood count and inflammation markers, liver function tests, renal function, serum protein electrophoresis, and immune fixation were all normal. There was no proteinuria. The microbiological findings of the stool cultures were initially negative for viruses, bacteria, helminths, and protozoa, and the serological tests excluded celiac disease and infections with the human immunodeficiency virus (HIV) or hepatitis A, B, and C viruses. Taking into account the patient's profuse diarrhea, steatorrhea, and pancreatic insufficiency, as well as a pancreatic mass suggested by abdominal ultrasound performed at another institution, the presence of pancreatic cancer was suspected.

To assess the pancreatic lesion, endoscopic sonography and computed tomography studies were performed. These studies revealed no abnormalities of the pancreas, but showed enlarged retroperitoneal lymph nodes. A biopsy was performed during endoscopic sonography examination. Pathohistological examination, including immunohistochemistry, initially suggested B-cell non-Hodgkin lymphoma. Molecular analyses with immunoglobulin heavy chain gene rearrangement (IgH-R), however, showed pseudoclonality. Histology did not show evidence for IgG4-associated changes. In light of the clinical presentation, disease course, and the presence of B symptoms, we suspected exudative enteropathy due to an underlying MALT lymphoma, and performed positron emission tomography/computed tomography (PET/CT) imaging. The examination showed an isolated tracer enhancement in the duodenum without any other fluorodeoxyglucose (FDG)-avid regions. Results of additional laboratory studies, including normal interleukin-2 receptor, normal serum electrophoresis, negative immune fixation, and negative light-chain restriction in flow cytometric lymphocyte assessment, were also not indicative of lymphoma.

To determine the cause of FDG enhancement in the duodenum on PET/CT, we performed an esophagogastroduodenoscopy. Macroscopically, diffuse mucosal erythema in the stomach and patchy mucosal alterations of the duodenum were noted. Biopsies of the antrum and body of the stomach revealed chronic gastritis of moderate activity and the presence of *Helicobacter pylori*. Multiple duodenal biopsies excluded celiac disease and Whipple's disease. However, further histological analysis identified *Giardia lamblia* trophozoites adjacent to duodenal epithelium, thus establishing the diagnosis of intestinal giardiasis (Figure 1A, 1B). Stool cultures performed at a later time as part of the patient's follow-up revealed the pathognomonic *Giardia lamblia* cysts and a positive *Giardia* antigen test result.

Our patient received metronidazole as part of a *Helicobacter pylori* eradication therapy using 40 mg pantoprazole once daily, 500 mg clarithromycin twice daily, and 500 mg metronidazole twice daily for 2 weeks [4], thus providing an adequate treatment also for *Giardia lamblia* infection [3,4]. Two months later, the patient was well without diarrhea or edema, and his weight had returned to normal. Protein levels had returned to normal and stool cultures were negative for any pathogens, but there was still mild exocrine pancreatic insufficiency. Confirmation of successful eradication using the *Helicobacter pylori* fecal antigen test was scheduled to be performed 3 months later.

Discussion

Giardia lamblia is an intestinal protozoan with oral-fecal transmission. Infection is predominantly located in the upper GI tract,

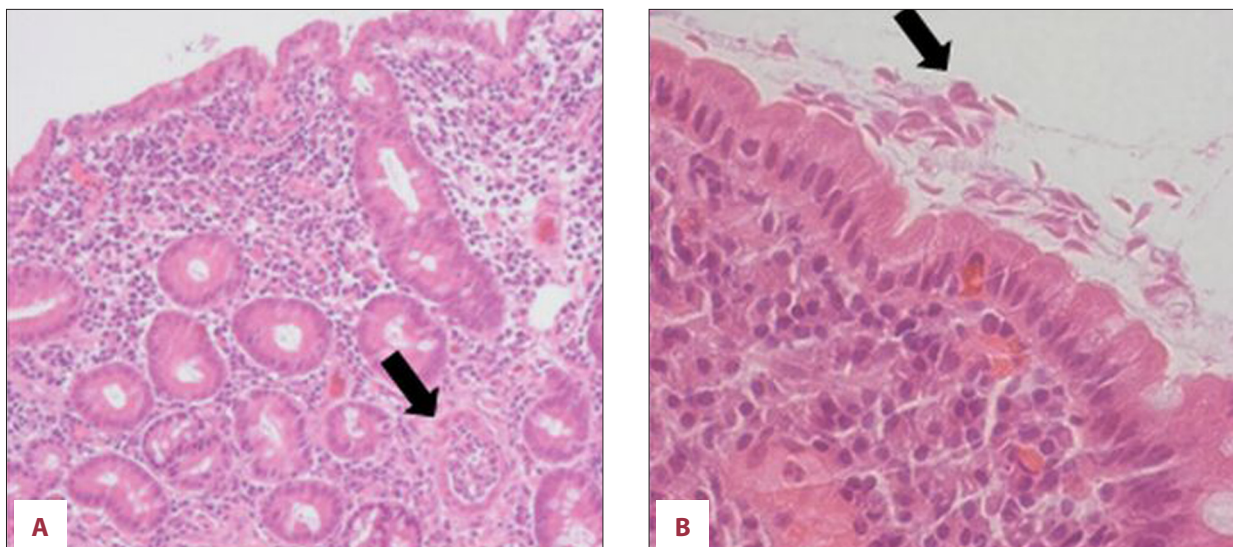


Figure 1. (A) Duodenal mucosa (H&E, 10×) with focally complete villous atrophy and moderate lymphoplasmocytic and granulocytic infiltration of the L. propria, cryptitis, and focal crypt abscesses (arrow). (B) Multiple *Giardia lamblia* trophozoites (arrow) adjacent to the apical duodenal epithelium (H&E, 40×).

particularly the duodenum, where trophozoites are absorbed into enterocytes [5]. Exudative enteropathy due to intestinal lambliasis in adults is rather uncommon, and to our knowledge only a few cases have been described in immunocompromised adults in the literature to date [6, 7]. Other pathogens causing exudative enteropathy in immunocompromised adults and children include *Cryptosporidium*, Gram-negative organisms, and *Entamoeba histolytica* [8].

Here, we described a case of an immunocompetent adult with intestinal giardiasis, which offers several educational facets. First, the fact that the initial stool cultures were negative for parasites caused a delay in establishing the correct diagnosis. Subsequent stool cultures then identified the pathognomonic *Giardia lamblia* cysts and a positive Giardia antigen test result. The initial negative result may have been due to the previously described intermittent fecal excretion of the pathogen [9]. Second, severe exocrine pancreatic insufficiency and retroperitoneal lymphadenopathy, combined with a suspected pancreatic mass, suggested a malignant process rather than an infection. Most likely, *Giardia lamblia* caused exocrine pancreatic insufficiency via inhibition of trypsin and subsequent loss of enzymatic conversion of pro-elastase to elastase in the duodenum [10]. After the initiation of treatment, we observed gradual recovery of the exocrine pancreatic function. Third, the finding of hypoglobulinemia acted as another diagnostic confounder. The low serum protein was most likely due to an exudative enteropathy caused by giardiasis-induced mucosal inflammation. Likewise, the patient's retroperitoneal lymphadenopathy and B symptoms were most likely the

result of the local inflammatory reaction [11]. The clinical suspicion of lymphoma prompted us to perform PET/CT imaging before standard GI tract endoscopic examination. This sequence of imaging studies does not represent standard of care in a patient with recurrent diarrhea, but was considered useful to exclude lymphoma. After a more detailed exploration of the patient's travel history, he reported frequent travel to Thailand and Greece, regions where *Giardia* is a common enteropathogen [12].

Conclusions

Although giardiasis is a common cause of gastrointestinal infection in infants and in developing countries, it should also be considered in the differential diagnosis of adults with chronic diarrhea, abdominal pain, and B symptoms. It is striking to note that the few published cases in developed countries involved immunocompromised adults, whereas our patient did not have an underlying immunosuppressive condition. The diagnosis of lambliasis should be based on a combination of stool cultures and serum serology. Therefore, in cases of high clinical suspicion, endoscopy and biopsy of the upper GI tract is recommended. The latter provides the opportunity for histological confirmation and assessment of the degree of duodenal damage.

Disclosure

The authors have nothing to disclose.

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