

Case Report

## A Case of Overwhelming Strongyloidiasis Cured by Repeated Administration of Ivermectin

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*Strongyloides stercoralis* is an intestinal nematode which infects a large portion of the world's population especially in warm climates. Because of an opportunistic nature of the parasite, immunocompetent hosts with infection confined to the intestinal tract are often asymptomatic, or if any, have moderate abdominal pain, diarrhea, and other non-specific complaints. Normal life cycle of the parasite is augmented by autoinfection in compromised hosts resulting in hyperinfection syndrome (Grove, 1989). In the worst situation, excessive parasites invade into various tissues to cause disseminated strongyloidiasis (Matsui *et al.*, 1982). Hyperinfection and/or dissemination are frequently found in individuals having immunodeficiency due to defective T-lymphocyte function or in those treated with immunosuppressants (Grove, 1989). In Japan, vast majority of severe strongyloidiasis cases were found in the Ryukyu Archipelagos where strongyloidiasis and adult T-cell leukemia/lymphoma (ATLL) are both endemic (Nakada *et al.*, 1984; Fujita *et al.*, 1985). In this paper we describe a case of overwhelming strongyloidiasis found in Miyakonojyo City, Miyazaki Prefecture. The patient was originated from Yonaguni, the southmost island of the Ryukyu Archipelagos. Repeated administration of ivermectin was required to reach complete cure.

### Case Report

The patient was a 46 year-old house wife. She was born and grown up in Yonaguni, Yaeyama-Gun, Okinawa Prefecture, from 1948 to 1966, and then moved into Miyakonojyo City, Miyazaki Prefecture. She has never been abroad. The patient has a past history of strongyloidiasis, which was diagnosed and treated during her temporally visit to her home town in Okinawa in 1990. Regretfully, this past illness was clarified only after the present diagnosis was made. On October 1994, she was suspected to have cholelithiasis and visited a regional hospital. Body temperature rose up to 38.8°C. Muscular defence was noted on the right upper abdominal wall and the Blumberg's sign was positive. Abdominal ultrasonography revealed the presence of gall bladder stones. Laboratory data were remarkable; total white blood cell count: 16,300/mm<sup>3</sup> with 4% eosinophils, CRP: (++) . She admitted to the hospital 5 days later to receive surgical operation for cholelithiasis. The patient's serum was positive for antibodies to human T-cell leukemia virus type-1 (HTLV-1). The presence of gall bladder stones was confirmed further by oral-drip infusion cholangiography and endoscopic retrograde cholangio-pancreatography (ERCP). During ERCP, duodenitis was suspected. By gastrofiberscopic observations, numerous small granular lesions covered with white plaques were seen in the duodenal mucosa. While the patient had been receiving preoperative examinations, she developed anemia,

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body weight loss, diarrhea and protein losing gastroenteropathy, and these symptoms gradually turned worse. Neither tumor nor ulcer were noted by barium enema. By colonofiberscopy, colonic mucosa from the caecum to the half way of the ascending colon was edematous and minute erythematous lesions scattered on the mucosa. On the 38th day of admission, a laboratory examiner in the hospital found a parasite larvae in her urine sediments and

suggested to the attending physician to perform stool examination. In a stool specimen, he found numerous actively moving larvae, which were identified as the rhabditiform larvae of *Strongyloides stercoralis* (Fig. 1). Her serum as well as stool specimen were sent to the Department of Parasitology, Miyazaki Medical College, for confirmation of the diagnosis. By a multiple-dot ELISA test, the patient's serum gave positive reaction against

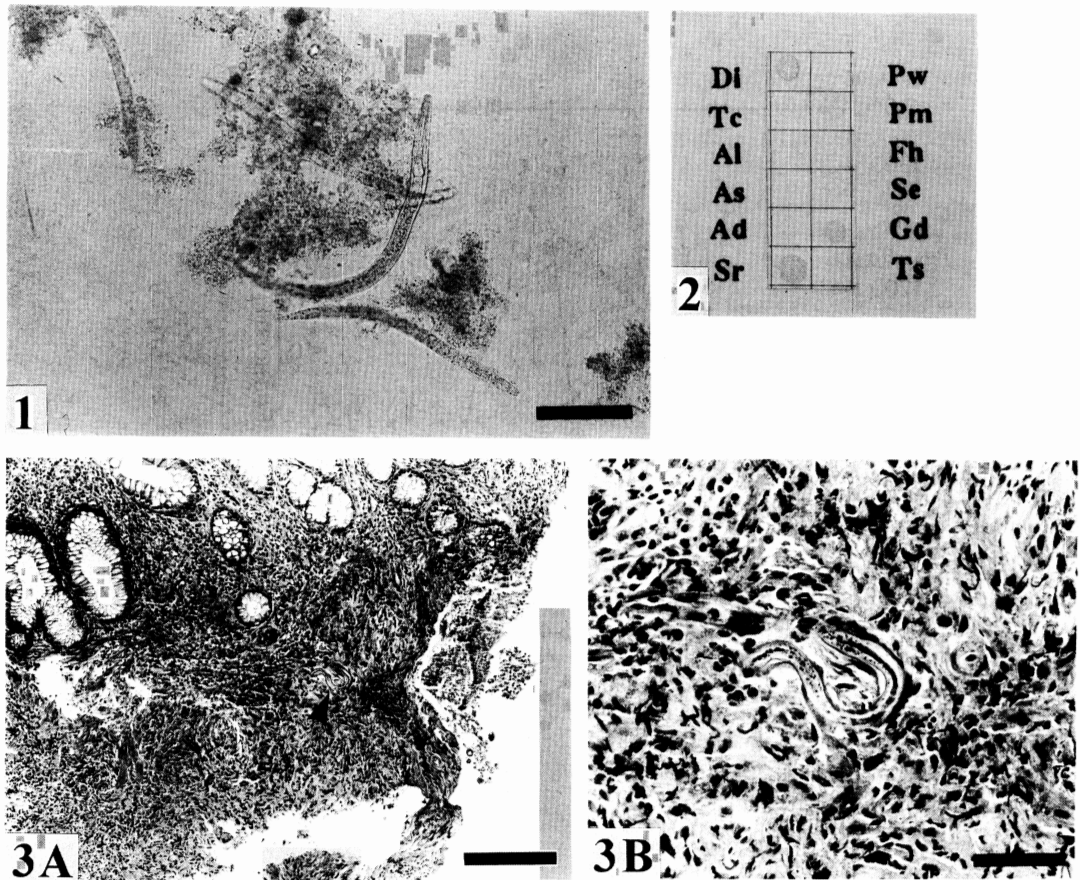


Fig. 1 *Strongyloides stercoralis* larvae found in the direct wet mount of the patient's stool.

Scale bar: 100  $\mu$ m.

Fig. 2 Multiple-dot ELISA of the patient's serum showing positive reaction against *S. ratti* antigen with moderate cross reaction against other nematode antigens.

Di: *Dirofilaria immitis*; Pw: *Paragonimus westermani*; Tc: *Toxocara canis*; Pm: *Paragonimus miyazakii*; Al: *Ascaris lumbricoides*; Fh: *Fasciola hepatica*; As: *Anisakis simplex* larvae; Se: *Spirometra erinacei-europei*; Ad: *Ancylostoma duodenale*; Gd: *Gnathostoma doloresi*; Sr: *Strongyloides ratti*; Ts: *Trichinella spiralis*.

Fig. 3 Granulomatous inflammation seen in the biopsied colonic mucosa (A) and its high-power view (B) showing longitudinal section of *S. stercoralis* larva (arrow head in A).

Scale bar: 200  $\mu$ m for (A), 50  $\mu$ m for (B).

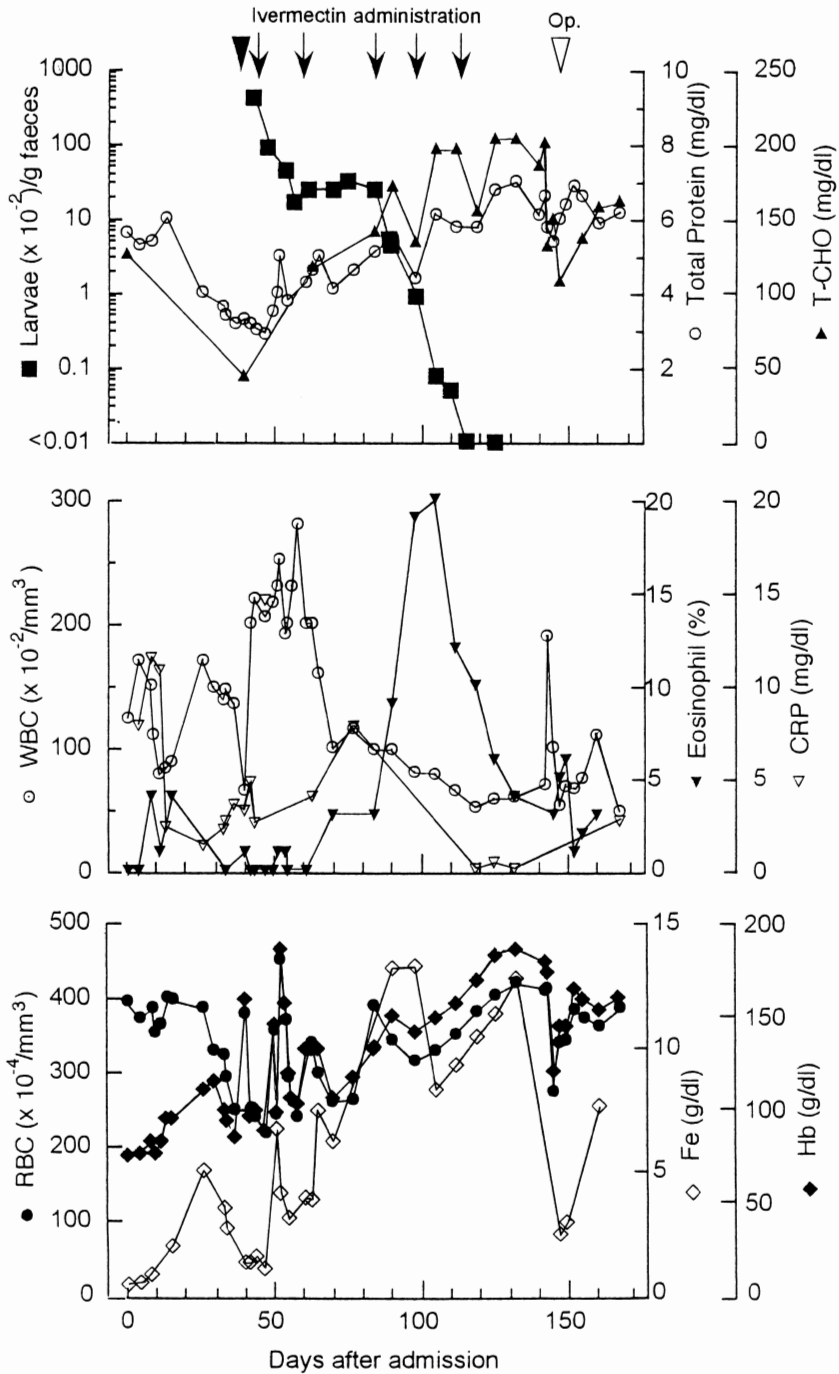


Fig. 4 Time course of larval output per gram of faeces (LPG), total protein, and total cholesterol (T-CHO) are shown in (A). Total white blood cell count (WBC), percentage of eosinophils, and CRP are summarized in (B). Red blood cell count (RBC), hemoglobin (Hb) and plasma iron (Fe) are given in (C). Arrows indicate the time of ivermectin administration. Closed arrow head; time of diagnosis; Open arrow head; time of surgical operation for cholelithiasis.

*Strongyloides ratti* antigen with moderate cross reactions against other nematode antigens (Fig. 2). Reexamination of the biopsied colonic mucosa revealed the presence of *S. stercoralis* larvae (Fig. 3) with massive inflammatory cell infiltration, which were overlooked at the first screening by the pathologist. The patient was treated with ivermectin (Mectizan®: 6 mg/tablet, Merk & Co., New Jersey, USA), which was kindly supplied from the Project Team for the Development of the Treatment of Tropical Diseases, the Ministry of Health and Welfare, Japan, through the courtesy of Prof. Y. Sato, Department of Parasitology, the University of Ryukyus, Okinawa, on 44, 59, 84, 98 and 112th days of admission. Soon after the start of chemotherapy, her symptoms gradually improved, and about one month after the treatment, her symptoms completely disappeared with normalization of laboratory data (Fig. 4). A transient leucocytosis due to neutrophilia and subsequent transient eosinophilia were observed after chemotherapy (Fig. 4). When the larvae became undetectable by stool examinations in direct smear, the completeness of the treatment was confirmed by a combination of AMS-III sedimentation concentration method, test tube filter paper cultivation technique, and the most sensitive agar culture method (Arakaki *et al.*, 1988).

### Discussion

Retrospectively, signs and symptoms of the present patient were typical for overwhelming strongyloidiasis. Although diarrhea, body weight loss, and protein-losing gastroenteropathy are the common features of severe infection with intestinal helminths, physicians in Japan nowadays often suspect such patients as having malignancy in gastrointestinal tracts and much attention is not paid for parasitic diseases. Similar problems were previously reported in cases of intestinal capillariasis (Nawa *et al.*, 1988) and metagonimiasis (Ichiki *et al.*, 1990). Together with the present case, all these cases should be diagnosed much more earlier by simple stool examination for parasite eggs/larvae as the first step of laboratory screening for diarrheal diseases.

Strongyloidiasis is considered as an opportunistic infectious disease where the severity of the

infection reflects host's immunological status. In immunocompetent hosts infestation can remain asymptomatic for years and overwhelming infection is seen in compromised hosts. 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). 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 (ATL) (Yamaguchi *et al.*, 1987). Although Miyazaki Prefecture is also known as an endemic area of HTLV-1 (Tachibana *et al.*, 1984), association of strongyloidiasis with ATL is rare probably because of the low prevalence of strongyloidiasis in this area (less than 1% in the 1940–50s; Tanaka, 1962).

Concerning chemotherapy for strongyloidiasis, pyruvium pamoate (Poquil®, Sankyo Pharmaceutical Co., Tokyo) and thiabendazole (Mintezol®, Merk/Ban-yu Pharmaceutical Co., Tokyo) has been used for long years. However, accumulated data in Okinawa Prefecture revealed that the efficacy of these drugs for the treatment of strongyloidiasis was significantly reduced by the concurrent HTLV-1 infection (Takara *et al.*, 1992; Sato *et al.*, 1992; Sato *et al.*, 1994). As alternatives for these drugs, applicability of albendazole (Toma *et al.*, 1993), mebendazole (Shikiya *et al.*, 1991a) and ivermectin (Shikiya *et al.*, 1991b) for the treatment of strongyloidiasis is currently examined in the endemic area with fairly successful results. The present patient was treated with ivermectin. Although administration of an ivermectin tablet (6 mg/tablet) at two weeks interval could reduce faecal larval excretion from the patient, additional three times of administrations at the same interval were required to reach complete cure. Even so, this drug seem to be highly effective with no or very minor side effects.

In conclusion, the present case highlighted the importance of stool egg/larva examination as the first step of laboratory examination for diarrheal diseases. Also, not only physicians but also surgical

pathologists and laboratory examiners should aware the presence of such cases.

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