bacterial pneumonia can complicate the picture.[2] A TB diagnosis was delayed by nearly 4 months from initial presentation in our patient, with ongoing disease progression contributing to the excessive fibrosis associated with the bronchial obstruction observed. After correct diagnosis and treatment, our patient still developed likely chronic bacterial pneumonia, distal to the bronchial obstruction. The abnormal white cell count (WCC) and CRP observed could have been due to TB alone but was presumed to be bacterial in origin given the clinical improvement documented with antibiotic treatment. Sputum and bronchoalveolar lavage samples did not isolate a bacteria but were performed while on antibiotics. The fact that children are more likely to develop primary *M. tuberculosis* infection with highly reactive regional lymph node enlargement, as well as the increased malleability and small size of their airways, increase the incidence of airway compression and other complications associated with intrathoracic lymph node disease.[3] Endobronchial disease has been observed in around 40% of children with TB requiring brochoscopic evaluation for airway obstruction,[4] with extrinsic lymph node compression—without endobronchial disease—in around 60%.[5] Either can result in partial obstruction with distal hyperinflation or complete obstruction with distal collapse, potentially complicated by secondary bacterial infection. Endobrochial TB may also be associated with bronchial spread and TB bronchopneumonia.[6] In children with airway obstruction resulting from possible TB disease, bronchoscopy has diagnostic and potential therapeutic value; careful consideration of infection control measures is essential.

The second teaching point is that unusual complications such as pneumothorax can occur. In our patient, this resulted from primary parenchymal disease with cavity formation. Pneumatocele development, due to the subsegmental ball valve effect produced by extrinsic compression, was considered to be less likely, given the thickness and irregularity of the cavity wall. Lung cavities in adults with pulmonary TB may precipitate a spontaneous pneumothorax,[7] but lung cavities are uncommon in young children.[6] However, young children may experience progressive parenchymal caseation with cavitation if there is uncontrolled progression of the primary Ghon focus or following complete bronchus obstruction with an expansile caseating pneumonia distal to the obstruction.[8]

The final teaching point is that the role of corticosteroids remains controversial in the treatment of associated airway obstruction. The role of corticosteroids in this situation is contentious[9] with very little evidence of benefit in pediatric lung disease. In adults, steroid therapy has been shown to reduce mortality in patients with severe forms of TB,[9] but only a small benefit was reported for pulmonary disease. In children, 1 small prospective study of airway obstruction due to hilar lymph adenopathy described faster clinical improvement and fewer complications when providing a course of oral prednisone.[10] In our case, prednisone 2 mg/kg/d was initiated on diagnosis of airway obstruction. This higher dose was chosen due to concurrent induction of hepatic enzymes by rifampicin, which increases steroid metabolism by approximately 50%. The airway fibrosis and persistent obstruction—despite steroid treatment—observed on follow-up may place our patient at risk of recurrent infection and bronchiectasis in this region in the future. However, in most children, the affected lung segments collapse with expansion of neighboring healthy parenchyma leading to complete resolution without any long-term sequelae.[11] Decompression of the external lymph nodes compressing the airway is a therapeutic option[12] but was not considered in our patient. Despite achieving a good treatment response, our patient may have benefitted from increased TB drug dosages in accordance with revised international guidance [isoniazid 10 mg/kg (range, 7–15 mg/kg), rifampicin 15 mg/kg (range, 10–20 mg/kg), pyrazinamide 35 mg/kg (range, 30–40 mg/kg)].[13]

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A Rare Complication of Giardiasis in Children

Protein-losing Enteropathy

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Abstract: Protein-losing enteropathy may develop as a complication of a wide spectrum of diseases. Three cases of giardiasis that presented with acute onset of hypoalbuminemia were documented, and resolution of protein loss after treatment was also confirmed. Thus, chronic enteric infections should be considered as an etiology of severe intestinal protein loss, particularly in children.

Key Words: giardiasis, protein-losing enteropathy, hypoalbuminemia

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Protein-losing enteropathy (PLE) is characterized by excessive loss of protein through the gastrointestinal (GI) tract, either because of systemic or GI disorders.[1] The protein loss in PLE is nonselective but is usually detected as hypoalbuminemia because of the slow turnover rate of albumin. In cases of severe hypopro-

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teinemia, the clinical picture may be complicated by ascites, pleural and/or pericardial effusion and edema and may also be associated with increased risk of infections.

Giardia lamblia, a protozoan parasite, is one of the most common causes of diarrheal disease and is relatively prevalent in developing countries where sanitary conditions are poor.[2] Giardiasis may present with a wide spectrum of clinical manifestations. However, selective PLE has rarely been documented in children with chronic *Giardia* infection.[3–5] This study reports 3 children who presented with severe hypoalbuminemia and intestinal protein loss in association with endoscopic and histopathologic evidence of giardiasis, with resolution after treatment.

PRESENTATION OF 3 CASES

Case 1 involved a previously healthy, 13-month-old boy with watery diarrhea and intermittent vomiting for 3 weeks and swelling of the face and abdomen for 1 week. Case 2 involved a 14-month-old girl who was referred to our hospital with suspected nephrotic syndrome. She had diarrhea, facial swelling and a distended abdomen for 2 weeks. Case 3 involved a 19-month-old boy with vomiting, diarrhea and swelling of the abdomen for 10 days before admission. Height-for-age and weight-for-height Z scores in case 1 were −0.6 and 0.95, respectively. Mild acute malnutrition was identified in cases 2 and 3 based on weight-for-height Z scores of −1.1 and −1.4, respectively. Physical examination of all 3 patients revealed pale skin, generalized edema and a distended abdomen without ascites or organomegaly. Laboratory results were similar, and all 3 patients had anemia, hypoproteinemia and hypoalbuminemia (Table 1). Biochemical examinations and repeated urine analysis excluded proteinuria and hepatic dysfunction, but serum vitamin B12, vitamin D and ferritin levels were lower than normal in all patients. Serum immunoglobulin levels were within normal limits, and sweat chloride tests and serology for celiac disease did not show any abnormality. Stool cultures failed to reveal pathogenic organisms in all patients. Although *Giardia* cysts and trophozoites were only detected on microscopic examination of the stool in case 3, stool analyses for *Giardia* antigen were repeatedly positive in all 3 patients. Fecal α-1 antitrypsin testing of stool samples was consistent with PLE in cases 2 and 3, but this test could not be performed in case 1. Upper GI endoscopy was performed in all patients to evaluate the intestinal mucosa. In case 1, multiple small erosions were observed in the duodenum, and duodenal biopsies showed villous flattening and significant inflammatory cell infiltration, mostly composed of lymphocyte and plasmocytes in the lamina propria (Figure 1A). *Giardia* trophozoites were detected by direct microscopic examination of duodenal aspirate. In case 2, examination of the upper GI tract revealed no mucosal abnormality, but histopathologic examination of duodenal biopsies identified villous clubbing and patchy lymphoplasmacytic and eosinophilic inflammation. Upper GI endoscopy showed edematous duodenal mucosa in case 3, with subtotal villous atrophy and lymphoplasmocytic inflammation on duodenal biopsy.

TABLE 1. Albumin Levels at Admission and at the 6th Month of Follow-Up

	At **A**dmission (g/d**L**)	At the 6th **M**onth (g/d**L**)
Case 1	1.3	3.8
Case 2	1.7	4.0
Case 3	1.9	3.9

Treatment and Follow-Up

On admission, intravenous albumin infusions were administered because of symptomatic severe hypoalbuminemia in all 3 patients. Metronidazole 20 mg/kg/day for 15 days was commenced in all patients. Dietary modification with high protein content was recommended, and vitamin B12, vitamin D and iron were also supplemented. After metronidazole treatment, signs, symptoms and laboratory findings were found to be dramatically improved. The first and second cases were reevaluated with upper GI endoscopy 3 months after cessation of treatment, and histopathologic examination demonstrated resolution of previous findings (Figure 1B). All patients have been asymptomatic, and their laboratory examinations have been normal for the last 12 months of follow-up (Table 1).

DISCUSSION

PLE is characterized by severe loss of serum protein into the intestinal lumen; therefore, hypoproteinemia is the most prominent clinical finding.[1] The differential diagnosis of hypoproteinemia also includes inadequate dietary intake, impaired synthetic capacity of the liver, proteinuria, lymphatic obstruction and widespread inflammation of vasculature, as in sepsis. Two of our patients had mild malnutrition, but this finding could not account for severe hypoalbuminemia. Fecal α-1 antitrypsin is a noninvasive test for the diagnosis of PLE[6] and was found to be higher than normal in 2 of our 3

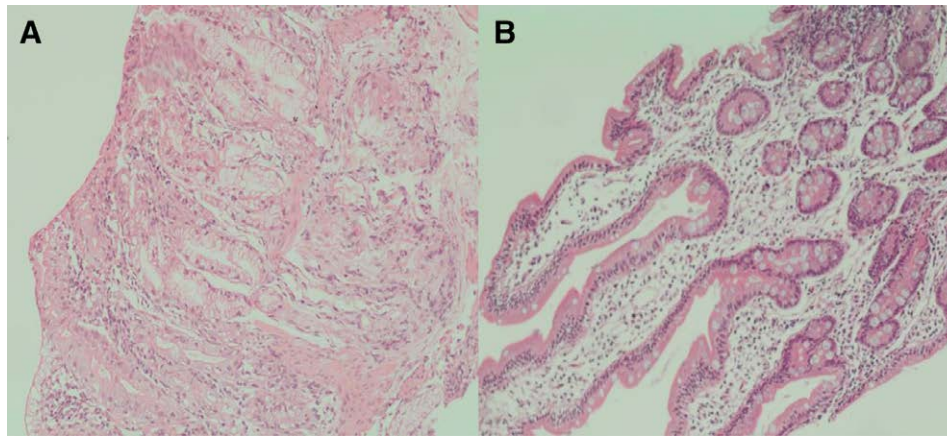


FIGURE 1. Histopathologic findings of duodenal mucosa before and after the treatment for giardiasis. A: Loss of intestinal villi in duodenal biopsies before treatment. B: Normal duodenal villi structure after the treatment.

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patients. Thus, PLE was suspected because of concomitant GI signs and symptoms in the absence of proteinuria or liver dysfunction.

Various causes of PLE are mostly secondary to enteric lymphatic obstruction, cardiac disorders associated with increased systemic venous pressure and mucosal inflammation, in association with defective enterocyte barrier function.[6] Several GI pathogens (*Strongyloides stercoralis*, *Salmonella, Shigella*, rotavirus) including *G. lamblia* can damage the intestinal mucosa and impair the enterocyte barrier function by disrupting the epithelial brush border and tight junctions. Giardiasis usually presents with mild symptoms such as abdominal pain and chronic diarrhea in immunocompetent individuals. However, children who are repeatedly exposed to contaminated water sources or those who are immunocompromised may present with a variety of symptoms, ranging from malabsorption to severe villous atrophy. Diarrhea was the predominant complaint in our patients. Abdominal distention and edema were other findings compatible with malabsorption. Anemia, vitamin deficiencies and low serum ferritin level may be associated with inadequate dietary intake or malabsorption, or both. Iron deficiency is a known complication of giardiasis; consistent with the literature, severe anemia was observed in all 3 cases.[7]

Examination of concentrated, iodine-stained wet stool preparations and modified trichrome-stained permanent smears has been the conventional approach to the diagnosis of *Giardia* infection. However, intermittent excretion of cysts and trophozoites in feces might hinder the detection of parasites despite multiple stool examinations. Therefore, molecular tests based on enzyme-linked immunosorbent assay for detection of *Giardia* antigens have high sensitivity and specificity and should be considered for initial diagnostic testing. One study compared microscopic examination of stool samples for parasites with stool antigen tests, and the sensitivity of the tests was reported as 83% and 95%, respectively.[8] Repeated stool examination for *Giardia* antigen was positive in all of our cases, and trophozoites were recognized on microscopic examination of feces in case 3. The reported sensitivity of stool examination is 85%, and repeated examinations contributed to the accuracy, while the microscopic analysis of duodenal aspirate for *Giardia* trophozoites had a sensitivity of 44%.[9] As a routine endoscopic procedure in our unit, duodenal aspirates are collected for microscopic analysis for *Giardia* trophozoites, which were detected in case 1. Identification of trophozoites within small intestinal biopsy specimens may require careful examination of multiple microscope fields, while direct sampling of duodenal aspirate in the same patient may improve sensitivity.[10]

Giardiasis is a known cause of non-celiac villous atrophy.[2,3] Consistent with the literature, duodenal biopsies of all cases in our study demonstrated villous abnormalities such as total or subtotal atrophy of intestinal villi and lymphoplasmocytic inflammation in the lamina propria of the intestinal epithelium. After treatment, follow-up endoscopies performed in 2 of the 3 patients demonstrated complete resolution of histopathologic findings. Thus, we clearly identified a causal association between PLE and giardiasis based on symptom resolution, in addition to laboratory and histopathologic findings. To our knowledge, this is the second published report demonstrating histopathologic recovery after treatment of *Giardia* infection.[3]

In conclusion, *Giardia* is a common cause of diarrhea, particularly in developing countries. It may rarely be complicated by PLE in association with common GI symptoms. Giardiasis is a treatable cause of PLE, which can be associated with severe comorbidities. Early recognition and treatment of *Giardia* infection presenting with PLE results in rapid clinical, laboratory and histopathologic recovery, thus, preventing malnutrition, particularly in growing children.

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MULTIFOCAL SKIN TUBERCULOSIS

Report of A Case

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Abstract: Tuberculosis (TB) is a severe problem in underdeveloped countries. Cutaneous TB is rare and often goes unrecognized. We report a Pakistani child with multifocal cutaneous and pulmonary TB. Microbiologic diagnosis was obtained when the abscesses were biopsied. Four-drug therapy produced rapid improvement of the lesions. A high level of suspicion must be maintained when evaluating children from countries at risk.

Key Words: tuberculosis, skin, bone, lung, mycobacterium

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Tuberculosis (TB) is a major global health problem. According to the World Health Organization,[1] one third of the world's population is thought to be infected with TB. In 2016, there were 10.4 million cases of active TB resulting in 1.3 million deaths. More than 95% of deaths occurred in developing countries. On the other hand, TB has become uncommon in high-income countries, especially among children. With the recent waves of migration, however, old diseases are reappearing and attention is required not to overlook the diagnosis of the atypical forms of TB. We report here the case of an adolescent girl who developed a multifocal form of cutaneous TB in addition to pulmonary involvement.

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