ACUTE NEUROSYCHOSTOSOMIASIS: TWO CASES ASSOCIATED WITH CEREBRAL VASCULITIS

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Abstract. Encephalitis and focal neurologic deficits can occur during the acute phase of schistosomiasis. We report two cases in which cerebral imaging showed cerebral vasculitis located in arterial junctional territories. These neurologic complications may be caused by eosinophil-mediated toxicity. Immediate treatment should consist of corticosteroids rather than specific antischistosomal drugs, which may aggravate the disorders.

INTRODUCTION

Acute schistosomiasis may be complicated by life-threatening neurologic involvement. This is an uncommon complication, described in 2.3% of 1,200 cases of acute Schistosoma japonicum infestation among soldiers during the Leyte campaign in 1944. It is pathophysiology remains unclear. The role of eggs or micro-emboli from the heart (during endomyocardial fibrosis) have been discussed. We report two new cases of brain involvement, complicating the acute invasive phase of schistosomiasis, where the signs point to cerebral vasculitis.

CASE REPORTS

The first patient was a 54-year-old man from Lebanon who had been living in Mali for several years was medically evacuated for confusion. He reported repeated exposure to fresh ground water in the Bamako region. Ten days before evacuation, he developed a high fever (40°C) and received presumptive treatment of malaria with quinine. The fever abated but he complained of disorientation, bewilderment, and irritability, and was diagnosed with a cerebellar syndrome and left hemiparesis. On admission, he was afebrile and had a Glasgow coma score of 9/15, persistent motor paresis, and confusion. There was no neck stiffness, jaundice, skin lesions, or spleen, liver, or node enlargement. His blood eosinophil count was 3,070/mm³ (normal < 500/mm³). The cerebrospinal fluid contained less than 1 cell/mm³, 4.8 mmol/L glucose, and 0.26 g/L protein; no bacteria or viruses were detected. Serologic test results for helminths (fascioliasis, schistosomiasis, filariasis, toxocariasis, trichinellosis, cystercerosis) and protozoa (trypanosomiasis, toxoplasmosis) were negative. Results of stool examination by Ritchie, Kato, and Baermann analysis with direct microscopic examination were negative for parasite eggs and larvae. Urine sample analysis was made by the direct microscopic examination of a centrifugated urine specimen and results were negative for parasite eggs. Circulating immune complexes (6.9 µg/mL) and antibodies to phospholipids (11 IU antiphospholipid IgG, normal < 5 IU; Harris’ method) were detected. Test results for antineural and antinative-DNA antibodies were negative. Blood cultures and test results for malaria were also negative. The C-reactive protein level was 119 mg/L (normal < 5 mg/L). Electrocardiography showed inverted ST waves in leads V3 to V5. The troponin Ic level was normal and cardiac kinetics was regular and homogeneous. Results of echocardiography were normal. Magnetic resonance imaging (MRI) of the head showed multiple infarcts bilaterally in the cortex and white matter (sempioval centrum), suggestive of cerebral vasculitis. Cerebral involvement during the invasive stage of helminthiasis (i.e., trichinellosis, hookworm, strongyloidiasis, ascariasis) was suspected, and albendazole was prescribed (800 mg/day for 5 days) because of its broad spectrum. His neurologic status improved slowly and he was transferred to another unit before being seen again four months later.

Serologic test results for schistosomiasis based on hemagglutination (Cellognost-Schistosomiasis; Chiron-Behring, Marburg, Germany) and indirect immunofluorescence (Schistosoma mansoni in-house prepared antigen; Laboratoire de Parasitologie-Mycologie, Groupe Hospitalier Pitié-Salpêtrière, Paris, France) were then positive (hemagglutination = 1:320, indirect immunofluorescence = 1:800), thus showing seroconversion for schistosomiasis. The other serologic test results for helminths and protozoa were negative and the patient still complained of psychomotor slowing and insomnia. Praziquantel, 40 mg/kg (one dose), was prescribed, but the patient returned to Mali and was lost to follow-up.

The second patient was a 21-year-old French man (tourist) who was hospitalized for persistent myalgias, headache, dry cough, loss of appetite, and fever (38–39°C). One month earlier, he developed a maculopapular rash just after bathing in a lake in the Dogon area of Mali. His eosinophil count was 2,000/mm³, and acute schistosomiasis was suspected. Electrocardiography showed inverted ST waves in lead V4. The troponin level was 13.9 µg/L (normal < 0.2 µg/L). Results of echocardiography were normal. Aspartate and alanine aminotransferase levels were 89 IU/L and 215 IU/L, respectively (normal < 40 IU/L). Multiple stool and urine samples were negative for parasite eggs, larvae, and adult forms. Serodiagnosis of schistosomiasis was positive by indirect immunofluorescence (1:800) (S. mansoni in-house prepared antigen; Laboratoire de Parasitologie-Mycologie, Groupe Hospitalier Pitié-Salpêtrière, Paris, France) and by hemagglutination (1:512) (Cellognost Schistosomiasis; Chiron-Behring, Marburg, Germany). Tests for circulating antigen in blood smears were not performed. Treatment with praziquantel (40 mg/kg)
was started. Two days later, he abruptly developed mental
confusion, anosognosia, disrupted flow of thought, and splin-
ter hemorrages under his nails. His temperature was normal.
An MRI of the head showed multiple bilateral brain infarcts;
they were located in the border zone and were suggestive of
cerebral vasculitis (Figure 1). Anticardiolipid antibody titra-
tion results were positive (IgM 28 IU, normal < 15 IU). Com-
puted tomography of the heart was normal, with no signs of
myocarditis or endomyocardial fibrosis.

Steroid therapy (prednisone, 1 mg/kg) was started, and the
symptoms disappeared within 48 hours. Four months later, S.
haematobium eggs were found by direct microscopic exami-
nation of centrifugated urine samples from both the patient
and five of his friends who had bathed in the same lake.

DISCUSSION

Neurologic complications generally occur in the later stages
of schistosomiasis and are caused by a granuloma reaction
around eggs or adult forms in the brain. However, neuro-
logic deficits have also been described during the acute phase
of schistosomiasis, which is also known as invasive schistoso-
miasis or Katayama fever. The acute phase occurs 2–6 weeks
after bathing in infected waters. It is an uncommon compli-
cation: for example, only 2.3% of 1,200 U.S. soldiers with
acute schistosomiasis developed neurologic disorders during
The Philippines campaign of World War II. In contrast, neu-
rochisomiasis can be life-threatening. It has been sug-
gested that these disorders may be caused by cardiogenic ce-
rebral emboli secondary to endomyocardial fibrosis induced
by eosinophil toxicity.

We describe here two cases of acute neuroschistosomiasis
in which cerebral vasculitis was the most likely cause of the
neurologic manifestations. Neurologic complications of acute
neuroschistosomiasis potentially include headache, confusion,
seizures, loss of consciousness, focal deficiencies, visual impair-
ment, ataxia, urinary incontinence, and motor paralysis. They usually disappear either spontaneously or after steroid therapy. It is interesting that in one of our patients neurologic symptoms occurred early after praziquantel therapy.

The pathophysiology of acute neuroschistosomiasis is un-
clear. Sarrazin and others incriminated cardiogenic emboli
secondary to endomyocardial fibrosis (EMF), but such disease usually occur during prolonged hypereosinophilia. Cere-
bral MRI showed multiple brain infarcts suggestive of wide-
spread cerebral vasculitis or cerebral embolism in our two
patients and also in three previously reported cases. Clinical examination of one of our patients showed splinter hem-
rorrhages, which are another sign of vasculitis, whatever its origin. This sign can be seen during endocarditis and other disorders causing vasculitis. Other features supporting the responsibility of vasculitis rather than embolism in the onset of neurologic complications are the rapid efficacy of steroid
therapy in one of our patients, the onset of cerebral disorders
after treatment with praziquantel in the other patient, and the
lack of cardiac involvement in both cases. Furthermore, similar clinical and pathophysiologic features pointing to micro-
thrombi in cerebral vessels have been described during the
course of trichinellosis, another helminthic disease. In addition, in these latter series, there was no parasite larvae in the brain of autopsied patients, and imunoallergic toxicity was the major pathophysiologic finding reported to explain these
signs.

One striking finding in our two patients, together with the
patients with trichinellosis referenced above, was their marked eosinophilia. Recent reports mention the toxicity of
eosinophilic granules for endothelial cells. Major basic pro-
tein and eosinophil cationic protein can damage nearby tis-
sues, especially endothelia. Endothelial cells can express ad-
hesion molecules such as platelet activating factor (PAF) and
vascular cell adhesion molecule, which attract eosinophils and
promote their adherence. Eosinophils also express adhesion
molecules such as intercellular adhesion molecule-1 and re-
ceptors for PAF, which augment the thrombotic effect.

Major basic protein and peroxide released from eosinophil
granules have direct toxicity for endothelial cells and muscle
cells of the heart, which potentially results in endomyocar-
dial fibrosis. Signs of cardiac vasculitis and necrosis have been seen at biopsy in patients with EMF. Furthermore, eosinophil-derived neurotoxin is directly toxic for nerve tis-
sue.

Thus, eosinophil-mediated toxicity, leading to vasculitis and small-vessel thrombosis, is the most likely pathophysi-
ologic mechanism in acute neuroschistosomiasis. This would explain how acute schistosomiasis with hypereosinophilia can be associated with neurologic deficits in the absence of car-
diac involvement. Antibodies to phospholipids and circulat-
ing immune complexes could contribute to these complica-
tions.

Encephalopathy can occur when circulating eosinophil
counts are persistently high, as in idiopathic hypereosino-
philia without evidence of EMF. Recent MRI studies of
patients with idiopathic hypereosinophilia have shown mul-
tiple lesions in the cortical and subcortical regions located in

**Figure 1.** Magnetic resonance imaging (T2 flair) of the second patient showing border zone infarcts suggestive of cerebral vasculitis (arrows).
arterial junctional territories, a pattern similar to that seen in acute neuroschistosomiasis.\textsuperscript{16}

Consequently, acute neuroschistosomiasis should be treated with corticosteroids rather than praziquantel, which can trigger neurologic complications as in our second patient. Furthermore, a clinical deterioration, including neurologic involvement in one patient, has recently been reported in 40% of 10 patients with acute schistosomiasis treated with praziquantel.\textsuperscript{17} In contrast, corticosteroids can attenuate the neurologic and cardiac toxicity of eosinophils and also the hypersensitivity reaction to parasite toxins.\textsuperscript{6,12} Subsequently, treatment with praziquantel should be postponed until neurologic recovery.

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