### Title
- Eosinophilia, a marker of asymptomatic Strongyloides infection, in a young patient with extrapulmonary tuberculosis

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

**SUMMARY** *Up to 150 words summarising the case presentation and outcome (this will be freely available online)*

*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 1,348/µl). *S. stercoralis* and *Hymenolepis nana* were detected serologically and in feces examinations. This case demonstrates that clinicians should search for *S. stercoralis* infection in tuberculosis patients who have epidemiologic risk factors and/or laboratory signs of eosinophilia, even if other symptoms and signs of helminths infection are less obvious.

**BACKGROUND** *Why you think this case is important – why did you write it up?*

*Strongyloides stercoralis* infection is a common and neglected public health problem in Latin America, sub-Saharan Africa, and Southeast 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 feces examination [2].

**CASE PRESENTATION** *Presenting features, medical/social/family history*

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 complained of 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 complained of swelling in her neck. She had no relevant past medical or allergic history. She did not have fever, cough, dyspnea, abdominal pain, diarrhea, or a history of taking any medication.

**INVESTIGATIONS If relevant**

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 computed tomography scans were also normal, except for a mass with a maximum diameter of 44 mm in the right supraclavicular region. Enhanced magnetic resonance imaging revealed a mass with ring-enhancement, a septal wall structure and an internal necrotic change. The laboratory examination results included mild eosinophilia (eosinophils 1,348/µl). HIV (ELISA) and HTLV-1 (CLEIA) 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 polymerase chain reaction 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 etiology of the eosinophilia was not known and a differential diagnosis was established.

**DIFFERENTIAL DIAGNOSIS If relevant**

- Parasitic infections primarily with helminths (strongyloidiasis, schistosomiasis, ascariasis, trichinosis, hookworm, filariasis)
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- Medication-associated eosinophilia
- Atopic dermatitis
- Hypereosinophilic syndrome
- Asthma
- Eosinophilic granulomatosis with polyangiitis
- Acute / chronic eosinophilic pneumonia
- Episodic angioedema with eosinophilia
- Eosinophilic esophagitis
- Tumor associated eosinophilia

A parasitological etiology was evaluated by microscopic examination of a direct fecal smear and by formalin-ethylacetate sedimentation, which showed several rhabditiform larvae of *S. stercoralis* and *Hymenolepis nana* (Figure 1 and 2). *S. stercoralis* infection was confirmed serologically using a *S. stercoralis*-specific IgG antibody (SRL, Japan), which yielded positive results.

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 If relevant

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 feces examination was normal. Eosinophilia decreased from 1,348 cells/µl to 482 cells/µl after 10 days of treatment with the anti-parasitic 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 fecal examination (direct fecal smear and culture) after 2 months of treatment was also normal.

DISCUSSION Include a very brief review of similar published cases

**TB treatment and *S. stercoralis* hyperinfection**

Previous reports of co-infection 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 immuno-competent host chronic *S. stercoralis* infection can become an overt hyperinfection in the presence of tuberculosis. Another case of *S. stercoralis* hyperinfection occurred in a patient with extrapulmonary TB (pleural effusion) without any immuno-suppressive 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 TB patients.

**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 helminths
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* titer >1:80, the cut-off in a series of Italian patients was 0.829, with an optimal cut-off value of 700/µl 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 fecal 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 epidemiologic 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%) [1]. Khieu et al. 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 *Hymenolepis 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, fecal 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% confidence interval: 17.4–20.4%) [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 co-infection of TB and *S. stercoralis* infection should be suspected even in patients in high-income countries.

**LEARNING POINTS/TAKE HOME MESSAGES 3 to 5 bullet points – this is a required field**

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 immune-competent hosts, the possibility of *S. stercoralis* co-infection should be considered in TB patients.

Knowledge and caution regarding the potential for *S. stercoralis* infection are essential even in high-income countries.

**REFERENCES Vancouver style (Was the patient involved in a clinical trial? Please reference related articles)**


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**FIGURE/VIDEO CAPTIONS** *figures should NOT be embedded in this document*

- Figure 1. Microscopic view of *Strongyloides stercoralis*
- Figure 2. Microscopic view of *Hymenolepis nana*

**PATIENT’S PERSPECTIVE** *Optional but strongly encouraged – this has to be written by the patient or next of kin*

- Not applicable.

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