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Gastroduodenal strongyloidiasis infection causing protein-losing enteropathy: A case report and review of the literature

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ABSTRACT

Strongyloides stercoralis is an intestinal nematode in which adult worms in the host small intestine can cause strongyloidiasis. Symptoms in immunocompromised patients might range from diarrhea and bleeding to sepsis and even death. A 56-year-old patient presented with a 2-month history of weight loss, vomiting, and diarrhea. The patient had type 2 diabetes mellitus (T2DM) and was on long-term prednisone for chronic kidney disease. The results of the gastric emptying test and head magnetic resonance (MRI) were normal. A blood test revealed increased IgE levels, eosinophilia, and hypoalbuminemia. Parasitic larvae were not discovered during stool analysis. Gastroscopy revealed chronic nonatrophic gastritis with erosions and dilation of lymphatic vessels of the duodenum. Small-bowel capsule endoscopy suggested dilation of lymphatic vessels of the small intestine. Colonoscopy revealed no abnormalities. Finally, a histopathology examination identified *S. stercoralis* pervasion in the gastric antrum and duodenum. The patient was treated with albendazole and discharged successfully. In conclusion, we discovered *S. stercoralis* as a cause of protein-losing enteropathy in a patient with a long-term oral corticosteroid therapy and T2DM. The diagnosis was made through histopathology, once parasitological examination was negative. Therefore, health professionals should stay alert to *S. stercoralis* infection in immunocompromised patients with vague gastrointestinal symptoms. More sensitive methods should be applied in the diagnosis.

1. Introduction

Strongyloidiasis is a soil-borne helminth illness. More than 600 million people worldwide are affected by *S. stercoralis*, and in many tropical and subtropical countries, *S. stercoralis* diseases affect between 10% and 40% of the population [1]. Strongyloidiasis cases are scattered in China, as shown by the *S. stercoralis* global distribution map [2].*S. stercoralis* infection is usually chronic and asymptomatic. However, in immunocompromised patients it can evolve to a severe form, hyperinfection and/or disseminated disease. Groups at risk of develop severe strongyloidiasis includes HTLV- 1 coinfected patients, alcoholics, patients in chronic use of corticosteroid and individuals with diabetes mellitus. When *S. stercoralis* infects the duodenum, it can cause persistent vomiting and ultimately result in intestinal malabsorption [3].

Protein-losing enteropathy (PLE) is the loss of protein from the digestive tract. The causes of protein-losing enteropathy are intestinal disease, intestinal pressure, and lymphatic obstruction. Elevated intestinal pressure can also be caused by right heart stress or

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liver cirrhosis. Intestinal lymphangiectasia is characterized by disturbance of lymphatic drainage of the small intestine with dilated intestinal lymphangiopathy. Laboratory findings in patients with PLE show mainly a decrease in serum concentrations of the following components: albumin, γ globulin (IgA, IgG, IgM), fibrinogen, cholesterol, etc.

Here, we report a 56-year-old patient with complaints of vomiting and diarrhea for two months and a long history of chronic kidney disease and diabetes mellitus who was finally diagnosed with gastroduodenal strongyloidiasis that was found in gastroduodenal biopsies.

2. Case presentation

A 56-year-old man (weight 49 kg, height 170 cm, BMI 16.96 kg/m^2 , resting blood pressure 117/86 mm Hg , resting heart rate 88 bpm) was admitted to our hospital on June 17th, 2022, with a history of vomiting and diarrhea during the previous 2 months. Additionally, he complained of discharging watery stools without experiencing any abdominal pain or distention, according to his clinical history. He had been admitted to the local hospital on April 10th, 2022. Proton pump inhibitors, painkillers and antibiotic treatment did not help the patient's condition during hospitalization. He then came to our hospital for further treatment. He had chronic kidney disease and was on long-term oral prednisone 4# QD and triptolide 2# BID treatment. He also had type 2 diabetes mellitus for two years without receiving treatment. He denied eating unclean food or leaving Zhejiang province in China. No family history of ulcerative colitis, Crohn's disease or other known gastrointestinal disease was reported.

Physical examination revealed mild anemia, swelling of the face and lower extremities, and tenderness of the abdomen. Laboratory examinations revealed mild anemia with hemoglobin of 103 g/L (normal range 120–160 g/L), a 12.1% eosinophil level (normal range 0.5%–5%), a total IgE evaluation of 1856 (normal range 20–200) KU/L, and a negative stool occult blood test result. Low levels of total serum protein 42.3 (normal range 60–80) g/L and albumin 27.6 (normal range 35–50) g/L, a low level of fibrinogen 0.63 (normal range 2–4) g/L, a low level of cholesterol 1.76 (normal range 3.12–5.68) mmol/L, and a high level of lactate dehydrogenase 365 (normal range 109–245) U/L were the main abnormal findings in biochemical tests. Despite the patient's history of chronic kidney illness, urine protein testing was negative, indicating that the patient's hypoalbuminemia was not caused by chronic kidney disease.

The symptomatic treatment regimen involved integrated treatment for chronic kidney disease, stomach protection, antiallergic treatment, regulation of intestinal flora and albumin supplementation. The patient's symptom of diarrhea had improved with the aforementioned therapies, but there was still vomiting. We thus performed a further MRI of the head, and the lack of any notable abnormalities allowed us to rule out central vomiting. The patient had a history of diabetes, and his blood sugar control was poor. We performed the gastric emptying test to exclude vomiting caused by diabetic gastroparesis. The result showed that there were no significant abnormalities, and the gastric half-emptying time (T1/2) was 15.4 minutes. Full abdominal enhancement computed tomography (CT) recommended multiple dilated effusions of the small intestine with little liquid level, peritoneum of abdomen and pelvic cavity, omental and mesentery obscurity. Additionally, the abdominal pelvis had a tiny amount of fluid.

Then, we performed painless gastroscopy and colonoscopy on the patient. Gastroscopy revealed chronic nonatrophic gastritis with

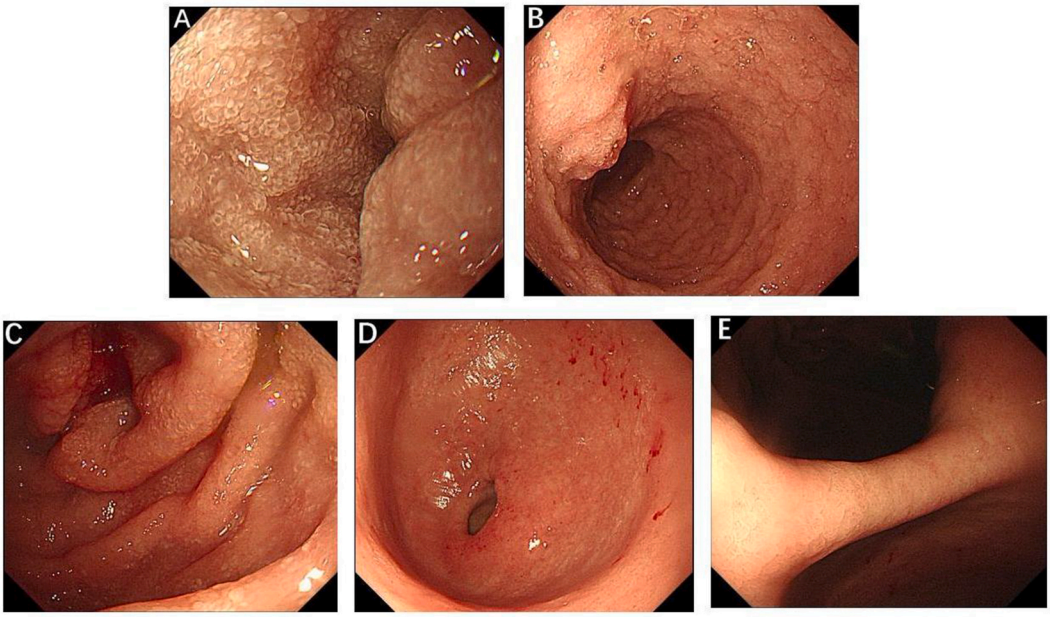

Fig. 1. Gastroscopy revealed chronic nonatrophic gastritis with erosion and dilatation of lymphatic vessels in the duodenal bulb and descending region. A. Bulb of duodenum; B. Descending part of duodenum; C. Junction of duodenal bulb and descending part; D. Gastric antrum; E. Gastric angle.

erosion and dilatation of lymphatic vessels in the duodenal bulb and descending region [Fig. 1(A–E)]. The colonoscopy showed atrophy of the villi in the terminal ileum [Fig. 2(A–D)]. We followed up with capsule endoscopy to assist in diagnosis. Capsule endoscopy suggested atrophy of the small intestine villi and multiple lymphangiectasias in the small intestine [Fig. 3(A and B)]. Human albumin 10 g BID intravenously was administered, and the patient still presented with progressive hypoalbuminemia. A fecal α1-AT clearance test was not performed. By combining endoscopic findings with laboratory findings, we considered the patient to have PLE and/or celiac disease. We performed the celiac disease antibody test, which was negative; therefore, celiac disease was excluded, and the diagnosis of PLE was specified.

Biopsies were taken from the antrum, duodenum, and terminal ileum, which were then sent for pathological review. Microscopically, the infection of *S. stercoralis* was found in the mucosa of the antrum and duodenum [Fig. 4(A and B)]. Finally, the patient was determined to have *S. stercoralis* infection. We chose to administer oral anthelmintic therapy. The patient received treatment with albendazole 400 mg once a day for 14 days. He was discharged. When we followed up with the patient 2 months later, he was in good health, and the symptoms, such as vomiting and diarrhea, had been resolved. The timeline illustrating progress of the case is shown in Fig. 5.

3. Discussion

Strongyloides stercoralis is an intestinal nematode in which adult worms in the host small intestine can cause strongyloidiasis. The filariform larvae, the infectious form of the parasite, invade the skin of the affected individuals, through which they migrate to the lungs either by hematogenous or lymphatic spread. Then, they ascend up in the tracheobronchial tree until they are swallowed into the gastrointestinal tract, where they mature [4] and put people in an infectious state. Symptoms after infection may differ according to the immunity condition. Many factors in immunosuppressed patients can induce disseminated hyperinfection. These risk factors include diseases associated with impaired cell-mediated immune function and medical interventions associated with immunosuppression. The degree of infection, invasion site, and human immune system function are all strongly correlated with the pathogenic effect of *S. stercoralis*. For example, when the larva irritate lung, pulmonary symptoms, including dyspnea, cough, and sputum discharge, were recorded in 15.7% of S. stercoralis-infected cases [2].Dermato-logic manifestations such as recurrent urticaria can occur, as can larva currens, pruritic linear streaks located along the lower trunk, thighs, and buttocks as a result of migrating larvae [5].Disseminated hyperinfection, which can invade the brain, liver, lung, kidney, urinary system, and digestive system, can be caused in patients with weakened immunity or use of corticosteroides and immunosuppressants. Furthermore, diffuse tissue damage may result from disseminated hyperinfection.

Adult *S. stercoralis* can irritate the mucosa of the small intestine mechanically Mild infection can manifest as hyperemia of the intestinal mucosa. Severe infection can reveal erosion of the intestinal mucosa, ulceration and even perforation of the intestine, which may also affect the stomach and colon. In addition to fever, anemia and hypoalbuminemia, patients may also present with nausea,

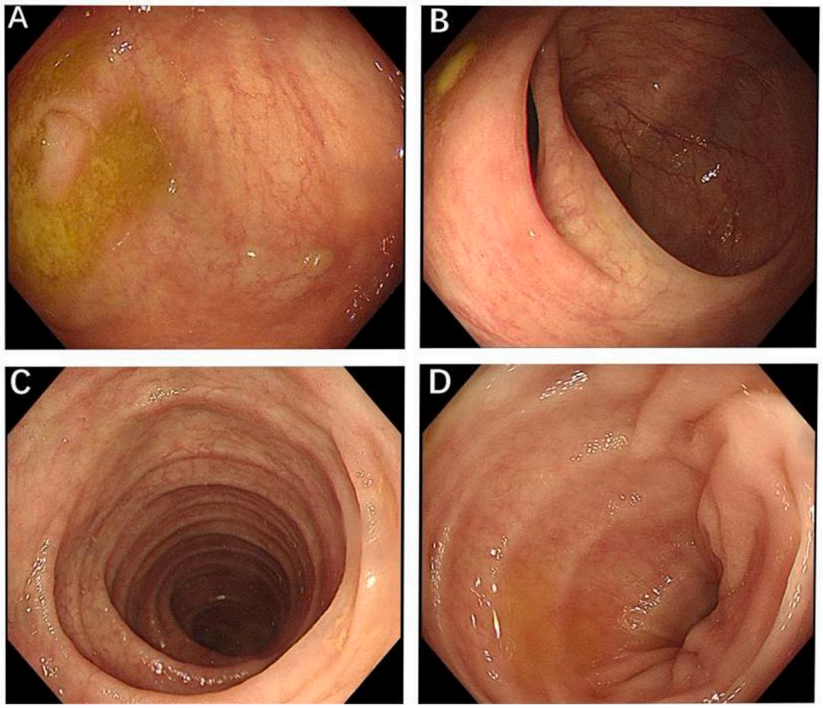

Fig. 2. The colonoscopy showed atrophy of the villi in the terminal ileum. A. The appendix hole; B. ileocecal valve; C, D. Terminal ileum.

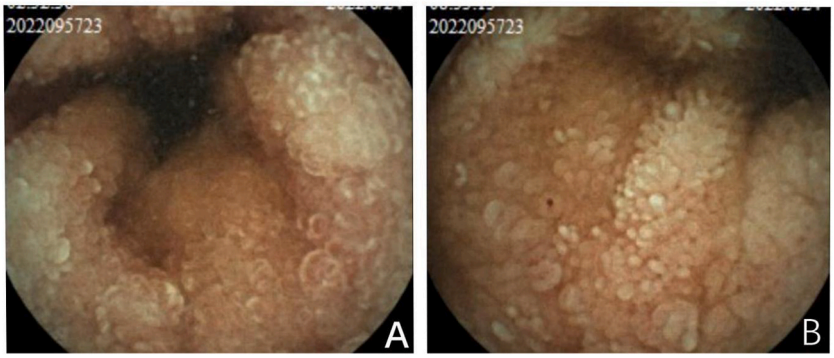

Fig. 3. Capsule endoscopy suggested multiple lymphangiectasias in the small intestine. A. Jejunum; B. Ileum.

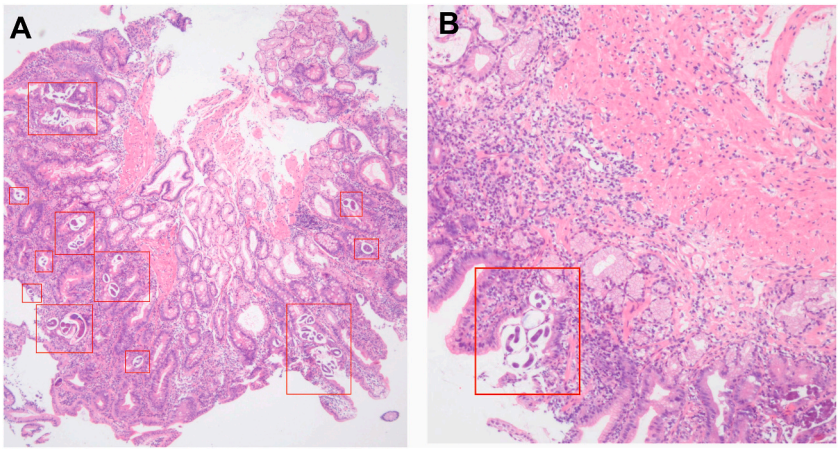

Fig. 4. Pathological findings showing S. stercoralis infection. **A**: hematoxylin–eosin staining × 50**; B**: hematoxylin–eosin staining × 100.

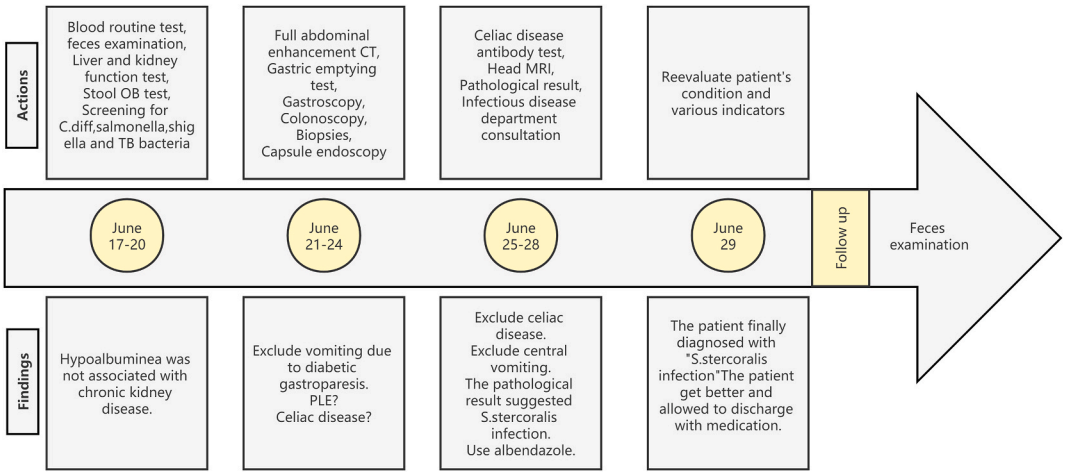

Fig. 5. Case progress timeline.

vomiting, abdominal pain, diarrhea and other symptoms. Hyperinfection frequently presents with significant gastrointestinal symptoms. Peripheral edema or ascites can occur as a consequence of PLE, prompting acute or deteriorating hypoalbuminemia [6].

In this patient, the gastrointestinal infection included clinical symptoms such as protein-losing enteropathy with diarrhea and vomiting. Peripheral eosinophilia is another common sign of infection, albeit it is nonspecific and typically rare in immunocompromised patients because eosinophils are suppressed [7]. At the same time, the elevation of total serum IgE levels, usually related to

eosinophilia has also been reported in *S.stercoralis* infection. As a result, we must pay closer attention to individuals who are receiving ongoing corticosteroid treatment or chemotherapy, transplant recipients, or those who have any other immunosuppressive condition when screening for strongyloidiasis [8]. These factors could raise the parasite burden and accelerate the autoinfectious process, resulting in a hyperinfection state that could later develop into a severe disseminated disease. Our patient has a history of T2DM , some studies have shown that inadequate control of blood sugar level in diabetes patients will lead to susceptibility to infection [9], including parasite infection [10]. However, the relationship between diabetes and *Strongyloides* infection remains controversial, with both positive [11] and negative [12]. Hyperinfection is characterized by the presence of numerous larvae in stool and/or sputum, as well as worsening of gastrointestinal and pulmonary symptoms. Using a variety of methods to identify *S. stercoralis* will also increase the diagnostic accuracy [13].

Strongyloides larvae are usually found in stool samples, while it also can be found in other samples such as sputum, duodenal aspirates, gastric biopsies, cervical smear or CSF liquid, the latter in disseminated *Strongyloides infection.* [14]*Strongyloides* larvae can be found using a variety of techniques, including direct smear, Baermann, Harada Mori, and agar plate culture, also a molecular approach such as ELISA on serology [13]· [15].The parasitological methods with higher sensitivity are Baermann and the agar plate culture, however, they are cumbersome, time-consuming and are not currently deployed in most laboratories. Serological methods, such as ELISA, are an alternative to diagnosis, but they have several limitations and their use in laboratory routine is still very restricted. Molecular methods are only used in a research setting. Therefore, stool examination is still considered the primary technique for the detection of *S.stercoralis* infection. The survey found that stool tests were the most convenient but had a low sensitivity and typically required three consecutive tests. Parasitic larvae were also not discovered in our patient's stool examination. Due to a delay in larva detection in this case, the patient was admitted to the internal medicine ward with a possible diagnosis of duodenitis and chronic atrophy gastritis. Duodenal biopsies helped us made the accurate for identifying larvae in this patient with gastrointestinal symptoms, and this finding was further demonstrated in our case in the histopathological examination after hospitalization for 9 days. However, duodenal biopsy is an invasive method, this invasive method should be perhaps be recommended only in selected cases for example in an of immunosuppressed patient to maximize the chance of detecting larvae when a prompt diagnosis is essential [14]. We conducted comprehensive endoscopic examinations and underwent biopsies simultaneously on patients, which may lead to bleeding, infection, and there is also a certain probability that larvae will not be detected. As a result, the endoscopic tissue biopsies are not a usual method to identify larvae.

In our case, the results of protein-losing enteropathy showed that protein leakage was caused by *S. stercoralis* infection. Then, we searched for articles published in PubMed from January 2000 to December 2022 using the terms "protein-losing enteropathy" and "strongyloidiasis" to identify the characteristics of people infected with *S. stercoralis* with protein-losing enteropathy (Table 1). In this search, we found that endoscopy often revealed chronic gastritis or severe erosive duodenitis, with or without eosinophilic infiltration [4,16]. We can also see larvae of the *strongyloides* in these areas [4,17].However, in another case from before 2000, they performed X-ray, which showed duodenal dilatation and a delay in the third part of the loop with abnormal motility [18]. Our patient underwent full abdominal enhancement CT, which suggested that the small intestine had gas effusion and dilation. We also performed capsule endoscopy in which the small intestine lymphatic vessels were dilated. The results also revealed the involvement of the small intestine mucosa. Compared to other cases, our results were in line with them.

Zhejiang Province in China is located in a subtropical zone. However, Zhejiang Province has rarely reported cases of strongyloidiasis. Therefore, when we made the primary diagnosis, the patient's primary complaints were evaluated as different diagnoses than strongyloidiasis. After the parasites were discovered during the gastric and duodenal biopsy, the patient was given a definitive diagnosis. In the present case, we believe that a confluence of high-risk conditions for *S. stercoralis* hyperinfection, such as imbalance of intestinal flora, malnutrition, chronic kidney disease, corticosteroid use and diabetes lead to this clinical presentation. We all know that an immunosuppressed patient may develop hyperinfection syndrome or disseminated infection, both of which are associated with high rates of morbidity and mortality [18]. Therefore, it is crucial to screen for *S. stercoralis* infection before undergoing tissue transplantation, cancer treatment, or corticosteroid therapy. To prevent the adverse events brought on by a delayed diagnosis, we should therefore pay more attention to using a combination of methods to diagnose *S. stercoralis* in these states.

Oral ivermectin is the preferred method of treatment for uncomplicated infections [16]. Possible alternatives include albendazole and thiabendazole. Thiabendazole showed more adverse events, while albendazole showed less efficacy than ivermectin [8]. It was advised to administer ivermectin until symptoms improved and a test for larvae had been negative for at least 2 weeks (duration of autoinfectious cycle) [4,5]. Finally, the patient received 14 days of 400 mg/day albendazole. When we followed up with the patient 2 months later, he was in good health, and the symptoms, such as vomiting and diarrhea, had been resolved.

There are several limitations in our study. Firstly, these highly sensitivity parasitological methods like Baermann and the Age Plate Culture which are cumbersome, and time-consuming and are not currently deployed in the clinical laboratory department of our hospital. However, we did bacteria smear of stool and examine fecal parasite eggs microscopically before and after treatment. On July 17th, the patient in the out-patient for follow-up, we review the blood routine test and examine fecal parasite eggs microscopically suggesting that all the indicators are normal. In addition, his gastrointestinal complaints had already disappeared. Secondly, we did not perform a fecal a1-AT clearance test which has a high specificity in diagnose PLE. We combined laboratory findings with endoscopic findings also helped us to diagnosed. Thirdly, ivermectin is not available in China, we then chose albendazole for deworming treatment. However, there is a study has pointed out that treatment of soil transmitted helminths infected individuals with albendazole was associated with an increase in insulin resistance after 12 month [19],which means the treatment may result in worsening glucose metabolism so we need to carry out a long-term follow-up to spy the patient's blood sugar.

Table 1
Characteristics of strongyloidiasis infection accompanied by protein-losing enteropathy.

Age	Sex	Complaints	Laboratory test	Endoscopic finding	Biopsy	Treatment	Reference
53	F	No specifically described	hypoalbuminemia, stool sample found larvae	not mentioned	Duodenal, proximal jejunal and distal jejunal biopsy showed larvae of strongyloides	1 recovered on ivermectin	J Clin Gastroenterol. 2012; 46(7):575-80
26	M	diarrhea for 10 days	Moderate anemia, hypoalbuminemia, stool sample found larvae	Upper gastroendoscopy showed presence of increased gastro-esophageal reflux with mild diffuse gastritis	Duodenal biopsy showed larvae of strongyloides in the crypts	Albendazole 400 mg/day for 3 days	J Assoc Physicians India. 2003; 51:395–6
43	F	Abdominal pain and abdominal distension for 1 month	mild anemia, hypoalbuminemia, and hyponatremia	upper gastrointestinal endoscopy, there was diffuse erythematous mucosa, subtle mosaic pattern and attenuated gastric folds. Duodenum shows edematous mucosa showing patchy erythema upto proximal D2	Gastric biopsy showed adult worms, eggs, and rhabditiform larvae in the crypts	3 days course of tab ivermectin 10 mg and tab albendazole 400	Journal of Advances in Medicine and Medical Research. 2021:232–6

4. Conclusion

In China, *Strongyloides* is not a common cause of gastrointestinal symptoms. Hence, a thorough examination, particularly endoscopic tissue biopsies, is crucial for patients with significant gastrointestinal symptoms. Once the precise diagnosis has been made, ivermectin or albendazole should be used. Patients with vague gastrointestinal symptoms who are receiving corticosteroid therapy or have an immunocompromised condition should pay more attention to confirm the presence of parasites using various diagnostic techniques.

We describe a case of gastroduodenal strongyloidiasis that results in protein-losing enteropathy. The parasite was found during a histological examination, and the patient was diagnosed. Emphasis was placed on the characteristic histological features to avoid missing the diagnosis. Strongyloidiasis needs to be identified, diagnosed, and treated as soon as possible to prevent more severe consequences.

Author contribution statement

All authors listed have significantly contributed to the investigation, development and writing of this article.

Data availability statement

No data was used for the research described in the article.

Additional information

No additional information is available for this paper.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] D. Buonfrate, D. Bisanzio, G. Giorli, P. Odermatt, T. Fürst, C. Greenaway, M. French, R. Reithinger, F. Gobbi, A. Montresor, Z. Bisoffi, The global prevalence of strongyloides stercoralis infection, Pathog. Basel Switz. 9 (2020) 468.
[2] R. Varatharajalu, R. Kakuturu, Strongyloides stercoralis: current perspectives, Rep. Parasitol. (2016) 23.
[3] M.C.A. Teixeira, F.T.F. Pacheco, J.N. Souza, M.L.S. Silva, E.J. Inês, N.M. Soares, Strongyloides stercoralis infection in alcoholic patients, BioMed Res. Int. 2016 (2016), 4872473.

[4] W. El Hajj, G. Nakad, A. Abou Rached, Protein loosing enteropathy secondary to strongyloidiasis: case report and review of the literature, Case Rep. Gastrointest Med. 2016 (2016), 6831854.
[5] R. Mejia, T.B. Nutman, Screening, prevention, and treatment for hyperinfection syndrome and disseminated infections caused by Strongyloides stercoralis, Curr. Opin. Infect. Dis. 25 (2012) 458–463.
[6] P. Piranavan, P. Kalantri, D. Pandey, H.S. Bharadwaj, A. Verma, Strongyloides stercoralis hyperinfection syndrome: a neglected cause of abdominal pain, Cureus 12 (2020), e10671.
[7] G.G. Baaten, G.J. Sonder, T. van Gool, J.A. Kint, A. van den Hoek, Travel-related schistosomiasis, strongyloidiasis, filariasis, and toxocariasis: the risk of infection and the diagnostic relevance of blood eosinophilia, BMC Infect. Dis. 11 (2011) 84.
[8] A. Requena-Méndez, D. Buonfrate, J. Gomez-Junyent, L. Zammarchi, Z. Bisoffi, J. Muñoz, Evidence-based guidelines for screening and management of strongyloidiasis in non-endemic countries, Am. J. Trop. Med. Hyg. 97 (2017) 645–652.
[9] S. Knapp, Diabetes and infection: is there a link? - a mini-review, Gerontology 59 (2013) 99–104.
[10] F.O. Akinbo, S.O. Olujobi, R. Omoregie, C. Egbe, Intestinal parasitic infections among diabetes mellitus patients, Biomark Genomic Med 5 (2013) 44–47.
[11] E. McGuire, C. Welch, M. Melzer, Is Strongyloides seropositivity associated with diabetes mellitus? A retrospective case-control study in an East London NHS Trust, Trans. R. Soc. Trop. Med. Hyg. 113 (2019) 189–194.
[12] R. Hays, A. Esterman, P. Giacomin, A. Loukas, R. McDermott, Does Strongyloides stercoralis infection protect against type 2 diabetes in humans? Evidence from Australian Aboriginal adults, Diabetes Res. Clin. Pract. 107 (2015) 355–361.
[13] A. Amor, E. Rodriguez, J.M. Saugar, A. Arroyo, B. López-Quintana, B. Abera, M. Yimer, E. Yizengaw, D. Zewdie, Z. Ayehubizu, T. Hailu, W. Mulu, A. Echazú, A. J. Krolewieki, P. Aparicio, Z. Herrador, M. Anegagrie, A. Benito, High prevalence of Strongyloides stercoralis in school-aged children in a rural highland of north-western Ethiopia: the role of intensive diagnostic work-up, Parasit Vectors 9 (2016) 617.
[14] A. Requena-Méndez, P. Chiodini, Z. Bisoffi, D. Buonfrate, E. Gotuzzo, J. Muñoz, The laboratory diagnosis and follow up of strongyloidiasis: a systematic review, PLoS Negl. Trop. Dis. 7 (2013), e2002.
[15] F. Schär, U. Trostdorf, F. Giardina, V. Khieu, S. Muth, H. Marti, P. Vounatsou, P. Odermatt, Strongyloides stercoralis: global distribution and risk factors, PLoS Negl. Trop. Dis. 7 (2013), e2288.
[16] Y. Suputtamongkol, N. Premasathian, K. Bhumimuang, D. Waywa, S. Nilganuwong, E. Karuphong, T. Anekthananon, D. Wanachiwanawin, S. Silpasakorn, Efficacy and safety of single and double doses of ivermectin versus 7-day high dose albendazole for chronic strongyloidiasis, PLoS Negl. Trop. Dis. 5 (2011), e1044.
[17] S. Bharti, A. Singh, R. Kirti, N. Kumar, Gastroduodenal strongyloidiasis causing protein losing enteropathy – a case report and brief review of literature, J. Adv. Med. Med. Res. (2021) 232–236.
[18] P.F. Milner, R.A. Irvine, C.J. Barton, G. Bras, R. Richards, Intestinal malabsorption in Strongyloides stercoralis infestation, Gut 6 (1965) 574–581.
[19] R. Hays, P. Giacomin, L. Olma, A. Esterman, R. McDermott, The relationship between treatment for Strongyloides stercoralis infection and type 2 diabetes mellitus in an Australian Aboriginal population: a three-year cohort study, Diabetes Res. Clin. Pract. 134 (2017) 8–16.