Intestinal pseudo-obstruction caused by *Giardia lamblia* infection

Tommaso Pessarelli,1 Guido Basilisco,2 Luisa Spina,2 Mirella Fraquelli2

SUMMARY
A woman in her 40s presented with malaise, nausea, reduced appetite, abdominal distention, loose stools and weight loss. Symptoms had started 6 months earlier and worsened in the last 2 weeks. CT enterography showed hypotonic dilated small bowel loops in absence of any mechanical obstruction. Endoscopic examinations including capsule endoscopy did not reveal any obstructing lesion, but a delayed small bowel transit time of the capsule. Duodenal histology revealed Marsh 3a villous atrophy. Secondary causes of intestinal pseudo-obstruction and villous atrophy were investigated. *Giardia lamblia* trophozoites were found in the stools and in the duodenal biopsies. The patient’s symptoms quickly resolved after metronidazole treatment with complete normalisation of duodenal histology.

BACKGROUND
Intestinal pseudo-obstruction (IPO) is characterised by signs and symptoms of mechanical obstruction of the small or large bowel in absence of obstructive anatomical lesions.1 The condition may be acute or chronic. In acute IPO, a transient and reversible imbalance of excitatory and inhibitory neural factors is responsible for motor impairment and small bowel or colonic dilatation.2 In chronic IPO, the motor impairment is caused by permanent alterations of the smooth muscle, enteric nerves or interstitial cells of Cajal.3 Signs and symptoms of IPO lasting more than 6 months define the chronic form, which is a rare disease with an estimated prevalence of <1/100 000.4 Acute IPO may be secondary to severe trauma, drugs or infections. Chronic IPO may be idiopathic or secondary to such systemic diseases as scleroderma, amyloidosis, and neurological or infectious disorders. *Giardia lamblia* (also known as *G. intestinalis* or *G. duodenalis*)5 is the most common protozoal intestinal parasite isolated worldwide,6 7 with seroprevalence rates ranging from 2% to 7% in high-income countries8 to 20%–40% in resource-limited settings.9 In Northern and Central Italy, the estimated prevalence of giardiasis is around 2%.10 *G. lamblia* infection may present with acute symptoms including diarrhoea, malaise, abdominal cramps and weight loss or with chronic symptoms related to malabsorption.11 *G. lamblia* infection has shown to alter gastrointestinal (GI) motor function12–14 and to increase the risk of such functional bowel disorders as dyspepsia or irritable bowel syndrome (IBS).15–17 We have reported the case of a woman presenting with IPO caused by *G. lamblia* infection for whom the treatment of the infection led to the complete resolution of the condition.

CASE PRESENTATION
A female in her 40s was referred to our gastroenterology clinic because of malaise, nausea, reduced appetite, abdominal distention, loose stools (two evacuations per day without macroscopic blood) and weight loss (−Δ 5 kg, ie, 10% of body weight in the last 6 months). Symptoms had started 6 months earlier and significantly worsened in the last 2 weeks. Clinical evaluation revealed a cachectic woman with a body mass index of 18 kg/m² and with severe abdominal distention. Blood tests including glucose and thyroid function did not reveal any gross abnormality. Abdominal X-ray showed dilated small bowel and the presence of air–fluid levels. Abdominal ultrasound with intestinal assessment showed remarkable gastric dilatation with maximum gastric diameter of 6.5 cm and substantial residual food despite overnight fasting, distended ileal loops and an ‘onion bulb-shaped’ tract of small intestine compatible with intestinal intussusception (figure 1).

The patient reported a family history of ovarian cancer, coeliac disease and ulcerative colitis. She did not refer any foreign travel in the last year and any contact with either domestic or wild animals. Her profession was not at increased risk of infectious diseases. She also denied taking any medication or illicit drugs. The patient was hospitalised.

INVESTIGATIONS
CT enterography was performed (figure 2), showing dilated (diameter >3 cm)18 and bundling small bowel loops with diffuse air–fluid levels in absence of mechanical obstructing lesions and increased thickness or hyperenhancement of the small bowel wall.

Esophagogastroduodenoscopy showed a macroscopically normal mucosa. Multiple stomach biopsies showed mild gastritis; *Helicobacter pylori* was absent. Duodenal biopsies revealed intramucosal lymphoplasmocytosis with increased number of CD3+ intraepithelial lymphocytes (40 CD3+ intraepithelial lymphocytes out of 100 enterocytes) and villous atrophy, consistent with modified Marsh 3a type (figure 3). Coeliac disease was ruled out by normal levels of IgA, antitissue transglutaminase (anti-tTG), antigliadin IgG and IgA and antienthymus IgA, and negative genotyping of the human leucocyte antigens (HLAs) for HLA DQ-2 and HLA DQ-8.

Colonoscopy did not evidence any obstructing lesion. To further exclude a mechanical obstruction, capsule endoscopy was performed (after permissive patency capsule examination), revealing...
Case report

a diffusely normotrophic small bowel mucosa and a slowed (362 min) small bowel transit time (median small bowel transit time 157.0–240.5 min).19

Faecal calprotectin and blood count were normal as well as C reactive protein, procalcitonin plasma levels, vitamin B₁₂, electrolytes, iron levels and transferrin saturation. Folates were slightly reduced (3.1 ng/mL, normal levels >3.8 ng/mL).

The diagnosis of IPO was made on the basis of the presence of dilated small bowel loops with air–fluid levels and in absence of any mechanical obstruction assessed by cross-sectional imaging and endoscopy.

Secondary causes of IPO and of Marsh 3a villous atrophy were revised (see the Differential diagnosis section).

DIFFERENTIAL DIAGNOSIS
Our patient’s symptoms had begun 6 months earlier and worsened in the last 2 weeks. Therefore, the differential diagnosis of IPO considered both acute and chronic forms. Clinical history and physical examinations excluded the most frequent causes of acute pseudo-obstruction or Ogilvie’s syndrome including surgery, severe trauma or acute infections. The patient denied the use of drugs affecting GI motility such as opioids, anticholinergic, alpha-2-adrenergic agonists, antipsychotics, calcium channel blockers, and cytotoxic and dopaminergic drugs. Diabetes, hypothyroidism and hypoparathyroidism were ruled out by normal glycaemia, thyroid-stimulating hormone and serum calcium levels.

Clinical history and physical examination excluded progressive systemic sclerosis, Ehlers-Danlos syndrome and neurological disorders such as stroke, encephalitis, dermatomyositis and myotonic dystrophy. Amyloidosis was ruled out by normal gastric biopsies. Absence of anti-Hu antibodies and antigliutamic acid decarboxylase antibodies excluded any paraneoplastic or autoimmune form of pseudo-obstruction.20–22

 Infective causes of acute and chronic pseudo-obstruction were considered. Bacterial stool cultures for Shigella, Salmonella and Campylobacter were negative as well as interferon gamma release assay and serologies for HIV, Epstein-Barr virus, cytomegalovirus, Borrelia burgdorferi, Toxoplasma gondii, Toxocara and Strongyloides stercoralis.22

Differential diagnosis of Marsh 3a villous atrophy considered coeliac disease, which was ruled out by negative serology and negative HLA DQ-2 and DQ-8 genotyping. Enteropathy-associated T-cell lymphoma was unlikely as strongly associated with coeliac disease. Drug-related villous atrophy was excluded as our patient did not take such medications as olmesartan, ipilimumab, colchicine, mycophenolate mofetil, methotrexate and azathioprine. Tropical sprue is an endemic condition in certain parts of the world such as South Asia, the Caribbean, and Central and South America, but it is unlikely in Italy. Crohn’s disease may cause villous atrophy but was excluded by cross-sectional imaging and normal faecal calprotectin. Collagenous sprue and Whipple disease were excluded by histological examination of duodenal biopsies. Common variable immunodeficiency was unlikely because of the normal levels of IgM and IgG and the reported normal response to vaccines. Small intestinal bacterial overgrowth was excluded by normal glucose breath test.23

The diagnosis of giardiasis was considered among the causes of Marsh 3a villous atrophy.24 The research of ova and parasites in the stools revealed the presence of trophozoites and cysts of G. lamblia. The parasite was found in the duodenal biopsies at a second look after the finding on stool examination (figure 4).

Autoimmune enteropathy, another rare cause of villous atrophy, was unlikely as it requires a diagnosis of exclusion.23

Figure 1 Doughnut or bull’s eye sign at abdominal ultrasound, suggestive for small bowel intussusception.

Figure 2 CT enterography showing dilated and bundling small bowel loops without mechanical obstructing lesions or increased thickness of the small bowel walls.

Figure 3 Duodenal biopsy showing intraepithelial lymphoplasmacytosis with incremented number of CD3+ intraepithelial lymphocytes (40 CD3+ intraepithelial lymphocytes out of 100 enterocytes) and villous atrophy, consistent with modified Marsh 3a.
Daughter also had metronidazole.

Abdominal distension and diarrhoea, successfully treated with:

Figure 4 Revised duodenal biopsies showing Giardia lamblia trophozoites (arrows) in the duodenal lumen close to the mucosal surface.

TREATMENT

The patient was treated with metronidazole, 500 mg three times a day for 7 days with rapid regression of symptoms.

OUTCOME AND FOLLOW-UP

Three month after treatment, upper GI endoscopy was repeated and multiple duodenal biopsies displayed normotrophic villi, with slight residual lymphoplasmocytic infiltration, and normal levels of CD3+ intra-epithelial lymphocytes (figure 5). G. lamblia trophozoites were absent in the duodenal biopsies and in the stools. Abdominal ultrasound showed no more signs of small bowel loops dilatation. After 3 months, the patient was asymptomatic with 3 kg body weight increase. Her 18-month-old daughter also had G. lamblia in the stools. She reported abdominal distension and diarrhoea, successfully treated with metronidazole.

DISCUSSION

We reported the case of a female patient with IPO caused by giardiasis. According to our search through the PubMed and Google Scholar databases, this is the first reported case of giardiasis presenting with a dilated small bowel mimicking IPO. The rapid and complete resolution of both symptoms and small bowel dilatation after Giardia eradication suggests that small bowel dilatation was due to an imbalance of reversible mechanisms controlling the intestinal tone. Gut tone is under the influence of cholinergic muscarinic excitatory and adrenergic, cholinergic nicotinic and nitric oxide (NO)-like inhibitory transmitters. An increased release of NO has been shown to play a pivotal role in the control of infections with numerous microbes including G. lamblia. In vitro studies showed that NO inhibits G. lamblia growth, and studies on NO synthase-deficient mice revealed a reduced clearance of the parasite in vivo. These findings raise the hypothesis that an enhanced release of NO might underlie the reduced small bowel tone in our patient. In line with this hypothesis, a significant increase in NO synthase-containing cells has been reported in the myenteric plexus of the small intestine of patients with chronic IPO, suggesting that NO overproduction may be related to the pathogenesis of ileal dilatation in these patients.

G. lamblia infection has been recognised as one of the causes of postinfectious IBS and functional dyspepsia (FD). The pathogenesis of these syndromes after bacterial or parasitic infection is probably multifactorial and is still insufficiently understood, but increased levels of inducible NO synthase associated with mast cell degranulation were found in the duodenal biopsies of subjects with IBS and FD, suggesting that NO dysregulation might be involved in the mechanism of postinfectious IBS and FD.

G. lamblia infection caused a histopathological pattern in our patient which was almost indistinguishable from that of coeliac disease. In this condition, anti-tTG and negative HLA DQ-2 and DQ-8 genotyping maintained their diagnostic ability to discriminate between coeliac disease and giardiasis. This result is in line with the almost 100% negative post-test probability previously reported for negative HLA DQ-2 and DQ-8 genotyping in patients with a clinical suspicion of coeliac disease. The recognition of the parasite in the duodenal lumen of our patient occurred only after a second look, suggesting that diagnosis might be difficult for the pathologist. In line with this observation, 18% of false negatives were reported in a retrospective histological analysis of duodenal samples from 567 cases of giardiasis presenting with celiac-like duodenal histology. In this context, the microscopic analysis of duodenal aspirate might have represented another diagnostic option, although not superior to the analysis of duodenal biopsies when available.

Abdominal ultrasound with intestinal assessment showed the presence of transient small bowel intussusception that was not confirmed at CT enterography. The transient nature of small bowel intussusception was previously reported in an observational study of 25 paediatric patients, none of whom had persistent intussusception requiring surgery. In this study, four patients with persistent symptoms had an underlying disease requiring treatment, two of them with giardiasis, suggesting that G. infection may predispose to transient small bowel intussusception.

Contributors TP, LS and MF conceived of the presented idea. TP and GB developed the text. GB and MF supervised the findings of this work. All authors followed the clinical development of the case, discussed the results and contributed to the final manuscript.

Funding This study was partially funded by Italian Ministry of Health, Current research IRCCS.

Competing interests None declared.

Patient consent for publication Consent obtained directly from patient(s).

Provenance and peer review Not commissioned; externally peer reviewed.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

Figure 5 Duodenal biopsies 3 months after metronidazole treatment showing normotrophic villi with normal levels of CD3+ intraepithelial lymphocytes.
Case report

Learning points

► *Giardia lamblia* infection could rarely present as intestinal pseudo-obstruction.
► The histological diagnosis of giardiasis via duodenal biopsies is possibly difficult but should be considered, particularly for patients presenting with duodenal atrophy.
► Transient small bowel intussusception at abdominal ultrasound with intestinal assessment should raise suspicion of *G. lamblia* infection.

ORCID ID
Tommaso Pessarelli http://orcid.org/0000-0002-8817-144X

REFERENCES


Copyright 2022 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit [https://www.bmj.com/company/products-services/rights-and-licensing/permissions/](https://www.bmj.com/company/products-services/rights-and-licensing/permissions/)

Become a Fellow of BMJ Case Reports today and you can:
► Submit as many cases as you like
► Enjoy fast sympathetic peer review and rapid publication of accepted articles
► Access all the published articles
► Re-use any of the published material for personal use and teaching without further permission

Customer Service
If you have any further queries about your subscription, please contact our customer services team on +44 (0) 207111 1105 or via email at support@bmj.com.

Visit casereports.bmj.com for more articles like this and to become a Fellow.