Seizures and Cerebral Schistosomiasis

Luiz Eduardo Betting, MD; Clodoaldo Pirani, Jr, MD; Luciano de Souza Queiroz, MD, PhD; Benito Pereira Damasceno, MD, PhD; Fernando Cendes, MD, PhD

Background: Schistosoma mansoni is a parasitic trematoid worm that infects humans. Schistosomiasis is endemic in parts of South America, sub-Saharan Africa, the Middle East, and some Caribbean islands. Disorders of the liver and gastrointestinal tract are the most common clinical manifestations. The central nervous system is not usually affected. The most common neurologic manifestation is transverse myelitis. In some circumstances, the eggs of S mansoni are found in the brain, causing inflammatory reaction.

Objective: To describe a young Brazilian patient with partial epileptic seizures caused by a granulomatous lesion due to S mansoni.

Conclusion: In endemic areas or in patients with a positive epidemiological history, schistosomiasis must be considered as a possible diagnosis of seizures, particularly when they are associated with granulomatous lesions on magnetic resonance imaging.

Arch Neurol. 2005;62:1008-1010

CHISTOSOMIASIS IS CAUSED BY a parasitic tropical trematoid worm that resides in the veins of its vertebrate definitive host. It is endemic in South America, sub-Saharan Africa, the Middle East, and some Caribbean islands. Infections are caused by transdermal penetration of the parasite. The 3 main species of schistosoma are Schistosoma mansoni, Schistosoma japonicum, and Schistosoma hematobium. Central nervous system involvement may occur in chronic schistosomiasis caused by any schistosome species, but especially by S japonicum. The possible mechanism of central nervous system involvement is the embolization of eggs or ectopic migration of adult worms. We describe a patient with partial seizures caused by cerebral S mansoni.

REPORT OF A CASE

In July 2000, a 26-year-old man presented with a first simple partial seizure episode described as a burning sensation in the fourth and fifth fingers of the left hand that spread to the ipsilateral aspect of the forearm, followed by clonic movements of the left eyelid, left side of the mouth, and upper part of the arm, and then by a brief period of confusion. That same day, he had 2 more episodes with the same symptoms. There was no evidence of tonic-clonic movements (secondary generalization). Phenytoin therapy (300 mg/d) was initiated, with good seizure control. Three months later, he had 2 more similar episodes. During the 3-month period, he had been taking phenytoin regularly, and no other treatment was introduced. After the new seizures, he was referred to our service. The dosage of phenytoin was increased to 350 mg/d, and the patient was admitted for evaluation.

A computed tomographic scan demonstrated a right parietal lesion. Magnetic resonance imaging showed a heterogeneous right parietal and insular corticosubcortical lesion with mass effect and a hyperintense signal on T2 sequences (Figure, A, B, and C). Histologic examination of a stereotactic biopsy specimen of the lesion revealed S mansoni eggs in epithelioid and giant cell granulomas (Figure, E and F). The results of biochemical and cytologic analysis of a cerebrospinal fluid sample were normal, as were those of immunologic analysis for S mansoni. A complete blood cell count showed eosinophilia, and a stool sample was positive for S mansoni.

Prednisone (1 mg/kg per day for 1 week, with gradual withdrawal during the following 3 weeks) and praziquantel (2 doses at 20 mg/kg per day) therapy was initiated. One month later, magnetic reso-
nance imaging showed complete resolution of the lesion (Figure, D), and 5 months later, the phenytoin therapy was gradually discontinued. Electroencephalography, which was performed before (1 examination), during (1 examination), and after (3 examinations) treatment, showed no evidence of epileptiform activity. The patient was still seizure free and taking no medications 2 years after the phenytoin therapy was discontinued. An echocardiogram and a thoracic angio–computed tomogram were negative for right-to-left shunts, which are a possible pathway for *S. mansoni* eggs to enter the arterial system and reach the brain. The findings of spinal magnetic resonance imaging were normal.

**COMMENT**

Five species of *Schistosoma* are known to infect humans: *mansoni*, *mekongi*, *intercalatum*, *haematobium*, and *japonicum*. All infections follow direct contact with fresh water that harbors the larval forms of the parasite known as cercariae. *Schistosoma mansoni* larvae enter the human circulation by penetrating the skin. After several days, pairs of worms migrate to the inferior mesenteric veins. Egg production begins 4 to 6 weeks after infection and continues for the life of the worm, usually 3 to 5 years. The eggs pass through the blood vessel lumina and the intestinal mucosa. They are finally shed in the feces. The life cycle is complete when the eggs hatch, releasing miracidia that infect specific freshwater snails (*Biomphalaria* species). Miracidia will then develop into sporocysts and produce cercariae (free-swimming larvae).

There are 3 stages of clinical presentation of schistosomiasis:

1. Immediate. In this stage, a maculopapular eruption may arise at the site of penetration immediately after infection.
2. Acute. This stage is frequently encountered in areas of high transmission rates. Common symptoms include fever, headache, generalized myalgia, pain in the right upper quadrant of the abdomen, bloody diarrhea, and respiratory problems. Hepatomegaly and splenomegaly may be present. Aseptic meningitis is rare.
3. Chronic. This stage results from the host’s immune response to schistosome eggs and the granulomatous reaction evoked by the antigens they secrete. Disorders of the gastrointestinal tract and liver are the most common clinical manifestations, which usually represent the sites of maximal accumulation of the eggs.4,5 Central nervous system manifestations are more commonly seen in *S. japonicum* infections; the usual presentation is focal or generalized tonic-clonic seizures and focal deficits.6 Transverse myelitis is the most common neurologic manifestation of *S. mansoni* infection, which rarely affects the brain. Patients with the tumoral form of *S. mansoni* infection6 are usually male and young; headache, focal neurologic deficits, and seizures are the main manifestations.

Pitella et al6 described 4 patients with cerebral *S. mansoni* infection and reviewed 7 additional cases that were reported in the literature between 1984 and 1995. Since then, few cases have been described.7-10 The real prevalence is estimated to be higher than has previously been published. Autopsy studies in endemic areas showed *Schistosoma* species in more than 28% of the examined brains, including 4% with *S. mansoni* infection.11 In Brazilian pa-
tients with fatal hepatosplenic schistosomiasis, autopsies showed 26% with brain involvement.12

The pathogenesis of cerebral schistosomiasis is not completely understood. The clinical findings are attributable to an inflammatory response from the host to the eggs in the brain. It is likely that the eggs enter the brain by embolization through venous shunts as a result of hepatic and pulmonary hypertension. Aberrant migration of the worms is another possibility. Some authors believe that the cerebral form is caused by aberrant migration of the worms to the vertebral venous plexus (Batson plexus). In the absence of valves, the worms migrate and produce eggs directly in the brain.8,9

Confirmation of the diagnosis is difficult. Neuroimaging (computed tomography and magnetic resonance imaging) usually shows a tumoral lesion with mass effect and heterogeneous contrast enhancement mainly at the cerebellum and more rarely at the thalamus and the temporoparietal, occipital, and frontal regions.6,8-10 Antibody detection in samples of blood or cerebrospinal fluid is useful in only a few specific circumstances. Eosinophilia is not a constant finding in cerebrospinal fluid analysis. Phthisia is not a constant finding in cerebrospinal fluid analysis. Definitive diagnosis is made by pathologic examination. Histologic analysis shows exudative necrotic granulomas and the parasite’s eggs.

The therapeutic decision in patients with new-onset seizures should be made based on the type of seizures and on the epilepsy syndrome. The present case represents an example of symptomatic epilepsy with localization-related seizures. Antiepileptic drug monotherapy is considered the best method to treat epilepsy. For partial seizures, carbamazepine and phenytoin have a similar profile and are considered first-line drugs.13 Carbamazepine is usually associated with fewer adverse effects. On the other hand, phenytoin is available for intravenous administration and doses may be divided twice daily. Long-term antiepileptic drug therapy in patients with cerebral schistosomiasis is rarely indicated, although there are no specific guidelines for the minimum duration of treatment.11 In our patient, we decided to discontinue phenytoin therapy after good evidence that his seizures were controlled and that his granulomatous lesion had completely resolved.

Excellent treatment responses for central nervous system schistosomiasis can be achieved with antiparasitic drugs and corticosteroids. Oxamniquine and praziquantel are the most effective antiparasitic drugs to use for treating schistosomiasis. They induce the death of the adult worm, although the exact mechanism is unknown.1 Partial or total surgical intervention, with good outcome, has also been described. However, the patients who underwent surgical treatment did not have a previous etiologic diagnosis.6-10 The “gold standard” treatment for cerebral S mansoni schistosomiasis remains to be determined. After 3 weeks of treatment, there should be almost complete resolution of the lesion and the symptoms. Patients who have a positive epidemiological history or live in an endemic area and who have suggestive clinical and radiological features must be investigated for cerebral schistosomiasis.

Accepted for Publication: April 20, 2004.
Correspondence: Fernando Cendes, MD, PhD, Department of Neurology, University of Campinas–UNICAMP, Cidade Universitária, Campinas, São Paulo, Brazil, CEP 13083-970 (fcendes@unicamp.br).

REFERENCES