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CASE REPORT

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Recurrent paralytic ileus associated with strongyloidiasis in a patient with systemic lupus erythematosus

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Abstract We present an interesting case of recurrent paralytic ileus due to strongyloidiasis in a woman who was being treated with corticosteroids and immunosuppressants for systemic lupus erythematosus (SLE). She was also a carrier of human T-cell leukemia virus type I. She had a history of strongyloidiasis 8 years earlier. Recurrent episodes of paralytic ileus due to strongyloidiasis occurred during treatment of her SLE with corticosteroids. Ivermectin was given and improved the symptoms. This case shows that symptomatic strongyloidiasis can be induced in immunocompromised hosts by immunosuppressive therapy. It is important to rule out strongyloidiasis prior to starting immunosuppressive therapy in patients from endemic areas.

Key words Corticosteroids · Cyclophosphamide · Human T-cell leukemia virus type I (HTLV-I) · Paralytic ileus · Strongyloidiasis · Systemic lupus erythematosus (SLE)

Introduction

Strongyloidiasis is a disease of tropical regions, so the endemic areas in Japan are Okinawa and Amami. *Strongyloides stercoralis* infection is observed in 11.2% of the inhabitants of these regions.[1] Many of the symptomatic patients are considered to be immunocompromised hosts. Patients with strongyloides can develop ileus, protein-losing enteropathy, and diarrhea, especially when treated with immunosuppressants or corticosteroids, while severe strongyloidiasis is occasionally fatal as a result of systemic infection. We report an interesting case of strongyloidiasis in a woman from Okinawa. She had a history of strongyloidiasis 8 years earlier. When she was treated with corticosteroids for systemic lupus erythematosus (SLE), recurrent paralytic ileus occurred and was later revealed to be due to strongyloidiasis. Ivermectin was given and improvement of her symptoms was noted. Immunosuppressive therapy with steroids or chemotherapeutic agents may cause symptomatic strongyloidiasis in susceptible patients.

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Case report

A 54-year-old Japanese woman was admitted to Kitasato University Hospital for evaluation and treatment of lupus nephritis on February 2004. She had been born in Okinawa Prefecture. In 1976, she emigrated to Brazil and worked as a farmer. In 1986, she returned to Japan and lived in Kanagawa Prefecture as a housewife. From 1990, she noted episodes of abdominal fullness, but these improved without treatment. In April 1994 she visited a local hospital, suffering abdominal distension and pain for ileus.

Because she continued to have episodes of abdominal distension, she attended the Department of Gastroenterology at Kitasato University East Hospital in September 1994. Gastroduodenoscopy showed enteritis, and *Strongyloides* larvae were identified in mucosal specimens obtained by biopsy, so she was diagnosed as having paralytic ileus due to strongyloidiasis. In December 1994, she was treated with mebendazole (100 mg twice a day). Treatment was continued intermittently over about 8 months. After the completion of treatment, stool examination did not detect strongyloides.

In 2000 she visited a local hospital, with a respiratory tract infection. Blood tests were performed and thrombocytopenia was noted. She was referred to the Department of Rheumatology at Kitasato University Hospital. Systemic lupus erythematosus was diagnosed by polyarthritis and laboratory tests (positive for antinuclear antibodies and anti-DNA antibodies, as well as having pancytopenia). In 2001, her polyarthritis and pancytopenia worsened, so she

started treatment with prednisolone (PSL) at 15 mg/day. In February 2004 (the PSL dose was 8 mg/day), urinalysis revealed red blood cell casts and proteinuria. In September, she was admitted to our hospital for evaluation and treatment. Physical examination showed a middle-aged woman with a temperature of 36.0°C, heart rate of 62 beats/min, respiration rate of 14 breaths/min, and blood pressure of 158/92 mmHg. No pulmonary or abdominal abnormalities were found. She had noted a weight gain of 2 kg (her weight was 51.9 kg) and pretibial edema. The electrocardiogram and chest X-ray film were normal. On admission, laboratory tests showed a hemoglobin of 9.0 g/dl and a white blood cell count of 4600/μl (81.9% neutrophils, 12.1% lymphocytes, 2.0% eosinophils, and 4.0% monocytes). Urinalysis showed 3+ proteinuria and 2+ hematuria. Examination of the sediment showed 8–10 erythrocytes per high-power field, 5–10 leukocytes per high-power field, granular casts, and hyaline casts. She also had proteinuria (5.5 g/day), a total protein of 5.5 g/dl, serum albumin of 2.5 g/dl, serum creatinine of 0.8 mg/dl, and daily creatinine clearance of 54.7 ml/min. Stools were negative for occult blood and microscopy of a stool sample was not performed. The complement levels were normal: C3 was 71 mg/dl (normal: 76–160), C4 was 9 mg/dl (normal: 14–44), and CH_{50} was 19 IU/ml (normal: 25–45). Antinuclear antibody was positive at a titer of 1:1280 (both the homogeneous type and the speckled type). Anti-DNA antibody was also positive at 77 IU/ml, but HBs antigen and anti-HCV antibody were negative. Ultrasonography showed normal-sized kidneys and no ascites or pericardial effusion.

Percutaneous renal biopsy was performed 14 days after hospitalization, and was diagnosed as lupus nephritis (Class IV-S(A/C): active and chronic lesions: diffuse proliferative and sclerosing lupus nephritis in the 2003 classification of lupus nephritis). She was treated with methylprednisolone (mPSL) at 500 mg for 3 days, followed by prednisolone at 50 mg/day. On the 40th hospital day, her proteinuria decreased to 2 g/day and there was 1+ hematuria. Because of sustained proteinuria, she was treated with intravenous cyclophosphamide (500 mg) on the 47th hospital day. On the 68th hospital day, she developed vomiting. On examination, no bowel sounds were heard. Abdominal X-ray films showed an abnormal gas collection in a large and small bowel with niveau under the diagnosis of paralytic ileus (Fig. 1). Conservative treatment was provided (fasting, continuous suction through a nasogastric tube, and intravenous infusion). Her symptoms improved after gastric tube insertion, but stool examination was performed because there was a history of strongyloidiasis. Stools were positive for occult blood, and microscopic examination of a stool sample revealed *Strongyloides* larvae (Fig. 2A,B). On the 71st hospital day, gastroduodenoscopy showed duodenal inflammation, and biopsy revealed *Strongyloides* larvae in the mucosa. Paralytic ileus due to strongyloidiasis was diagnosed, and she was given 6 mg of Ivermectin on the 70th and 84th hospital days. Microscopic examination of a stool sample demonstrated no *Strongyloides* larvae on the 84th hospital day. Then it was noticed that her human T-cell leukemia virus type I (HTLV-I) antibody titer was >356.

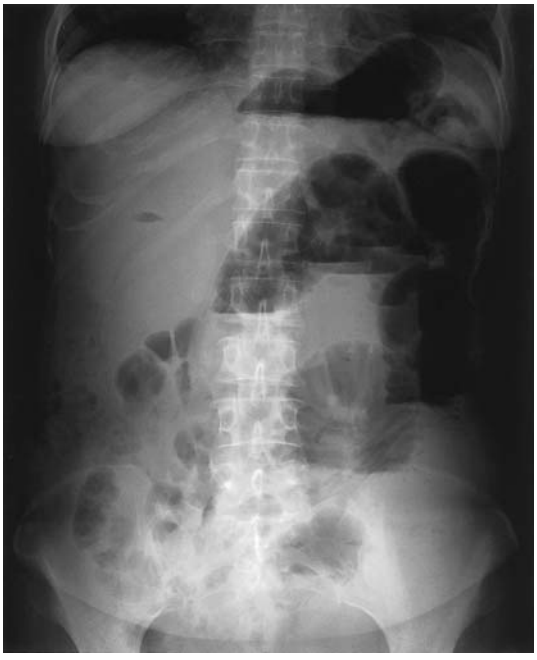

Fig. 1. X-ray film of the abdomen showed niveau of the small intestine, the so-called herring-bone sign

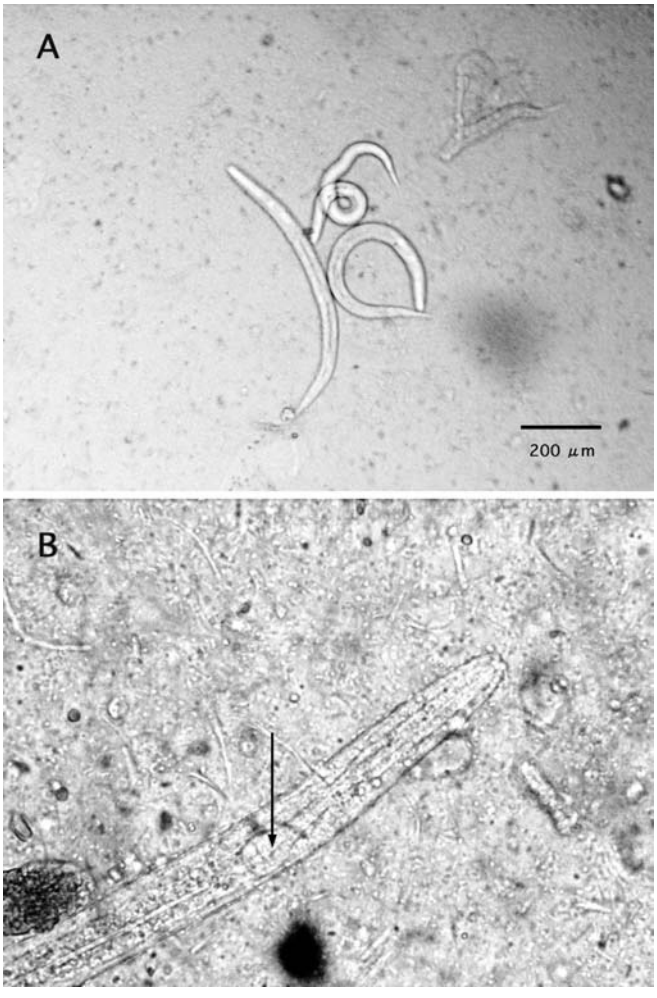

Fig. 2. A Rhabditiform larva of *Strongyloides stercoralis* separated from the stool of the patient. **B** The larva had a muscular esophageal structure, indicated by the *arrow*

Peripheral blood adult T-cell leukemia (ATL) cells were negative throughout the clinical course. We gave a second intravenous cyclophosphamide pulse (500 mg) on the 96th hospital day and microscopic examination of a stool sample subsequently demonstrated no *Strongyloides* larvae. On the 100th hospital day, she was discharged on PSL at 15 mg/day. Urinalysis showed 1+ proteinuria (0.7 g/day) and 1+ hematuria, while the sediment contained 1–5 leukocytes per high-power field. Other tests showed the following: total protein 5.4 g/dl, serum albumin 3.6 g/dl, serum creatinine 0.6 mg/dl, and daily creatinine clearance 74.8 ml/min. The C3, C4, and CH_{50} levels were 61 mg/dl, 14 mg/dl, and 28 IU/ml, respectively, and anti-DNA antibody was positive at 3 IU/ml. Since the patient's discharge from hospital, larvae have not been discovered in the stool.

Discussion

Strongyloidiasis is a parasitic infection caused by *Strongyloides stercoralis*, which is distributed widely in tropical and subtropical areas. South Kyushu and Okinawa are the regions where it commonly occurs in Japan, and it was reported that strongyloidiasis affects 11.2% of the inhabitants.[1] *Strongyloides stercoralis* has two parts to its life cycle: free-living and parasitic. Infectious filariform larvae invade percutaneously and travel via the blood or lymph to the lungs. After passing into the airways, the larvae are swallowed and then inhabit the mucosa of the duodenum and proximal jejunum. In addition, so-called autoinfection occurs when filariform larvae metamorphose in the bowel and reinfect the bowel. The infection thus continues throughout life or for many years with new generations of parasites owing to autoinfection. Disseminated strongyloidiasis can occur when the host becomes seriously ill.[2] To make a diagnosis of strongyloidiasis, the parasite should be detected in the stools or duodenal juice, or the ova should be found. In addition, endoscopic examination may allow diagnosis by detecting parasites in the duodenum, or by biopsy of atypical inflammatory changes of the jejunal mucosa.[3] In our present case, we were able to prove the diagnosis by stool examination and duodenal biopsy. Symptoms of strongyloidiasis are not specific, but diarrhea, loose stools, abdominal pain, malaise, and loss of weight are common.[2] In severe cases, paralytic ileus can develop. Paralytic ileus in our case may have been caused by massive intestinal infestation with *Strongyloides stercoralis*.[4]

There have been 25 reported cases of strongyloidiasis-related ileus (15 in Japan and 10 in foreign countries). The age at diagnosis was 2–82 years, with elderly and middle-aged (>50 years old) patients accounting for about half. There were 15 males and 10 females. Recurrent ileus was not reported overseas, but was found in 3/15 cases in Japan. The risk factors for strongyloidiasis include (1) immunosuppressive therapy (chronic steroid administration), (2) malignancy, (3) immune deficiency (malignant lymphoma, adult T-cell leukemia/lymphoma, etc.),[5] (4) organ transplantation, (5) surgery, (6) pregnancy/delivery, (7) nutritional deficiency and chronic alcoholism, and (8) other causes (diabetes mellitus, SLE, anti HTLV-1 antibody).[6] Among these factors, immunosuppressive therapy was performed for 4/15 cases in Japan and 4/10 overseas. In addition, HTLV-I antibody was positive in 6/15 cases in Japan, but was negative (or not investigated) in the overseas cases. Okinawa is an endemic area for HTLV-I. Nakada et al. reported that 39% of patients with *Strongyloides stercoralis* infestation were positive for HTLV-I proviral DNA, and suggested that *Strongyloides* and HTLV-I-infected cells or HTLV-I itself may interact with each other, or that depression of cell-mediated immunity by HTLV-I allows the development of *Strongyloides* hyperinfestation.[7] Our patient was also seropositive for HTLV-I.

Systemic lupus erythematosus patients are immunocompromised hosts, but they rarely develop strongyloidiasis, and we found only 10 reports during our search of the literature (Table 1).[8–17] The duration of SLE before the onset of strongyloidiasis was variable (5 weeks to 12 years), but all of the patients reported therapeutic contents were using corticosteroids. Symptoms that resembled those of

Table 1. Case reports of *Strongyloides stercoralis* in patients with systemic lupus erythematosus

Sex	Age (years)	Disease duration	Therapy	Nematode search specimen	Outcome	Area	First author[Ref.]
F	18	NR	PSL 60 mg/day + IVCY 1 g/month	Stool, sputum	Survived	Australia	Potter[8]
NR	NR	3 y	NR	NR	Died	USA	Lemos[9]
F	38	2 y	PSL 20 mg/day	Blood vessel	Died	USA	Reiman[10]
F	67	1 y	PSL 15 mg/day	Sputum, stomach, intestines	Died	Japan	Setoyama[11]
F	44	12 y	NR	Sputum, duodenum, lymph node	Died	Argentina	Finkielman[12]
F	43	4 m	PSL	Sputum, stool	Died	USA	Livneh[13]
M	59	7 y	PSL 30 mg/80 mg (alternative day)	Stool, sputum	Survived	USA	Wachter[14]
F	43	2 y	PSL 30 mg/day	NR	Survived	USA	Webster[15]
M	66	5 w	PSL 120 mg/day	Jejunum	Survived	USA	Berger[16]
M	23	3 y	PSL 60 mg/day	Duodenum, stool	Survived	USA	Rivera[17]
F	51	4 y	PSL 35 mg/day	Duodenum, stool	Survived	Japan	Present case

Age, age at onset of disease; NR, not recorded; PSL, prednisolone; IVCY, intravenous cyclophosphamide; y, years; m, months; w, weeks

SLE were found occasionally, such as abdominal pain, respiratory failure, and cerebral disease. Accordingly, when we encounter such symptoms, we have to distinguish a flare-up of SLE disease activity from strongyloidiasis. The present patient was diagnosed as having active SLE and was treated with high-dose corticosteroids and intravenous cyclophosphamide pulse therapy. This treatment plus being an HTLV-1 carrier induced the development of strongyloidiasis.

Strongyloidiasis causes anemia, eosinophilia, hypocholesterolemia (due to abnormal fat absorption), and hypoalbuminemia (due to protein-losing enteropathy).[18] Anemia and hypoalbuminemia were found in our patient, but there is a possibility that these changes developed with increased SLE activity (lupus nephritis, etc.), and distinguishing the symptoms of SLE from strongyloidiasis is difficult. Although our patient had the nephrotic syndrome, her cholesterol level was lower at the time of hospitalization, so we cannot exclude the possibility of latent *Strongyloides stercoralis* infestation. On the other hand, eosinophilia is not found in serious cases[19] or cases treated with corticosteroids,[20] even if there is infestation with *Strongyloides stercoralis*. Because eosinophilia was not found in our case, it seems difficult to judge the presence or absence of *Strongyloides stercoralis* only on the basis of eosinophilia in patients on systemic steroid therapy.

In recent years, the occurrence of nephrotic syndrome due to strongyloidiasis itself has been suggested. Mori et al.[21] reported a nephrotic syndrome patient with eosinophilia who developed ileus, epigastralgia, and malabsorption due to strongyloidiasis. Percutaneous renal biopsy revealed minimal change nephrotic syndrome and the patient recovered with Thiabendazole treatment. In the present case, rather than strongyloidiasis, it seems likely that nephritis was a symptom of SLE, because it developed along with markers of increased disease activity such as an increased anti-DNA antibody titer, hypocomplementemia and renal pathological findings.

As pharmacotherapy for this patient, we used Ivermectin (6 mg) orally twice every 2 weeks. No *Strongyloides* larvae were seen on microscopic examination of stool samples after the first treatment on the fourth day. In recent years, oral Ivermectin has been increasingly used for strongyloidiasis,[22] but it is clear that its efficacy is lower in patients with a greater disease burden.[23]

In conclusion, our case emphasizes that immunosuppressed individuals treated with immunosuppressants should be assessed for possible parasite infestation by stool examination prior to starting therapy, if the patient was a resident or born in endemic areas.

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