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Short Communication

Brain schistosomiasis in mice experimentally infected with *Schistosoma mansoni*

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ABSTRACT

Introduction: Human neuroschistosomiasis has been reported in the literature, but the possibility of modeling neuroschistosomiasis in mice is controversial. **Methods:** In two research laboratories in Brazil that maintain the *Schistosoma mansoni* life cycle in rodents, two mice developed signs of brain disease (hemiplegia and spinning), and both were autopsied. **Results:** *S. mansoni* eggs, both with and without granuloma formation, were observed in the brain and meninges of both mice by optical microscopy. **Conclusions:** This is the first description of eggs in the brains of symptomatic mice that were experimentally infected with *S. mansoni*. An investigation of experimental neuroschistosomiasis is now feasible.

Keywords: Schistosomiasis. Experimental neuroschistosomiasis. Brain schistosomiasis.

The World Health Organization estimates that between 200 and 300 million people worldwide are infected with *Schistosoma* and that 800 million people are at risk of infection[1]. In Brazil, approximately 4 to 6 million people are infected with *Schistosoma mansoni*[2].

Central nervous system (CNS) involvement in schistosomiasis can occur during acute primary infections[1,2]. Cerebral complications were reported in 2.3% of 1,200 cases of acute *S. japonicum* infection in soldiers in the Philippines in 1944 during World War II[3]. However, neurological complications generally occur during chronic hepatointestinal schistosomiasis[4]. In fact, autopsies conducted in endemic areas have identified *Schistosoma* species in up to 28% of the studied brains (4% with *S. mansoni* infection). In particular, Pitella et al.[5] reported the presence of *S. mansoni* eggs in 25% of the brains of autopsied patients in Brazil who died from hepatosplenic schistosomiasis.

The clinical neurological manifestations of schistosomiasis are caused by an increase in intracranial pressure, and the focal signs are triggered by the masses produced by granulomas, depending on the site of the cerebral lesions. The initial signs and symptoms include headache, focal or generalized seizures, ataxia, nystagmus, nausea and vomiting, intracranial hypertension and neurological deficits[6,7].

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Aloe et al.[8] described eggs, both with and without granuloma formation, in CD-1 mice infected with 60 *S. mansoni* cercariae (Puerto Rican strain). However, the mice did not present the signs or symptoms of brain disease. Additionally, Silva et al.[9] observed very few eggs in the brains of small percentages of BALB/c, C57BL/6 and Swiss albino mice that were infected once or five times with 30-50 cercariae (Feira de Santana strain) and concluded that the model was not suitable for studying neuroschistosomiasis. Given these limited findings, we decided to further investigate murine neuroschistosomiasis. Our research question addressed whether *S. mansoni*-infected mice in our animal facilities would present the signs or symptoms of brain involvement, and if so, whether these signs and symptoms are correlated with the presence of eggs or granulomas in the brain.

Male and female Webster mice (2 or 18 months old) were obtained from our animal facility (Centro de Pesquisas René-Rachou, Belo Horizonte, Brazil) and maintained in our laboratory. The mice were subcutaneously inoculated with 50 *S. mansoni* cercariae (LE strain) isolated from *Biomphalaria glabrata* (Planorbidae) snails. Note that we routinely maintain approximately 100 infected mice in our laboratory[10]. Four months after infection, one mouse (#1) developed right hemiplegia, rendering survival unlikely.

A similar procedure was conducted in a laboratory in Bahia (Centro de Pesquisas Gonçalo Moniz-Fiocruz). Fifty BALB/c mice were infected with 50 *S. mansoni* cercariae (Feira de Santana strain) each, and 8 months after infection, one mouse (#2) also developed right hemiplegia and spinning.

The mice in both laboratories were sacrificed by cervical fracture after being anesthetized with pentobarbital. During the autopsies, the livers, lungs and brains were retrieved for

examination. All of the animal procedures were approved by the local ethics committees for animal research.

The livers, lungs and brains that were obtained during the autopsies were fixed in 10% buffered formaldehyde. After 24 hours, the tissue fragments were embedded in paraffin, and 4-µm sections of the tissues were cut using a Spencer microtome. The tissue sections were then stained with hematoxylin and eosin (H&E) and examined by light microscopy.

Well-formed granulomas were frequently observed in the meninges **(Figure 1)**. Additionally, eggs with miracidia surrounded by small granulomas **(Figures 2** and **3)** or without granuloma formation were observed in the brains of both mice. *S. mansoni* eggs were also identified in the livers and lungs of the mice. The granulomas were in the productive phase, with slight fibrosis, which suggested that the chronic phase of infection had already begun.

For many years, we have observed evidence of brain disease (hemiplegia, spinning and urinary retention) in mice infected with *Schistosoma mansoni*, but these mice were considered to have other diseases, such as labyrinthitis or cerebral infections. As such, the mice were not considered to be useful for the experiments being conducted and were typically omitted from studies.

Recently, as we were studying human neuroschistosomiasis, we began to suspect that the manifestations in mice may be signs of brain involvement[12,13]. Surprisingly, *Schistosoma mansoni* eggs and granulomas were identified in the CNS of symptomatic animals. However, during autopsy, it was not possible to identify which areas of the brain were affected. Therefore, no neurological relationship between our microscopic findings and the clinical signs of cerebral involvement, such as hemiplegia and spinning, could be established in this study.

This preliminary report on spontaneous brain involvement in experimental murine schistosomiasis is intended to inform other investigators of the possibility of a mouse model of neuroschistosomiasis.

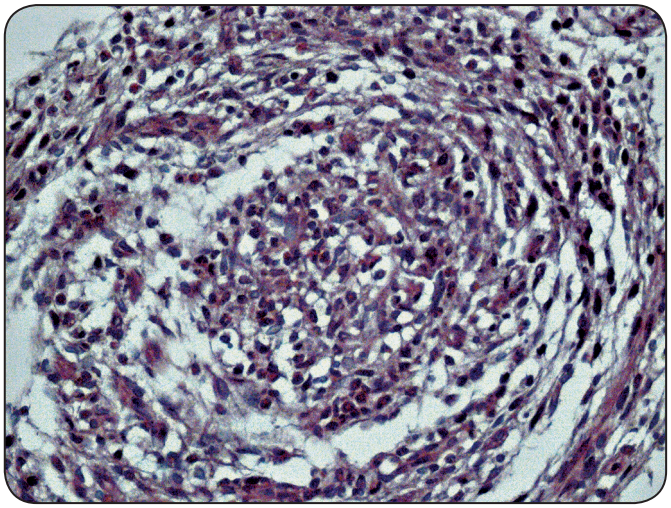

FIGURE 1 - Mouse 2. A well-formed granuloma with numerous eosinophils. No *Schistosoma mansoni* eggs can be observed in this lesion (H&E, 400X).

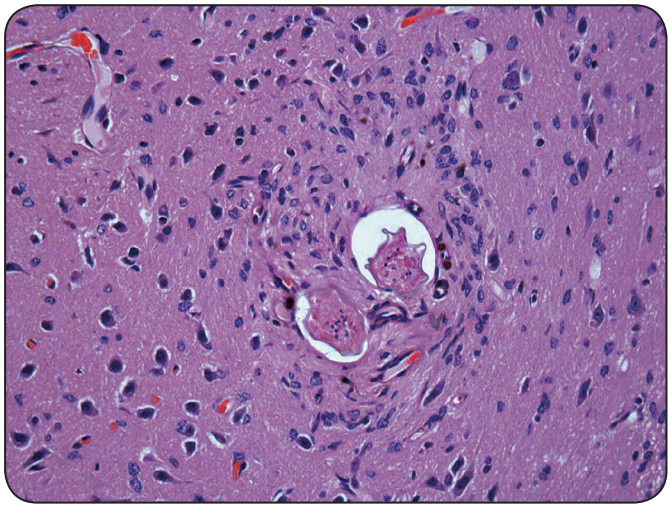

FIGURE 2 - Mouse 2. Two eggs containing miracidia and a small granuloma around the eggs (H&E, 400X).

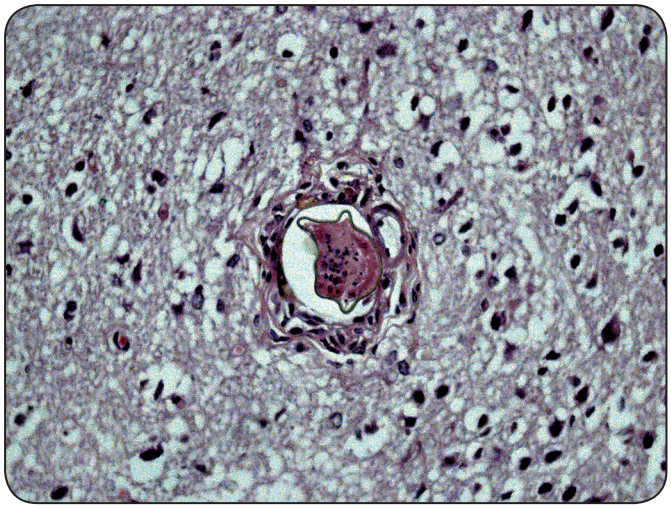

FIGURE 3 - Mouse 1. A perivascular *Schistosoma mansoni* egg containing a miracidium and surrounded by a small number of inflammatory cells in the brain (H&E, 400X).

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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