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Case Report

Internal Medicine Section

Strongyloides stercoralis Infestation Manifesting as Protein Losing Enteropathy and Dyselectrolytaemia in an Immunocompetent Adult: A Case Report

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ABSTRACT

Strongyloides stercoralis is an intestinal nematode which persists as chronic asymptomatic infection for several years. Clinical manifestations become apparent long after initial infection which includes non specific gastrointestinal (GI) symptoms like pain abdomen, nausea, vomiting, altered bowel habits or weight loss. Larval reproduction can lead to disseminated infection in the immunocompromised. Very rarely, hyperinfection or disseminated strongyloides can lead to ulceration, bleeding, small bowel obstruction, colitis or ascites. In severe cases, electrolyte disturbances and protein losing enteropathy may occur. We present a unique case of intestinal infestation of *Strongyloides stercoralis* in a 42-year-old immunocompetent male with a rare manifestation of protein losing enteropathy and dyselectrolytaemia without any GI symptoms at the outset, whose presentation was anasarca and initial investigations including work-up for cardiovascular, hepatic and renal causes of anasarca were unremarkable except for hypoalbuminaemia and electrolyte abnormalities and notable absence of peripheral eosinophilia. The diagnosis was arrived at by simple and conventional investigations like stool microscopy which demonstrated the Strongyloides larvae and upper GI endoscopy aided the biopsy which was confirmatory. He responded to appropriate medical treatment. Helminthic infestation should be kept in mind as a rare cause of malabsorption syndrome manifesting as protein losing enteropathy in a tropical and endemic country like India. These are treatable causes and respond to specific cost-effective antihelminthic treatments.

Keywords: Gastrointestinal symptoms, Helminthic, Malabsorption

CASE REPORT

A 42-year-old male presented to the Emergency Department (ED) with generalised body swelling for one month, which was insidious in onset and gradually progressive. He had history of loose stools for ten days one month prior to hospitalisation, which were intermittent, watery and non mucoid. He consulted a local physician and was treated with oral antibiotics, antidiarrhoeal agents and probiotics for the same whose details were not available. There was no history of passage of blood in stools, vomiting, abdominal pain, abdominal distension, jaundice, dyspnoea, decreased urine output, passage of frothy urine, haematuria, fever or loss of appetite. He used to consume alcohol once or twice in a week for 10 years which he left two months ago. He denied history of any past medical illness.

At the ED, he had blood pressure of 110/70 mmHg, pulse rate of 90/min, regular and normal volume, respiratory rate of 18 breaths/min regular and abdominothoracic, oxygen saturation of 99% on room air and temperature of 99°F. His capillary blood glucose was 158 mg/dL. Physical examination revealed presence of facial puffiness and pitting oedema of all limbs. There was no pallor or icterus and jugular venous pressure was normal. Systemic examination was unremarkable. Chest X-ray posteroanterior (PA) view done at ED revealed no abnormality. Ultrasonography (USG) of abdomen showed normal liver echotexture and no evidence of any free fluid. Laboratory investigation findings are presented in [Table/Fig-1].

Remarkably, there was hypoproteinaemia (3.35 g/dL), hypoalbuminaemia (1.42 g/dL) and electrolyte abnormalities in the form of hyponatraemia, hypokalaemia, hypocalcaemia, hypophosphataemia and hypomagnesaemia. There was hypolipoproteinaemia and low serum iron and total iron binding capacity with normal transferrin saturation and ferritin. Urine

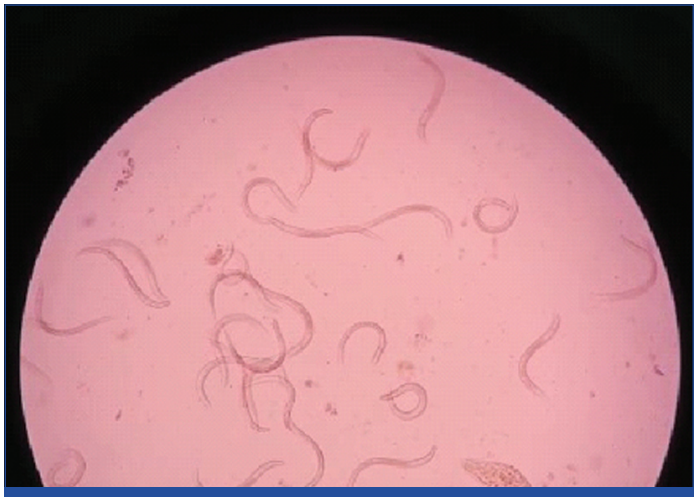
Parameters	Values
Haemoglobin	11.7 g/dL
Total Leucocyte Count (TLC)	9300/mm^3
Differential Leucocyte Count (DLC)	N60L20
Platelet count	2.58 lakh/mm^3
Blood urea/S. creatinine (mg/dL)	8/0.53
S.Na$^+$/S.K$^+$ (mEq/L)	114/2.7
Total protein/S.albumin (g/dL)	3.35/1.42
S. Ca2$^+$/Corrected Ca2$^+$ (mg/dL)	6/8.064
S.Phosphate/S.Magnesium	2.2/1.6 (mg/dL)
S. uric acid (mg/dL)	2.5
Total bilirubin/Direct bilirubin	0.90/0.31 (mg/dL)
Alanine transaminase (IU/L)	60.3
Aspartate transaminase (IU/L)	40.5
Alkaline phosphatase (IU/L)	225
Gamma-glutamyl transaminase	46 IU/L
Prothrombin time	13 seconds
International Normalised Ratio	1.22
HBsAg/HCV/HIV I and II	Negative
Fasting blood sugar/postprandial blood sugar	103/156 (mg/dL)
HbA1c (Glycated Haemoglobin)	6.2%
Peripheral smear	Normocytic normochromic RBCs with normal leucocytes and platelets
Iron profile	S.iron-25 mg/dL, S.ferritin-190 ng/mL, Transferrin saturation-33%, Total Iron Binding Capacity-75 mg/dL

Lipid profile	Total cholesterol- 73 mg/dL, Triglyceride-97 mg/dL, Low-density lipoprotein 30 mg/dL, High density lipoprotein -14 mg/dL, Very low-density lipoprotein -19 mg/dL
S. Vitamin B12	830 pg/mL
S.folic acid	4.72 ng/mL
S. 25 hydroxy Vitamin D3	30 ng/mL
Urine routine examination and microscopy	protein-absent, sugar-absent, no pus cells or RBCs per high power field
24 hour urinary protein	0.51 g

[Table/Fig-1]: Baseline investigations at admission. S: Serum

analysis revealed absence of proteinuria, which prompted a search for enteric protein loss in the face of low serum electrolytes and lipoproteins, hinting towards malabsorption.

The patient was managed conservatively with i.v. albumin infusions (20% human albumin 100 mL daily) and correction of electrolyte abnormalities was done by necessary supplementations based on laboratory values. Immunoglobulin A (IgA) anti tissue transglutaminase (tTG) was sent to rule out celiac sprue, which was 3.06 U/mL (negative). Stool routine and microscopic examination revealed numerous strongyloides larvae [Table/Fig-2], reduced bacterial flora and acidic pH and no occult blood.



[Table/Fig-2]: Image of microscopic examination of wet mount preparation of stool specimen of the patient showing larvae of *Strongyloides stercoralis* (40x).

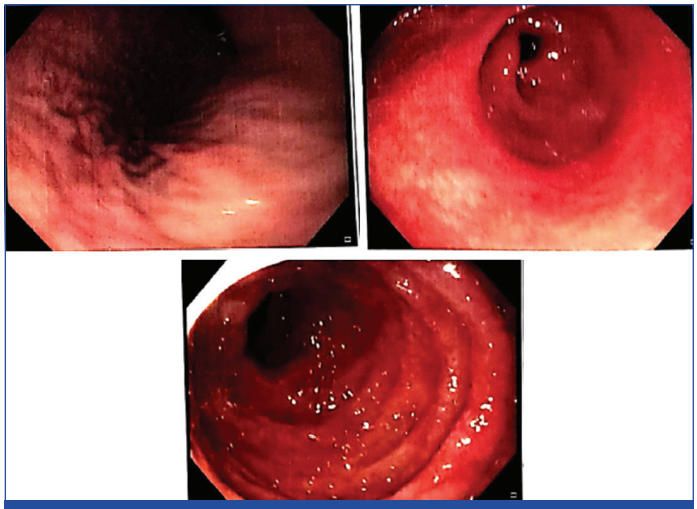
Upper GI endoscopy showed reduced number of villi in duodenum with presence of scalloping and erosions [Table/Fig-3]. Duodenal biopsy revealed filariform larvae of *Strongyloides stercoralis*, crypt hyperplasia with regenerative atypia and dense mixed inflammatory infiltrate in lamina propria suggestive of chronic active duodenitis with *Strongyloides stercoralis* infestation [Table/Fig-4].

Thus, the patient was diagnosed as a case of strongyloidiasis with protein losing enteropathy and dyselectrolytemia and started on Ivermectin 200 mcg/kg/day and given 12 mg oral tablet (weight of 60 kg) once daily for two doses. Stool microscopic examination repeated thereafter revealed no abnormality signifying complete clearance of strongyloides infestation.

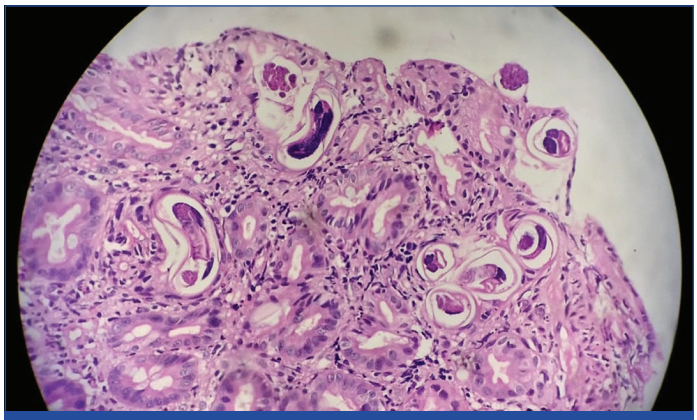
During the course of the anthelmintic treatment and supportive measures, swelling of limbs and face gradually disappeared. The patient was discharged after 15 days of hospitalisation with residual swelling confined to both feet till ankles and serum albumin level of 3.1 g/dL.

The following table [Table/Fig-5] shows the trend of improvement in albumin and electrolyte levels in the patient during the course of hospital stay.

During the follow-up visit after one month, the patient had minimal residual swelling confined to both ankles. His serum albumin was



[Table/Fig-3]: Images of upper GI endoscopy of the patient showing reduced villi with duodenal scalloping with erosions.



[Table/Fig-4]: Microscopic image of histopathology of duodenal biopsy of the patient showing filariform larvae of *Strongyloides stercoralis*, crypt hyperplasia with regenerative atypia and dense mixed inflammatory infiltrate in lamina propria (40x stained with H&E).

Parameters	Day 5	Day 8	Day 10	Day 14
S. albumin (mg/dL)	1.8	2.4	2.7	3.1
S. Na^+ (mEq/L)	118	125	130	134
S. K^+ (mEq/L)	3.0	3.3	3.71	3.9
S. $Ca2^+$ (mg/dL)	6.7	7.0	7.1	7.8
S. Phosphate (mg/dL)	2.5	3.8	4.0	3.9

[Table/Fig-5]: Albumin and electrolyte levels during hospital stay. S: Serum

3.3 g/dL and serum electrolytes were within normal ranges. Repeat stool microscopic examination was unremarkable.

DISCUSSION

The case study demonstrated hypoalbuminaemia as the cause of the patient's swelling of limbs and face, associated with electrolyte abnormalities which turned out to be protein losing enteropathy in the absence of other systemic signs and suggestive investigations. It was stool examination aided by endoscopic duodenal biopsy which helped to arrive at a diagnosis of strongyloides infestation, remarkably in absence of peripheral blood eosinophilia.

It becomes paramount in a tropical country like India, which is endemic to parasitic and helminthic infections, to strongly suspect helminthic infestations in causes of protein losing enteropathy.

Regions of Southeast Asia, Africa, and Western Pacific together account for up to 75% of strongyloides infections globally [1]. Regional prevalence in tropics and subtropics exceeds more than 30% [2]. *Strongyloides stercoralis* can undergo free living as well as parasitic cycle of development. Rhabditiform larvae passed in stools transform into filariform larvae which humans acquire after contact with fecally contaminated soil via penetration of skin or

mucous membranes. The infectious larvae reach the lungs via bloodstream, ascend the tracheobronchial tree and are swallowed, thus reaching the intestine. They mature into adult forms which lay eggs in the intestinal mucosa. Rhabditiform larvae are released after hatching, which are passed in stools or they directly transform into filariform stage and penetrate colonic wall or perianal skin and enter the bloodstream, resulting in continued internal infection. This autoinfection allows it to persist for decades [3].

In uncomplicated cases, patients are asymptomatic or have mild cutaneous or GI symptoms. Recurrent urticaria, often involving the buttocks and wrists is the most common cutaneous manifestation [3]. Migrating larvae can elicit a serpiginous eruption, larva currens ("running larva") which is pruritic, raised, erythematous and advances as rapidly as 10 cm/h along the course of larval migration [3]. Adult worms burrow into the duodenojejunal mucosa and can cause abdominal (usually midepigastric) pain, nausea, diarrhoea, GI bleeding, mild chronic colitis and weight loss. Small-bowel obstruction can develop with early, heavy infection. Hyperinfection can lead to malabsorption. In disseminated strongyloidiasis, larvae may invade lungs, Central Nervous System (CNS), peritoneum, liver, and kidneys. Bacteraemia may develop because of the passage of enteric flora through disrupted mucosal barriers which can lead to Gram-negative sepsis, pneumonia, or meningitis [3].

Autoinfection is kept in check by host immune response, waning of which due to glucocorticoids or other immunosuppressants results in infections with Human T-Lymphotropic Virus type 1 (HTLV-1) or uncommonly HIV, which leads to hyperinfection with generation of large numbers of filariform larva. Conditions associated with impairment of cell mediated immunity or medical interventions causing immunosuppression are risk factors for severe diseases like HTLV-1 infection, HIV infection, malignancy, hypogammaglobulinaemia, congenital immunodeficiency, malnutrition/administration of steroids or cytotoxic drugs, solid organ or haematopoietic stem cell transplants, etc., [4,5].

Cases of strongyloidiasis presenting as protein losing enteropathy have been reported earlier [6-9]. In all these cases, the patients already had an established or known immunocompromised condition as a predisposing factor for such presentation. Janardhanan S et al., reported gastroduodenal strongyloidiasis with protein losing enteropathy and anaemia in an elderly diabetic man who was on Disease Modifying Antirheumatic Drugs (DMARDs) and Non Steroidal Anti-inflammatory Drugs (NSAIDs) for rheumatoid arthritis [6]. Bharti S et al., reported it in a 46-year-old woman who was on steroids for joint pains [7]. Wang Y and Zhang X reported similar presentation in a 56-year-old male who was diabetic and had Chronic Kidney Disease (CKD) and was on long-term prednisone [8]. In the present case, there was no established immunocompromised state prior or detected to be such in the period of hospitalisation. Elshamy MHA et al., also reported similar presentation in a 62-year-old immunocompetent female [9]. However, all these cases had GI manifestations at the time of presentation which was notably absent in the present case and therefore it posed a diagnostic dilemma.

Peripheral blood eosinophilia and increased IgE levels were evident in the case reported by Wang Y and Zhang X [8] which was not there in the other cases including the present case [6,7]. Stool examination was unremarkable in all of these while it was the stepping stone to diagnosis in the present case. In all of them, diagnosis was clinched by endoscopic changes and histopathology, which also settled the dilemma in the present case.

Lastly, clinical response and recovery was evident in all of these cases after anthelmintic treatment. The present patient improved after two doses of ivermectin as described earlier. The first case received two doses of ivermectin repeated after a week [6], while the second case received ivermectin and albendazole combination [7] and the third and fourth cases were treated with only albendazole [8,9].

Bone marrow transplant recipients can manifest accelerated autoinfection cycle, resulting in hyperinfection and/or disseminated strongyloidiasis leading to multiorgan system invasion [10].

Stool examination finding of rhabditiform larvae is diagnostic. In uncomplicated cases, very few larvae may be passed and about one-third cases only are detected by stool microscopy. Use of serial examinations, agar plate detection method or Polymerase Chain Reaction (PCR) improves the diagnostic yield [3]. Serologic testing using Enzyme Linked Immunosorbent Assay (ELISA) is a sensitive method for diagnosis but should be employed in patients with suggestive geographic history, peripheral blood eosinophilia and/or candidates for steroid or other immunosuppressive therapy [3]. As stool examination finding of strongyloides larvae unravelled the diagnosis in the present case, serologic testing was not required due to the absence of factors to be considered for ordering it, as mentioned before.

Larvae may also be demonstrated in duodenojejunal aspirates or biopsies, which in the present case settled the diagnosis. Endoscopic findings include thickened gastric folds, mucosal oedema, discolouration or erosions, epithelial haemorrhages, aphthous ulcers or loss of vascular pattern in colon [11]. In disseminated strongyloidiasis, larvae may also be obtained from potential sites of migration, including sputum, bronchoalveolar lavage fluid or surgical drainage fluid.

For treatment, efficacy of ivermectin 200/mcg/kg/day for one or two days has shown to be greater than albendazole 400 mg daily for three to seven days and comparable with that of thiabendazole (25 mg/kg per day for three days). In a meta-analysis including seven trials and more than 1100 patients with chronic strongyloidiasis, cure rates for ivermectin were found to be superior to albendazole and comparable with thiabendazole (74-84%, 48%, and 69%, respectively) [12]. Ivermectin should be extended for 14 days or at least seven days after parasites have been eradicated in disseminated infections. In potentially immunocompromised patients, ivermectin course should be repeated after 14 days. Asymptomatic stages also need to be treated because of risk of subsequent dissemination and hyperinfection [3].

CONCLUSION(S)

The case highlights a very rare presentation of *Strongyloides stercoralis* infestation as protein losing enteropathy and electrolyte disturbance in the absence of any prior immunocompromise or relevant risk factors. It brings to light the need to consider searching for helminthic infections as one of the possible causes of protein loss from the gut, leading to severe hypoalbuminaemia manifesting as anasarca even when other GI or extraintestinal symptoms or signs are not present at the outset. This helps in guiding necessary and relevant investigations for confirmation and specific antihelminthic treatments are available which are curative and economical.

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