

Fatal Meningoencephalitis Caused by Disseminated Strongyloidiasis

Hsien-Hsueh Chiu^{1,2} and Shung-Lon Lai²

Abstract- A middle-aged aboriginal man with a history of alcoholism and gastrectomy was diagnosed as having bacterial meningoencephalitis based on the typical clinical manifestations, laboratory findings, and treatment responses. During the recovery stage, he developed consciousness disturbance, seizures, severe diarrhea, and respiratory failure that led us to search for other possibility of the diagnosis. The eosinophilia and repeated stool examinations helped us to make the diagnosis of disseminated strongyloidiasis. In this patient the initial bacterial meningitis was followed by *S. stercoralis* hyperinfection. Despite treatment with strong antimicrobial agents, the patient died. This case could serve as a reminder to physicians to be alert for strongyloidiasis superimposed on bacterial meningitis.

Key Words: Strongyloidiasis, Meningoencephalitis, Hyperinfection syndrome

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INTRODUCTION

Strongyloidiasis caused by *Strongyloides stercoralis* is usually asymptomatic or mildly symptomatic in the gastrointestinal system. It may persist for many years but could occasionally progress to a disseminated state with a high mortality rate. Disseminated strongyloidiasis mostly occurs in immunosuppressed patients. The presenting symptoms may include abdominal pain and distension as well as pulmonary and neurological complications, or even septicemia and shock⁽¹⁾. In 1973, Neefe et al. were the first to document central nervous system (CNS) involvement with *S. stercoralis*⁽²⁾. Thereafter more cases of CNS involvement were reported, most

based on autopsy findings. However, among the 27 cases of strongyloidiasis ever reported in Taiwan⁽³⁾, no proven case of meningoencephalitis was documented. We report herein a case of meningoencephalitis caused by strongyloidiasis occurring in Taiwan. We emphasize the possible association of strongyloidiasis with bacterial meningitis.

CASE REPORT

A 60-year-old right-handed aboriginal man, who had a history of alcoholism and gastrectomy, was sent to a local hospital because of irrelevant speech in late September, 2004. After an episode of convulsive

From the Departments of ¹Chinese Medicine, and ²Neurology, Chang Gung Memorial Hospital, Kaohsiung, Taiwan.
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Reprint requests and correspondence to: Shung-Lon Lai, MD., Ph.D. Department of Neurology, Kaohsiung Chang Gung Memorial Hospital, No. 123, Ta-Pei Road, Niao-Sung Hsiang, Kaohsiung, Taiwan.
E-mail: carlos@adm.cgmh.org.tw

seizure, his consciousness deteriorated rapidly. He was transferred to our hospital on October 2, 2004. Elevated body temperature to 38.6°C, neck stiffness, and confusion were noted on admission. Neurological examination revealed that he was confused and delirious, but the pupils and oculocephalic responses were normal. The ability of movement was symmetrical in the limbs. The plantar responses were flexor on both sides. There was no clue of drug- or substance-related disorder and of hypoglycemia.

The serum laboratory study showed marked leukocytosis with a white blood cell count of $33.1 \times 10^9/L$. The differential count shows segments 90.5%, lymphocytes 4%, and eosinophils 1%. The biochemistry data showed an elevated GOT level of 71 U/L, otherwise (including renal function and serum electrolytes) were within normal limits. Mild infiltration of the right lower lung field was noted on the plain film. Brain computed tomography showed generalized cortical atrophy. Excessive beta activity was noted in the first EEG examination, which revealed no epileptiform discharge. The CSF showed marked pleocytosis of $2490 \times 10^6/L$ (neu-

trophil 64%, lymphocyte 20%, monocyte 16%), along with an elevated protein level of 5.19 g/L, and a low glucose level of 38 mg/L. CSF cytology revealed no tumor cells. Vancomycin and ceftriaxone were given under a tentative diagnosis of bacterial meningoencephalitis. Tuberculosis, cryptococcosis, herpes simplex, and Japanese B encephalitis were ruled out by microbiological investigations.

After treatment with antibiotics for three days, his clinical condition improved. He was no longer febrile and was able to communicate with his family in the aboriginal language. The follow-up CSF study showed improvement in pleocytosis ($40 \times 10^6/L$, neutrophil 55%, lymphocyte 37%, monocyte 8%), protein (2.77 g/L), and glucose (44 mg/L). Although the microorganism cultures from the blood, sputum, and CSF were all negative, the clinical pictures, laboratory findings and treatment responses supported the diagnosis of bacterial meningitis.

On October 7, excessive bile ran out from the nasopharyngeal tube, and severe diarrhea developed. Routine stool and KUB examinations showed nonspecif-

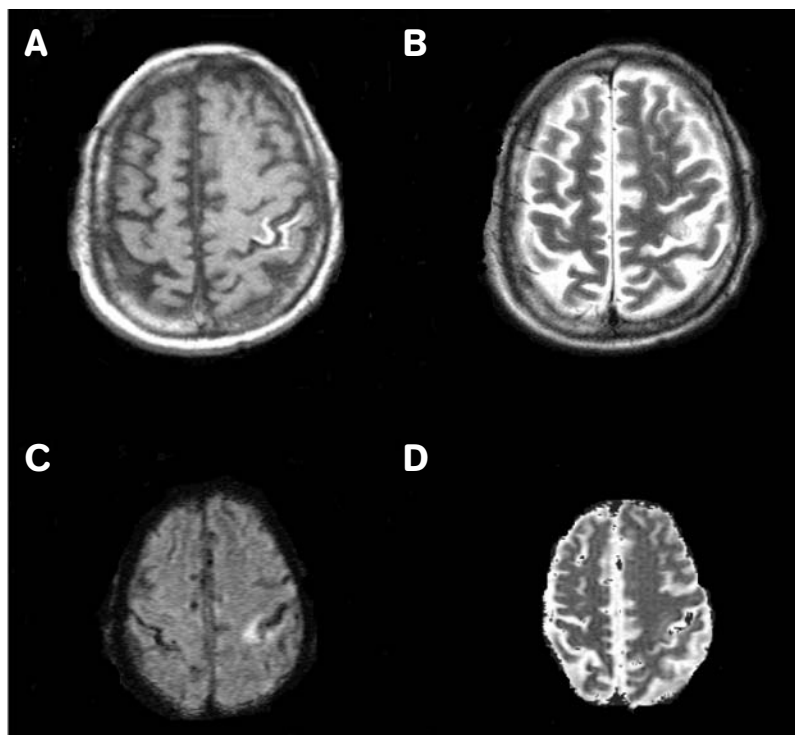


Figure 1. Brain MRI findings. The linear hyperintensities along left parietal cortical gyrus in T1-weighted image (A), in T2-weighted image (B), and diffusion-weighted image (C). Also note an hypointensity area with perifocal hyperintensity noted on the apparent-diffusion coefficient map (D).

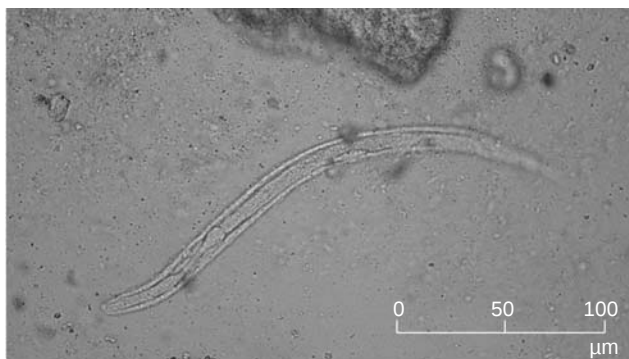


Figure 2. Rhabditiform larva of *S. stercoralis* in the feces.

ic findings. Abdominal sonography revealed alcoholic liver disease. His consciousness became dull, and low-grade fever (up to 37.6°C) developed again. MRI of the brain showed hyperintensity in T1-, T2- and diffusion-weighted images in the left rolandic area. This finding was compatible with an infarct with laminar necrosis (Fig. 1), but by itself could not explain his change in consciousness. On October 13, the patient was intubated because of respiratory failure, although there was only a very mild infiltration lesion in the lung. Focal seizures initially involving the left side of the face then marching to the left hand and lower limb were noted. Multiple epileptic foci in the right frontal and left central regions were noted in the follow-up EEG. The clinical seizures subsided after intravenous infusion of valproic acid, 400 mg q12h. On October 15, the body temperature was 34.6°C and the patient was in a confusional state. The 3rd CSF study showed pleocytosis of $39 \times 10^6/L$ (neutrophil 55%, lymphocyte 37%, monocyte 8%), protein 2.57 g/L, and glucose 56 mg/L.

On October 18, marked eosinophilia (12%) was noted. Because the previous eosinophil count was normal, drug allergy was suspected. Repeated routine stool examinations showed rhabditiform larvae of *S. stercoralis* (Fig. 2) in the feces. Despite of treatment with oral albendazole 400 mg twice a day beginning on October 20, the patient passed away on October 27 due to cardiopulmonary failure. There were a large amount of rhabditiform larvae of *S. stercoralis* in the feces to the last day of hospitalization.

DISCUSSION

Based on the clinical presentations of fever, headache, consciousness change, seizures, typical CSF findings, and good drug responses, a tentative diagnosis of bacterial meningoenkephalitis was made. The unusual manifestation that the condition deterioration again instead of a good initial response to antibiotics seemed against bacterial infections. The gastrointestinal, respiratory, and central nervous system functions all got worse. The final clues for a diagnosis of strongyloidiasis came from the elevated eosinophils and the larvae in repeated stool examinations. A hyperinfection state involving the gastrointestinal, respiratory, and central nervous systems seems to be the most likely explanation for the simultaneous manifestations from these multiple organ systems.

Gram-negative bacterial meningitis is a common complication of the hyperinfection state of strongyloidiasis. The rhabditiform larvae, instead of being excreted with the stool, may metamorphose into invasive filariform larvae within the patient's gastrointestinal tract and penetrate the intestinal wall. This may cause autoinfection and result in disseminated strongyloidiasis with hyperinfection in the digestive and respiratory systems. Bacteria from the flora in the bowel travel with *S. stercoralis* larvae and enter the blood circulation, thus, Gram-negative bacteremia or meningitis is common in the hyperinfection state⁽⁴⁾. Although the culture results were negative in this case, the initial clinical and CSF findings supported a diagnosis of bacterial meningitis, which was very likely related to the hyperinfection state.

Direct CNS infection caused by *S. stercoralis* has been very rare, because it is hard to decide which brain regions to sample in vivo. Very rarely, the filariform larvae are found directly in the CSF⁽⁵⁾. Meltzer et al. postulated that the neurological dysfunction is due to an infection of the CNS by *S. stercoralis* and/or the bacteria as well as the fungi traveling to the CNS with the larvae^(6,7). In 2002, Tsai et al. reported 27 patients with strongyloidiasis in southern Taiwan in a 10-year period⁽³⁾. There was only one case with consciousness change in that review, but the cause was not determined. In this case, the second phase of consciousness disturbance, the new

seizure foci, and the small cortical infarction are best explained by the direct invasion of filariform larvae into the CNS parenchyma or meninges⁽⁹⁾.

The hyperinfection state is usually associated with steroid use or AIDS infection. According to the medical history, this case did not take steroids, nor did he use any immunosuppressing agent before this event. Alcoholic liver disease was thought to be contributory to the immunocompromised state. In addition, the patient had history of gastrectomy. This might have played an important role in the enhancement of the autoinfection, because the rhabditiform larvae would then not be digested by the gastric acid in its life cycle, and have a greater chance of survival as well as multiplication into the infective filariform larvae. This would contribute to the hyperinfection syndrome, in which the filariform larvae migrate to different organs, leading to the tissue damage, local inflammation, anemia, and malnutrition. The relative risk (RR) of *S. stercoralis* infection was increased for patients who had recently used corticosteroids (RR= 3.3), who had a hematologic malignancy (RR= 5.28), or who had prior gastric surgery (RR= 11.5)⁽⁹⁾.

The diagnosis and treatment of strongyloidiasis remains a strategic issue, even when the patients are asymptomatic. Infection of *S. stercoralis* is usually only mildly symptomatic and may persist for many years. However, it could occasionally progress to the hyperinfection state with a high mortality rate. In this patient, an early diagnosis was difficult because of the lack of evidence for strongyloidiasis in the initial laboratory data. We presume that the hyperinfection state made the lung lesion worse in this case, though there was no larva found in the saliva. We used albendazole 800 mg per day, but still failed to stop the fulminant course of multiple organ failure.

This is the first case report of meningoencephalitis caused by *S. stercoralis* infection in Taiwan. The treatment response of the hyperinfection syndrome could be disappointing, and the mortality rate is usually higher than 50%. At any rate, earlier detection and prompt institution of albendazole might lead to a more favorable clinical course and outcome, although the CNS damage is usually irreversible. Local physicians should always

keep in mind that strongyloidiasis has not been eradicated in Taiwan. For the cases of bacterial meningitis, especially those of Gram-negative meningitis and a relapsing course under antibiotic therapy, a possible etiological factor of strongyloidiasis should not be overlooked.

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