Case Report: Pseudotumoral Form of Neuroschistosomiasis: Report of Three Cases in Ganzi, China

Heng Wan,* Hayashi Masataka, Li-Ping Zhang, and De-Fu Zheng

Department of Neurology and Functional Neurosurgery, West China Fourth Hospital of Sichuan University, Chengdu, People's Republic of China; Department of Neurology, Kofu City Hospital, Kofu, Japan; Department of Parasitology, Center for Disease Control and Prevention of Sichuan Province, Chengdu, People's Republic of China; Department of Neurology, Ganzi Tibetan Autonomous Prefecture People's Hospital, Ganzi, People's Republic of China

Abstract. The authors report three rare cases of neuroschistosomiasis lacking extracranial involvement. No parasitic eggs were detected in the stool with the Kato–Katz thick smear methods. Computed tomography of the brains showed hypodense signals, and magnetic resonance imaging showed isointense signals on T1-weighted images, hyperintense signals on T2-weighted images, and intensely enhancing nodules in the brain after intravenous administration of gadolinium. High-grade gliomas were suspected, and operations or radiosurgery was performed. Cerebral schistosomiasis was confirmed in all cases by biopsy of the brain lesions, revealing granulomas containing embedded *Schistosoma japonicum* eggs. All cases were definitively diagnosed as brain schistosomiasis japonica. Praziquantel and corticosteroids were administered, and the prognoses were good for all case patients. Although the aforementioned pattern of imaging examinations is not present in all cases of neuroschistosomiasis, a diagnosis of neuroschistosomiasis should be considered when this pattern of imaging is observed; cerebrospinal fluid serological exams are also recommended.

INTRODUCTION

Schistosomiasis is one of the most widespread parasitic infections in the world. The three major schistosome species known to infect humans are *Schistosoma haematobium* (endemic in Africa and the eastern Mediterranean), *S. mansoni* (endemic in Africa, the Middle East, the Caribbean, and South America), and *S. japonicum* (endemic primarily in China, Japan, and the Philippines). It is estimated that more than 1,000,000 humans in China are presently infected with *S. japonicum*.^{1,2} Although gastrointestinal system involvement with *S. japonicum* seems to be common, neuroschistosomiasis is rare. Cerebral schistosomiasis affects approximately 2–4% of infected persons and may be found mainly in the parietal, temporal, and occipital lobes and the cerebellum.^{3,4} In addition, almost all cases of brain schistosomiasis japonica are accompanied by hepatosplenomegaly.⁵ Here, the authors describe three cases of brain schistosomiasis japonica that were identified by pathological diagnosis and predominantly involved the cerebrum and cerebellum without affecting any other organs. Blood studies were normal, and no parasitic eggs were detected in the stool with the Kato–Katz thick smear methods for 2 consecutive days. These patients were all misdiagnosed and mistreated in the local hospital, and all of them came from or worked in the Ganzi region of the Sichuan province, one of the severe endemic areas of *S. japonicum* in China.⁶

CASE REPORT 1

A 57-year-old, right-handed workman was admitted to the hospital with left-sided parietal headaches. The headaches were throbbing in nature, radiated posteriorly for a few weeks, and were not accompanied by fever, convulsion, or

any other symptoms. The workman came from the Ganzi region of the Sichuan province, one of the endemic areas of *S. japonicum* in China. The workman was born in the Shanxi province and worked as a construction laborer in the Ganzi region. His medical history included a mild trauma from a traffic accident. During the previous few weeks, he had experienced intermittent episodes of headache, and there was no association with position or movement and no nausea or vomiting. The patient seemed to be a healthy man with no distress. His blood pressure, heart rate, and temperature were normal. A general physical examination proved to be unremarkable, with the patient exhibiting no rash, organomegaly, or lymphadenopathy. The neurological examination was also normal, with no visual defects identified by confrontation and no papilledema. Routine laboratory tests included an electrolyte test, renal and liver function tests, erythrocyte sedimentation rate, complete blood cell count, and stool test. Laboratory findings revealed a leukocyte count of 12,000/mL, an increased red blood cell count (caused by high-altitude living conditions), and no eosinophilia. Additionally, no parasitic eggs were detected in the stool with the Kato–Katz thick smear methods for 2 consecutive days. The cerebrospinal fluid (CSF) revealed normal levels of protein, glucose, and chloride. The CSF serological exams were ignored, because the cost was relatively high and the distance between the local Center for Disease Control and Prevention (CDC) and the hospital was large. The chest radiography and abdominal ultrasonography results were also normal. No hepatosplenic involvement was detected. Computed tomography (CT) of the brain showed hypodense areas in the left frontal lobe. Cerebral magnetic resonance imaging (MRI) was later performed and revealed a hypointense signal on T1-weighted images (Figure 1A), a hyperintense signal on T2-weighted images (Figure 1B), and intensely enhancing nodules in the left frontal lobe after intravenous administration of gadolinium (Figure 1C). Electroencephalograph (EEG) tracing revealed an asymmetrical slow wave in the left frontal areas with a 3- to 5-Hz slow-wave pattern (Figure 1D). The workman was treated with antibiotics for 10 days but still complained of dizziness and an aggravating headache. A

*Address correspondence to Heng Wan, Department of Neurology and Functional Neurosurgery, West China Fourth Hospital of Sichuan University, Renmin Nanlu, No. 18, Section 3, Chengdu, Post code 610041, People's Republic of China. E-mail: zeonguton@yahoo.cn

FIGURE 1. (A) MRI showing a hypointense signal on T1-weighted images in the left frontal lobe. (B) MRI showing a hyperintense signal on T2-weighted images in the left frontal lobe. (C) MRI showing intensely enhancing nodules in the left frontal lobe after intravenous administration of gadolinium. (D) EEG showing an asymmetrical slow wave in the left frontal areas with a 3- to 5-Hz slow-wave pattern.

high-grade glioma was suspected. He refused any surgical treatment, and a stereotactic radiosurgery was finally performed. However, the patient suffered from uncontrollable vomit and intracranial hypertension after radiosurgery, and a craniotomy was performed with this patient's consent. Microscopic examination showed that the lesions appeared to have light yellow or grayish-white spotted nodules with a poor blood supply. Examination of a frozen section of the resected lesions suggested that *S. japonicum* ova and granulomas were present. Pathologic examination of the biopsy specimen revealed sclerosing schistosomal granulomas scattered within the parenchyma of the cerebrum. The diagnosis was confirmed, and antischistosomiasis treatment was administered when the patient's condition had stabilized. The patient was concurrently treated with praziquantel (20 mg/kg per day) and dexamethasone (10 mg/day) for 14 days. The patient was discharged after 31 days and showed complete resolution of symptoms at the 3-month follow-up exam. The abnormal EEG findings had improved to almost normal patterns with a 9-Hz diffuse α -wave pattern.

CASE REPORT 2

A 16-year-old, right-handed schoolboy was admitted to the hospital with a history of headache, dizziness, vomiting, and double vision that started four weeks prior and was not

accompanied by fever, convulsion, or any other symptoms. The patient's family came from the Ganzi region. His parents denied any history of previous disease, and his medical history was unremarkable. On admission, the patient was found to have diplopia on left lateral gaze and horizontal nystagmus. No major neurological dysfunction was detected. Laboratory findings revealed a leukocyte count of 10,000/mL, an increased red blood cell count (caused by high-altitude living conditions), and no eosinophilia. The CSF revealed normal levels of protein, glucose, and chloride. The CSF serological exams were ignored because of the presumptive diagnosis of a neuroglial tumor. No parasitic eggs were detected in the stool with the Kato-Katz thick smear methods for 2 consecutive days. The chest radiography and abdominal ultrasonographic results were also normal. No hepatosplenic involvement was detected. A CT of the brain showed low-density areas in the left cerebellum (Figure 2A). MRI of the brain showed a left cerebellar lesion with mass effect compressing the surrounding tissues (Figure 2B). Contrast-enhanced images showed a mass-like structure and punctate nodules (Figure 2C and D). The patient was taken to the operating room with the presumptive diagnosis of a neuroglial tumor and subjected to a lateral suboccipital craniectomy 3 days after admission. A brown, brittle tumoral mass without a clearly defined margin within the cerebellar tissue was removed. Microscopic examination revealed schistosomal granulomas in the cerebellum. The diagnosis was confirmed after surgery. He was treated with

FIGURE 2. (A) CT showing low-density areas in the left cerebellum. (B) MRI showing a hypointense signal on T1-weighted images with mass effect compressing the surrounding tissues in the left cerebellum. (C, D) MRI showing a mass-like structure and punctate nodules in the left cerebellum after intravenous administration of gadolinium.

praziquantel (20 mg/kg per day) and prednisone (5 mg/day) and quickly improved. The patient was discharged after 23 days and showed no neurological impairment at the 3-month follow-up exam.

CASE REPORT 3

A 42-year-old, right-handed herdsman was admitted to the hospital after experiencing a mild bilateral frontotemporal headache for 6 weeks that was not accompanied by a fever, visual scintillation, or any other symptoms. The herdsman came from the Ganzi region. His medical history was unremarkable. During the prior few weeks, he had experienced intermittent episodes of headache and nausea. The patient seemed to be a healthy man, and his general physical examination was normal. Neurological examination showed a slight ataxic gait and incoordination of the movements of the right limbs. Laboratory findings revealed a leukocyte count of

11,000/mL, an increased red blood cell count (caused by high-altitude working conditions), and no eosinophilia. The CSF revealed normal levels of protein, glucose, and chloride. Although expensive and time-consuming, both the CSF serum indirect hemagglutination assay (IHA) and the enzyme-linked immunosorbent assay (ELISA) for schistosomes were carried out. No parasitic eggs were detected in the stool with the Kato-Katz thick smear methods for 2 consecutive days. The chest radiography and abdominal ultrasonographic results were also normal. No hepatosplenic involvement was detected. CT of the brain showed low-density areas in the right cerebellum (Figure 3A). MRI of the brain enhanced by intravenous contrast showed a heterogeneous, hyperintense area with irregular borders in the right cerebellar hemisphere (Figure 3B–D). The herdsman was treated with antibiotics for several days before receiving the CSF serology test results, but he still complained of an aggravating headache. A high-grade glioma was suspected, and a biopsy was performed. Examination of a

FIGURE 3. (A) CT showing low-density areas in the right cerebellum. (B) MRI showing a hypointense signal on T1-weighted images in the right cerebellum. (C, D) MRI showing a heterogeneous, hyperintense area with irregular borders in the right cerebellum after intravenous administration of gadolinium. (E, F) Pathologic examination of the biopsy specimen showing sclerosing schistosomal granulomas scattered within the parenchyma of the cerebellum.

frozen section of the biopsy tissue specimen suggested that *S. japonicum* ova and granulomas were present. Pathologic examination of the biopsy specimen revealed sclerosing schistosomal granulomas scattered within the parenchyma of the cerebellum (Figure 3E–F). At the same time, the positive CSF serology test results were also sent back. The diagnosis was confirmed, and the patient was treated concurrently with praziquantel (20 mg/kg per day) and dexamethasone (10 mg/day) for 14 days. The patient was discharged after 26 days and showed complete resolution of symptoms at the 3-month follow-up exam.

DISCUSSION

As previously mentioned, three major schistosome species are known to infect humans. *S. haematobium* predominantly affects the urinary tract, whereas *S. mansoni* and *S. japonicum* characteristically cause intestinal and hepatosplenic disease.^{6,7} Although schistosome eggs are small and can easily reach the brain, involvement of the central nervous system is a rare ectopic manifestation of schistosomiasis. Neuroschistosomiasis disease is caused by the host reaction to the presence of schistosome eggs.⁸ However, some people with eggs in the central nervous system may not develop symptoms.⁹

The following main four potential mechanisms may explain how eggs can exist in the brain. (1) Adult flukes ovulate schistosome eggs that settle in the intracranial blood sinus, forming a focus of infection. (2) Schistosome eggs that lodge into the portal venous system are carried to the brain by systemic circulation through the portosystemic ramus anastomoticus. (3) Schistosome eggs are passed to the brain through the left ventricle or vertebral vein.¹⁰ (4) Schistosome eggs produced by ectopic adult worms entered the main blood circulation when passing through the lungs and affected the brain diffusely.

Neuroschistosomiasis caused by japonica species may have more acute presentation as a diffuse encephalopathy with features including delirium, focal motor deficits, visual and speech disturbances, and increased intracranial pressure.¹¹ More commonly, intracranial granulomas may develop and present as mass lesions, which was seen in our report, sometimes many years after the initial infection. These granulomas often provoke focal or generalized seizures.¹² The presentation in pediatric patients is very similar to the presentation observed in adults.^{13,14} Some studies have suggested that seizures are common in the chronic stage, whereas increased intracranial pressure occurs in the acute stage.¹⁵

The diagnosis of cerebral schistosomiasis can be difficult; clinical findings are nonspecific, and laboratory changes, such as eosinophilia and evidence of schistosome ova in the stool or urine, may or may not be present, which was seen in this report.¹⁶ The Kato–Katz technique was widely used for the diagnosis of *Schistosoma japonicum* infection in China. However, the sensitivity of the Kato–Katz technique on stool specimen was around 65–83%.¹⁷

Increased total protein levels, pleocytosis, and eosinophilia (suggestive of parasitic infection) can sometimes be observed in the CSF. Blood tests may also show eosinophilia; however, peripheral eosinophilia is uncommon in chronic infections.¹⁸ Stool samples may also be negative for eggs in chronic infections.^{19,20}

CSF serological examinations may be useful for differential diagnosis.²¹ The sensitivity of IHA was 83.7–92.3% and the

specificity 55.8–67.3%, whereas the sensitivity of ELISA was 88.4–96.2% and the specificity was 38.4%.^{22,23} Zhou and others²⁴ used the Kato–Katz results as the gold standard reference: the specificity of the IHA was from 60% to 77%, the positive predictive value of this method was from 19% to 30%, and its sensitivity and negative predictive value were more than 97%. However, serology does not differentiate between past and current infections and is, therefore, less useful in patients from endemic regions. A positive serology (in blood and/or CSF) may initiate a trial treatment in cases with compatible brain lesions. Tissue biopsy and demonstration of ova remain the gold standard for diagnosis.²⁵

Neuroimaging examinations may be helpful for obtaining an accurate diagnosis. The leptomeninges and cerebral cortex are the most common sites involved, whereas the cerebellum, thalamus, hippocampus, midbrain, basal ganglia, choroid plexus, and white matter are less frequent sites of infection. In the mass form of cerebral schistosomiasis, CT typically reveals an enhancing mass lesion associated with edema and without calcification. MRI may show a heterogeneously enhancing mass with surrounding edema.^{26,27} However, such large granulomatous lesions provoking brain tumor-like syndromes may frequently be asymptomatic.²⁸ In other cases, MRI may show a nodular and linear enhancement pattern with associated vasogenic edema. In these instances, the pattern of contrast enhancement is more noteworthy than the associated vasogenic edema. Pathologically, this enhancement pattern correlates with a host granulomatous response to schistosome eggs. Although this pattern is not present in all cases of cerebral schistosomiasis, a diagnosis of cerebral schistosomiasis should be considered when it is observed.²⁹

The treatment of cerebral schistosomiasis is highly effective and safe. Praziquantel kills the adult worms, and corticosteroids, which can be used for all schistosomal subtypes, concomitantly reduce the granulomatous inflammation.³⁰

Surgical treatment should be used when cerebellar schistosomiasis leads to a mass effect of the posterior cranial fossa or when cerebral schistosomiasis leads to increased intracranial pressure. The goals of surgery are to resect the schistosomal granuloma and reduce the intracranial pressure. Microsurgery is effective for the total resection of lesions and can assist in the protection of the brain, increasing the cure rate.^{31,32}

The special MRI or CT patterns combined with CSF serological examinations may play an important role in the differential diagnosis of neuroschistosomiasis. In the meantime, we still recommend an aggressive diagnostic approach (such as a stereotactic biopsy) in confusing cases for confirming pathological diagnosis, because early diagnosis and treatment can minimize the resultant tissue damage and eliminate the parasite worm.^{33,34}

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Authors' addresses: Heng Wan, Department of Neurology and Functional Neurosurgery, West China Fourth Hospital of Sichuan University, Chengdu, People's Republic of China, E-mail: zeonguton@yahoo.cn. Hayashi Masataka, Department of Neurology, Kofu City Hospital, Kofu, Japan, E-mail: hayashi65@aurora.ocn.ne.jp. Li-Ping Zhang, Department of Parasitology, Center for Disease

Control and Prevention of Sichuan Province, Chengdu, People's Republic of China, E-mail: LibbyCheung@yahoo.com. De-Fu Zheng, Department of Neurology, Ganzi Tibetan Autonomous Prefecture People's Hospital, Ganzi, People's Republic of China, E-mail: zeonguton@163.com.

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