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Case Report

Immunoserologically Diagnosed *Strongyloides*-Pneumonitis with Pleural Effusion and Eosinophilia

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Strongyloidiasis caused by *Strongyloides stercoralis* is one of the commonest intestinal helminthiases in warm climates. Because of the migration route of the parasite, the respiratory tract is, next to the digestive tube, most directly and severely affected by *S. stercoralis* infection (Grove, 1989). While pulmonary involvement is minimal in light infections in immunocompetent hosts, severe pulmonary damage can occur either in heavy infections in competent hosts or severe, disseminated infections in compromised hosts. Therefore, respiratory symptoms are usually observed transiently in the early stage of massive infection or in the late stage of severe cases due to auto-infection and/or dissemination (Grove, 1989). In this paper we describe an unusual case of pulmonary strongyloidiasis diagnosed only by immunoserological methods. The patient suffered from pneumonitis with pleural effusion for over a month with increasing eosinophilia but never showed abdominal symptoms. Repeated faecal and sputum examinations were all negative for *S. stercoralis* larvae or other parasite eggs throughout the course of the disease.

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Case Report

The patient was a 51 year-old house wife born and grown up in Nichinan-City, Miyazaki, Japan. She has never been abroad. On 18 August 1994, she visited a primary physician because of high fever and cough. In spite of treatment with antibiotics her symptoms turned worse and pneumonitis was suspected by chest radiogram, so that she was transferred to a regional hospital on 13 September for further work-up. On the time of admission, total white blood cell was 12310/mm^3 with 21.0% eosinophils. C-reactive protein (CRP) was 14.9 mg/dl. Other laboratory data related liver and kidney functions were within normal range. The patient was negative for antibodies to human T-cell leukemia virus type-1 (HTLV-1). Chest radiogram (Fig. 1) and computed tomogram (CT: Figs. 2–5) showed bilateral pleural effusion and multiple infiltrations predominantly in the left lung. From these observations, she was strongly suspected to be infected with helminth parasites. Because neither parasite eggs nor larvae were detected by repeated stool examinations, her serum was sent to the Department of Parasitology, Miyazaki Medical College for immunoserological examination. By a multiple-dot ELISA test, the patient's serum and pleural effusion showed positive reaction against *Strongyloides ratti* antigen with weak cross reaction against other nematode antigens (Fig. 7). The reaction patterns of the patient's serum and pleural effusion were essentially identical with those of the sera obtained from

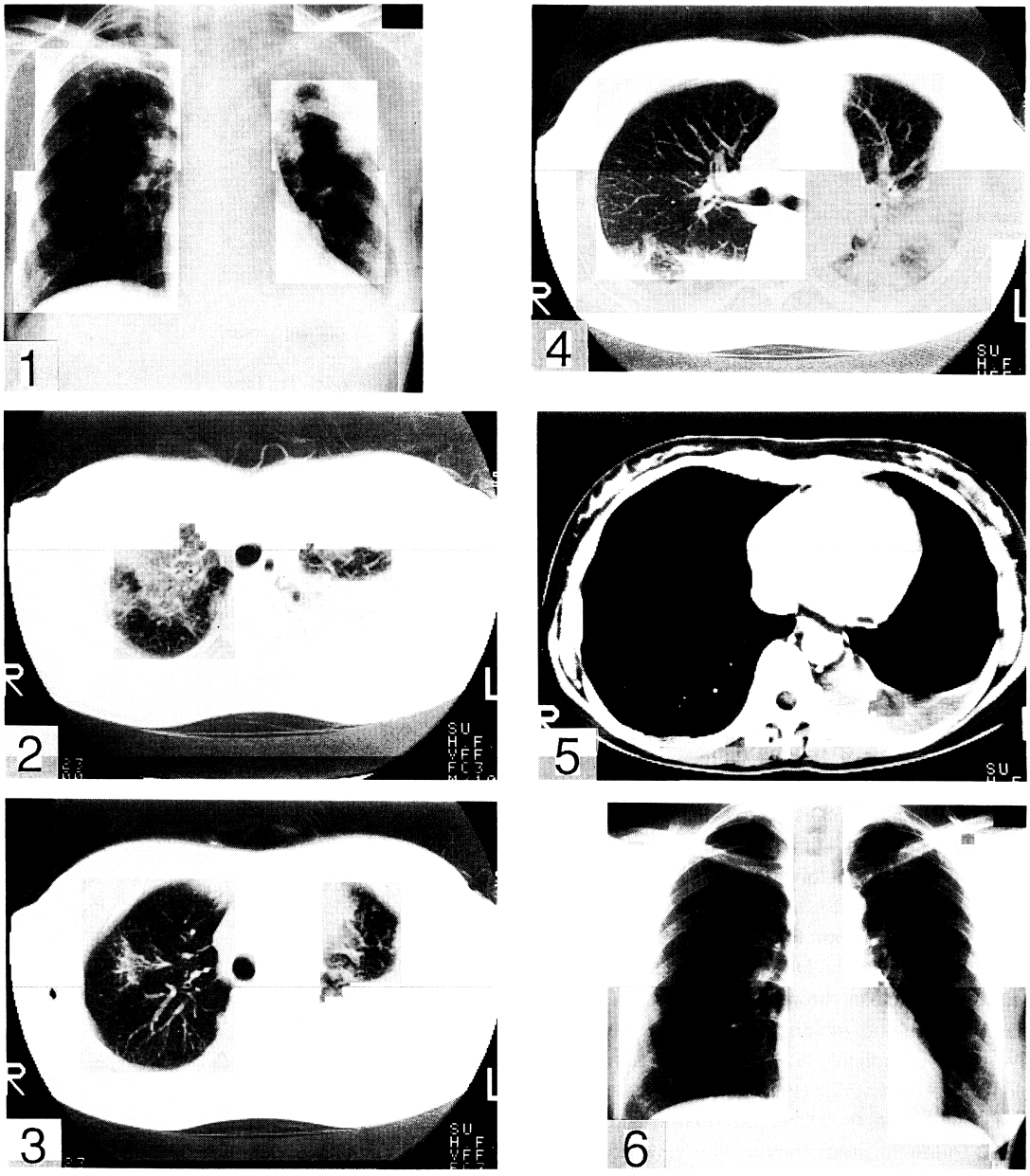

Fig. 1 Chest radiogram at the time of admission showing bilateral multiple diffuse infiltrations predominantly on the left lung field.

Figs. 2–5 Computed tomogram at the time of admission showing multiple diffuse infiltrations (Figs. 2–4) and bilateral pleural effusion (Fig. 5).

Fig. 6 Chest radiogram one month after chemotherapy. Note completely normalized appearances.

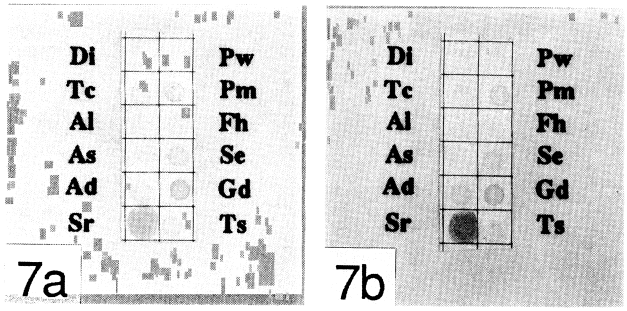

Fig. 7 Multiple-dot ELISA of the patient's serum (a) and pleural effusion (b) showing positive reaction against *S. ratti* antigen.
Di: *Dirofilaria immitis*, Pw: *Paragonimus westermani*, Tc: *Toxocara canis*, Pm: *Paragonimus miyazakii*, Al: *Ascaris lumbricoides*, Fh: *Fasciola hepatica*, As: *Anisakis simplex*, Se: *Spirometra erinacei*, Ad: *Ancylostoma duodenale*, Gd: *Gnathostoma doloresi*, Sr: *Strongyloides ratti*, Ts: *Trichinella spiralis*
Each spot was blotted with 1 μg/μl antigen (crude extract in phosphate buffered saline) and the sheet was blocked by incubating with 1% casein/Tris buffer. The sheet was incubated with 1:200 diluted patient's serum or pleural effusion at 37°C for 30 min, washed, and then incubated with peroxidase-labeled rabbit anti-human IgG at 37°C for 30 min. Peroxidase was detected using H_2O_2 and 4-chrolo-1-naphthol.

confirmed cases of strongyloidiasis (kindly supplied by Prof. Y. Sato, Department of Parasitology, the University of Ryukyus, Okinawa). She was treated successfully with albendazole (400 mg/day for 3 days from 7 October and 21 October), which was kindly supplied as an orphan drug distributed from the Project Team for the Development of the Treatment of Tropical Diseases, Ministry of Health and Welfare, Japan, through the courtesy of Prof. Y. Sato. About one month after the treatment, her symptoms completely disappeared with normalization of chest radiogram (Fig. 6) and peripheral blood cell counts (Fig. 8). During admission and subsequent follow-up study, larvae were never detected by repeated stool examinations in direct smear, AMS-III method, filter paper culture, and the most sensitive agar culture method. Nor were the larvae found in the sputum throughout the period examined. Further follow-up is now undergoing in our laboratories.

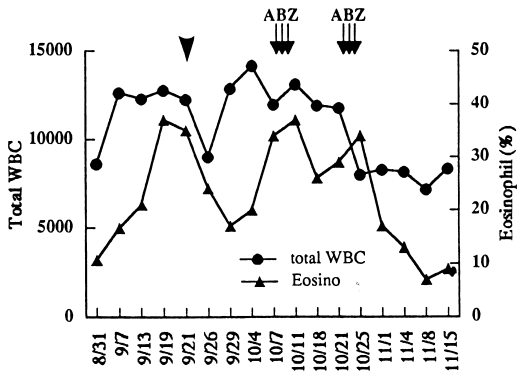

Fig. 8 Time course of white blood cell count and eosinophilia of the patient.
ABZ: albendazole, arrow head: time of immunoserological diagnosis.

Discussion

Because of the complicated life cycle of the parasite, strongyloidiasis is a systemic disease, though the mature adult is an intestinal nematode. Since filariform larvae migrate through the lungs as part of their life cycle, pulmonary complications should occur during the course of *S. stercoralis* infection. Strongyloidiasis is considered as an op-

portunistic infectious disease where the severity of the infection reflects host's immunological status. In immunocompetent hosts infestation can remain asymptomatic for years, and pulmonary complications are rather considered as the signs of overwhelming infection in the compromised host (Berger *et al.*, 1980; Bruno *et al.*, 1982; Shiroma *et al.*, 1990). Surprisingly, the patient reported here had no past history of serious illness nor had been treated with immunosuppressive drugs. Furthermore, parasite larvae were never detected by repeated stool examinations during admission or subsequent follow-up studies. Therefore, it seems quite probable that the patient was immunocompetent and that she had a massive infection immediately before the respiratory symptoms had first appeared.

In Japan, the Satsunan-Islands including Amami and Ryukyu Archipelagos have been known as the heavily endemic area. Even nowadays, the prevalence of strongyloidiasis in Okinawa Prefecture, covering the Ryukyu Archipelagos, is estimated to be 5–10% among the middle and upper-age brackets of the inhabitants (Sato 1986; Shiroma *et al.*, 1990). Although Miyazaki Prefecture was an endemic area of strongyloidiasis in the 1940s to 1950s, the prevalence at that time was less than 1% (reviewed by Tanaka, 1962) and further surveillance has never been carried out since that time. Since the patient has never been abroad nor had lived in heavily endemic areas, and since she showed no sign of immunosuppression, she was presumably infected recently somewhere in Miyazaki Prefecture. If this case were in fact caused by *S. stercoralis*, strongyloidiasis is still endemic at least in the southern part of Miyazaki Prefecture.

In Okinawa Prefecture over 50% of the strongyloidiasis patients were found to be infected concurrently with HTLV-1 (Nakada *et al.*, 1984) and this parasite was assumed as a leukemogenic co-factor of adult T-cell leukemia (Yamaguchi *et al.*, 1987). Although Miyazaki Prefecture, especially the area where the present patient is living, is also known as an endemic area of HTLV-1 (Tachibana *et al.*, 1984), the patient was negative for antibodies to HTLV-1, indicating that severe infection of the patient was not due to underlying concurrent infections with HTLV-1 viruses.

In the present study, the patient was diagnosed as strongyloidiasis by immunoserological examinations and diagnostic chemotherapy. In spite of vigorous pathological changes in the lungs, the parasite larvae were never detected in the stool or sputum specimens throughout the period examined. Tanaka (1958) reported that, after percutaneous infection with the infective larvae of *S. stercoralis* in human, rhabditiform larvae became detectable in the stool within a month or so. The exact reason why the larvae were not detected in the stool or sputum of the patient remains unclear. One possibility is that the causative parasite was *Strongyloides* spp. other than *S. stercoralis*. If this is the case, *S. fülleborni* should be considered because this species was frequently found in wild Japanese monkeys in the southern part of Miyazaki Prefecture (Horii *et al.*, 1982). Since *S. ratti* larval antigen was used for the dot ELISA test, further determination of the exact species of the causative parasite is necessary. Another possibility is that the patient might have an unnoticed infection with *S. stercoralis* in the past and became resistant to challenge infection. In experimental infection with *S. ratti* in rats (Moqbel, 1980), severe inflammatory response predominated by eosinophil infiltration was observed in lungs after challenge infection.

The patient was effectively cured by albendazole. Recently Shikiya *et al.* (1992) reported that, against *S. stercoralis*, ivermectin was superior to benzimidazole derivatives. At the present, both albendazole and ivermectin are available only as orphan drugs. We urge the earliest evaluation of these drugs in the chemotherapy of strongyloidiasis.

In conclusion, we demonstrated that severe pulmonary complications could occur in the early stage of strongyloidiasis in immunocompetent hosts. Physicians as well as parasitologists should be aware of such cases.

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