CASE REPORT

Eosinophilia, a marker of asymptomatic *Strongyloides* infection, in a young patient with extrapulmonary tuberculosis

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SUMMARY

Strongyloides stercoralis infection is a common and neglected public health problem in many areas of the world. Here we report the case of a 21-year-old woman who emigrated from Cambodia to Japan and presented with swelling of the right supraclavicular region of 2 months' duration. She had no other symptoms. Tuberculous lymphadenitis was diagnosed based on a fine-needle aspiration biopsy of the right supraclavicular lymph node. The laboratory examination revealed mild eosinophilia (eosinophils 1348/ μ L). *S. stercoralis* and *Hymenolepis nana* were detected serologically and in faeces examination. This case demonstrates that clinicians should search for *S. stercoralis* infection in patients with tuberculosis who have epidemiological risk factors and/or laboratory signs of eosinophilia, even if other symptoms and signs of helminths infection are less obvious.

BACKGROUND

Strongyloides stercoralis infection is a common and neglected public health problem in Latin America, sub-Saharan Africa and South-east Asia.¹ The clinical importance of *S. stercoralis* infection is related to the unique ability of the infecting organism to reproduce and persist within its host for decades. In people with T cell immune deficiencies, *S. stercoralis* causes hyperinfection syndrome, severe disseminated disease and, therefore, a high mortality.¹ However, asymptomatic *S. stercoralis* infection is difficult to diagnose because of the lack of clinical signs and symptoms, and the low sensitivity of a faeces examination.²

CASE PRESENTATION

A 21-year-old woman who emigrated from Phnom Penh, Cambodia, to Japan 3 months earlier presented with a swelling in her right supraclavicular region of 2 months' duration. She had slight pain for a few weeks in the area of the swelling, but it abated without any medication. She had no other symptoms. She had moved to Japan to work in a sewing factory. Because she had experienced difficulty in visiting a health facility in Japan, her guardian took her to our clinic shortly after she had swelling in her neck. She had no relevant medical or allergic history. She did not have fever, cough, dyspnoea, abdominal pain, diarrhoea or a history of taking any medication.

INVESTIGATIONS

On physical examination, she was alert. Her body temperature was 36.7°C, blood pressure was 121/76 mm Hg, respiratory rate 18 breaths/min and her initial oxygen saturation 99% at room air. The respiratory and abdominal examinations were normal. Remarkable findings included a hard swollen lymph node in the supraclavicular region. A chest X-ray showed no abnormality in the lungs. The neck, thoracic and abdominal plain CT scans were also normal, except for a mass with a maximum diameter of 44 mm in the right supraclavicular region. Enhanced MRI revealed a mass with ring enhancement, a septal wall structure and an internal necrotic change. The laboratory examination results included mild eosinophilia (eosinophils 1348/ μ L). HIV (ELISA) and human T-cell leukemia virus-1 (chemiluminescent enzyme immunoassay) screening tests were negative.

Fine-needle aspiration biopsy of the right supraclavicular lymph node was performed, and the specimen was subjected to Ziehl-Neelsen staining, culture and a PCR test. All were positive for *Mycobacterium tuberculosis*. Ziehl-Neelsen staining of a sputum specimen was negative. The patient was, therefore, diagnosed with tuberculous lymphadenitis. The aetiology of the eosinophilia was not known, and a differential diagnosis was established.

DIFFERENTIAL DIAGNOSIS

- ▶ parasitic infections primarily with helminths (strongyloidiasis, schistosomiasis, ascariasis, trichinosis, hookworm and filariasis)
- ▶ medication-associated eosinophilia
- ▶ atopic dermatitis
- ▶ hypereosinophilic syndrome
- ▶ asthma
- ▶ eosinophilic granulomatosis with polyangiitis
- ▶ acute/chronic eosinophilic pneumonia
- ▶ episodic angioedema with eosinophilia
- ▶ eosinophilic oesophagitis
- ▶ tumour-associated eosinophilia

A parasitological aetiology was evaluated by microscopic examination of a direct faecal smear and by formalin–ethyl acetate sedimentation, which showed several rhabditiform larvae of *S. stercoralis* and *Hymenolepis nana* (figures 1 and 2). *S. stercoralis* infection was confirmed serologically using a *S. stercoralis*-specific IgG antibody (SRL, Nagasaki, Japan), which yielded positive results.

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Figure 1 Microscopic view of *Strongyloides stercoralis*.

Tuberculous lymphadenitis with asymptomatic intestinal parasitic disease was diagnosed given the absence of a medication history and the definitive results of the stool and serological examinations. Other systemic diseases associated with eosinophilia and affecting the lung, skin and vascular system could be ruled out.

TREATMENT

Before the patient was treated for tuberculosis (TB), she was administered ivermectin, praziquantel and albendazole. Ivermectin is considered to be the most effective treatment for *S. stercoralis* infection.³ After 10 days, which included two administrations of ivermectin, her faeces examination was normal. Eosinophilia decreased from 1348 to 482 cells/ μ L after 10 days of treatment with the antiparasitic drugs. The patient was then started on a standard multiple-drug regimen for the treatment of TB (isoniazid+rifampicin+ethambutol+pyrazinamide) for a total recommended duration of 6 months.

OUTCOME AND FOLLOW-UP

After adequate treatment, the prognosis of the patient was generally good. The lymph node swelling diminished over a period of 2 months. A follow-up faecal examination (direct faecal smear and culture) after 2 months of treatment was also normal.

Figure 2 Microscopic view of *Hymenolepis nana*.

DISCUSSION

TB treatment and *S. stercoralis* hyperinfection

Previous reports of coinfection with TB and helminths are scarce. One involved a patient with miliary TB and *S. stercoralis* hyperinfection.⁴ That case illustrated that even in the immunocompetent host, chronic *S. stercoralis* infection can become an overt hyperinfection in the presence of TB. Another case of *S. stercoralis* hyperinfection occurred in a patient with extrapulmonary TB (pleural effusion) without any immunosuppressive risks except for TB.⁵ Corticosteroids are indicated for patients with extrapulmonary TB complicated by conditions such as meningitis, pleural effusions with severe respiratory difficulties, lymph node hypertrophy with bronchial or arterial compressions, severe hypersensitivity to TB drugs and life-threatening paradoxical reactions at the beginning of TB treatment.^{6,7} Patients treated with immunosuppressive agents, especially corticosteroids, are at risk of developing fatal disseminated forms of *S. stercoralis* infection.¹ Therefore, clinicians should be aware of the differential diagnosis of *S. stercoralis* in patients with TB.

Difficulty in screening for *S. stercoralis*

In clinical settings, however, there are two major considerations in the screening and diagnosis of *S. stercoralis* infection.

First, because >50% of *S. stercoralis* infections remain asymptomatic,⁸ proper screening of potentially infected individuals before immunosuppressive treatment is essential, but it is seldom carried out.¹ In our patient, mild eosinophilia was the only indicator of a helminth infection. Eosinophilia is not of specific diagnostic value in the clinical setting, but it is the sole marker of chronic asymptomatic parasitic infection caused by *S. stercoralis*.⁹ In an area under the receiver operating characteristic curve analysis of the eosinophil count for discriminating patients with an anti-*Strongyloides* titre >1:80, the cut-off in a series of Italian patients was 0.829, with an optimal cut-off value of 700/ μ L to predict *S. stercoralis* infection.⁹

Second, the ideal diagnostic approach in patients with suspected *S. stercoralis* infection has yet to be defined. Among the several approaches currently available, their diagnostic precision is unclear.² Direct faecal smears and the Kato-Katz method are relatively simple but of low sensitivity. The Baermann method, Koga agar plate culture and ELISA are of moderate to high sensitivity, but they are not widely available and are time consuming.²

Nonetheless, in patients with epidemiological risk factors and/or laboratory signs of eosinophilia, clinicians should search for *S. stercoralis* infection, even if other symptoms and signs of helminths infection are less obvious.

Evaluation of the epidemiological risks for *S. stercoralis*

Epidemiological prevalence data on *S. stercoralis* infection are available, but sparse.¹ In Southeast Asia, where the disease is highly endemic, infection rates of 17.5%, 23.7% and 26.2% have been reported in Cambodia, Thailand and Laos, respectively.¹ Only in Vietnam is the prevalence low (0.02%). Khieu *et al*¹ conducted a study of the prevalence of *S. stercoralis* infection in Northern rural Cambodia, based on the examination of two stool samples using the high-sensitivity Koga agar plate culture and Baermann methods.⁸ They found that *S. stercoralis* was a common intestinal parasite, with a prevalence of 44.7% of the examined population, whereas *H. nana* was detected in only 0.2%.⁸ These data suggest a very high risk for *S. stercoralis* infection in our patient.

In high-income countries, faecal contamination of the soil by *S. stercoralis* is rare, and the prevalence of infection is accordingly low.¹ However, *S. stercoralis* infection remains an issue for immigrants from endemic areas and for tourists visiting these countries.¹ Nonetheless, in high-income countries, there are several exceptions. For example, in Japan, epidemiological studies conducted in the Okinawa islands showed a moderate-to-high infection rate of 18.7% (95% CI 17.4% to 20.4%).¹ Other data on the population-based prevalence of *S. stercoralis* infection in other parts of Japan are lacking. In Australia, Aboriginal communities also have a high infection rate.¹⁰ Therefore, possible coinfection of TB and *S. stercoralis* infection should be suspected even in patients in high-income countries.

Learning points

- ▶ Immunosuppressive therapy, such corticosteroids, is a risk factor for *Strongyloides stercoralis* hyperinfection.
- ▶ Eosinophilia may be the sole marker of asymptomatic *S. stercoralis* infection.
- ▶ Even in immunocompetent hosts, the possibility of *S. stercoralis* coinfection should be considered in patients with TB.
- ▶ Knowledge and caution regarding the potential for *S. stercoralis* infection are essential even in high-income countries.

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Competing interests None declared.

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