Brain Magnetic Resonance Imaging Findings in Young Patients with Hepatosplenic Schistosomiasis Mansoni without Overt Symptoms

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Abstract. The purpose of this study was to describe the brain magnetic resonance imaging (MRI) findings in young patients with hepatosplenic schistosomiasis mansoni without overt neurologic manifestations. This study included 34 young persons (age range = 9–25 years) with hepatosplenic schistosomiasis mansoni, who had been previously treated. Patients were scanned on a 1.5-T system that included multiplanar pre-contrast and post-contrast sequences, and reports were completed by two radiologists after a consensus review. Twenty (58.8%) patients had MRI signal changes that were believed to be related to schistosomiasis mansoni. Twelve of the 20 patients had small focal hyperintensities on T2WI in the cerebral white matter, and eight patients had symmetric hyperintense basal ganglia on T1WI. There was a high frequency of brain MRI signal abnormalities in this series. Although not specific, these findings may be related to schistosomiasis.

INTRODUCTION

According to the World Health Organization, schistosomiasis affects more than 200 million persons in several countries in Africa, Asia, or America and remains a major public health problem.1,2 Schistosomiasis is an infection caused by digenetic trematode platyhelminths of the genus Schistosoma, and the three main species are S. mansoni, S. japonicum, and S. hematobium.3,4 The species S. mansoni infects approximately 12 million persons in Brazil, which characterizes this country as an endemic area.5 The most severe presentation of the disease is hepatosplenic schistosomiasis mansoni (HSM), which is characterized by splenomegaly, perportal fibrosis, portal hypertension, and upper digestive bleeding caused by rupture of esophageal varices.6 Ectopic schistosomiasis infection of the central nervous system (CNS) is unusual. Cerebral lesions are caused primarily by S. japonicum, whereas spinal cord lesions are usually caused by S. mansoni and S. haematobium.7,8 In patients in Brazil with fatal HSM, autopsies showed that 26% have brain involvement.9

Reports of magnetic resonance imaging (MRI) findings associated with CNS schistosomiasis have described exsudative lesions with variable enhancement patterns, such as diffuse, spotty, nodular, or central linear and nodular.3,8–13 There have been some isolated reports of brain MRI findings in patients with schistosomiasis mansoni. However, these cases are usually found in symptomatic patients with the granulomatous form of the disease. No systematic brain MRI studies of patients with HSM have been published. The purpose of this investigation was to prospectively describe brain MRI findings in young patients with HSM without overt neurologic symptoms who had been previously treated.

MATERIALS AND METHODS

Thirty-four young outpatients (age range = 9–25 years, mean ± SD age = 16.5 ± 3.4 years) with the proven severe form of HSM were included in this investigation. Twenty-four (70.6%) patients were male and 10 (29.4%) were female. All patients came from a region hyperendemic for schistosomiasis mansoni, Zona da Mata, a sugar cane plantation area in the State of Pernambuco in northeastern Brazil, which had a prevalence greater than 25%. Diagnosis was established by a positive Kato-Katz test result or a quantitative oogram performed by using three rectal biopsy specimens and abdominal ultrasound examination, which demonstrated Symmers fibrosis grades II and III. These patients had been previously treated with oxamniquine (20 mg/kg, single dose) and had undergone splenectomy, ligature of the left gastric vein, and auto-implantation of spleen tissue into a pouch of the major omentum. Patient ages at the time of surgery ranged from 8 to 16 years. Post-operative rather than pre-operative patients were chosen because many of these young persons with severe HSM at Hospital das Clínicas da Universidade Federal de Pernambuco had already undergone surgery.

Patients with other hepatic diseases (cirrhosis, congenital hepatic fibrosis, hepatitis), history of alcoholism, prior neurologic diseases, hypertension or other vascular diseases, and those using any drugs with liver and/or brain toxicity were excluded. Persons with contraindications to MRI examinations were also excluded.

Neurologic assessment. All patients underwent neurologic evaluation by an experienced neurologist. They underwent a comprehensive neurologic workup that included a detailed history and neurologic examination and a battery of neuropsychologic tests including Kohs and Wechsler tests. The Kohs test is a block design test used to analyze the cognitive capacity of children and adolescents. It is used mainly to test persons with language or hearing handicaps. The Wechsler Intelligence Scales are a series of standardized tests used to evaluate cognitive abilities and intellectual abilities in children and adults.

Magnetic resonance imaging of the brain. The MRI scans were conducted by using a 1.5-T Philips (Amsterdam, The Netherlands) Gyroscan System using standard axial, sagittal, and coronal spin-echo, T1WI (repetition time = 500–562 milliseconds, echo time = 14 milliseconds) with a matrix size of 143–203 x 512 pixels, and a slice thickness of 5 or 6 mm, with an inter-slice gap of 0.5–0.6 mm. Axial and coronal turbo spin-echo T2WI (echo time = 90–100 milliseconds with a repetition time of 2,022–4,811 milliseconds) and axial fluid
attenuated inversion recovery (FLAIR) images (repetition time = 6,000 milliseconds, echo time = 100 milliseconds, inversion time = 2,000 milliseconds) were also obtained. After paramagnetic contrast administration (standard dose of 0.1 mmol/kg of body weight), axial and coronal SE T1WI were performed. Diffusion images were obtained for only three patients and all normal.

The MRI scan was interpreted by two radiologists who were experts in neuroradiology. Both examiners viewed the images together and reached a consensus before writing reports. Results were categorized as normal and brain MRI findings that could possibly be related to schistosomiasis. Brain MRI-unrelated abnormalities were not included in the analysis.

**Ethical considerations.** The recommendations of the World Health Organization and the Declaration of Helsinki (1975) in terms of protecting the rights and well-being of persons studied were followed. At the end of the study, all patients were informed about the results of the examinations and received appropriate recommendations, treatment, and referrals. The ethical committee of Hospital das Clínicas, Universidade Federal de Pernambuco approved this study. The patients and/or their parents signed a consent form after a full explanation of the study was provided.

**Data analysis.** Results are expressed by their frequencies in percentages.

**RESULTS**

At neurologic examination, all patients were oriented in time and space. There were no signs of acute encephalitis or encephalomyelitis. No signs of slow-expanding intracranial lesions (headache, seizures, papilledema, visual abnormalities, speech disturbances, sensory impairment, hemiparesis, nystagmus, ataxia) were seen.

None of the patients had clinical symptoms of hepatic encephalopathy. However, intelligence and cognitive evaluation showed abnormal Kohs test results for 27 (79.4%) patients and abnormalities in Wechsler test results for 7 (20.6%) patients. Liver function test results for each patient were normal at the time of the MRI examination.

**MRI of the brain.** Nine (26.5%) of the patients in this series had normal brain MRI examination results. Of the 34 MRI procedures conducted, 25 (73.5%) showed abnormalities on T1 and/or T2WI. However, only 20 (58.8%) demonstrated lesions that could be related to schistosomiasis, although no enhancement with contrast material (CM) injection was seen.

Eight (40%) of 20 patients with brain MRI signal changes possibly related to schistosomiasis showed on T1WI bilateral and symmetrical hyperintensities that were restricted to certain brain areas, particularly globus pallidus, cerebral peduncles, or both. A variable degree of hypersignal was noted in these patients. In addition, hyperintensity at the floor of the fourth ventricle was observed in two patients. There was no radiologic counterpart on T2WI for these abnormalities. Typical examples of these changes are shown in Figure 1. The pituitary gland appeared homogeneously hyperintense on T1WI in one patient (Figure 1D).

The MRI findings of the brain in 60% (12 of 20) of the patients with significant signal changes showed small focal T2 and FLAIR hyperintensities involving the cerebral white matter (Figure 2). These focal areas of T2 hyperintensities were predominantly seen in the frontal lobes (91.7%) and 54.5% were bilaterally distributed. The number of hyperintensities in each person varied from four to ten and their sizes were less than 1 cm. Three of these patients had concomitant bilateral and symmetrical hyperintensities on T1WI in the globus pallidus and cerebral peduncles.

Two patients showed involvement of the corpus callosum. One of them had a small oval lesion with low signal on T1 and FLAIR and high signal by T2WI.

The distribution of the frequencies of the brain MRI signal abnormalities is shown in Table 1. The distribution of the frequencies of the brain MRI findings according to their categorization is shown in Table 2.

**DISCUSSION**

Schistosomiasis is a widespread disease in the developing world and is one of the most important helminthic infections in terms of public health. Patterns of schistosomiasis infection are shaped by two factors: host exposure and host immunity. The conditions responsible for evolution to severe forms of the disease are not completely clear although parasite burden seems to be a major determinant.14

Involvement of CNS may be observed with any of the clinical forms of schistosomal infection. In almost all symptomatic cases of neuroschistosomiasis mansoni (NS), involvement of the CNS starts in the early stages of infection, during disease evolution to its chronic forms, or concomitantly with the chronic intestinal and hepatointestinal forms.3 In situ ova deposition after anomalous migration of adult worms appears to be the main, if not the only, mechanism by which S. mansoni may reach the CNS in patients with the intestinal and hepatointestinal forms of the parasitosis. The mass effect produced by the heavy concentration of ova and granulomas in circumscribed areas of the spinal cord and brain explains the severe neurologic symptoms observed in these patients.

Although more frequent, CNS involvement associated with the hepatosplenic and cardiopulmonary forms is almost always asymptomatic. The random distribution of ova in the CNS of patients with these forms suggests that ova are carried there mainly as emboli by the arterial system or through retrograde venous flow.3,4,8,15,16 Because of the discrete inflammatory reaction elicited by the sparsely distributed ova, neurologic symptoms attributable to ova deposition are not present in most neuroschistosomiasis mansoni patients with the hepatosplenic and cardiopulmonary forms.7,15–17

To the best of our knowledge, this investigation reports the largest number of HSM patients studied with brain MRI signal abnormalities. Every patient included in this study had been previously treated and none had any neurologic complaints. None of them had brain MRI abnormalities consistent with the tumoral form of cerebral schistosomiasis. The images did not reveal abnormal enhancement after the administration of the paramagnetic contrast material.

The few reported cases of cerebral schistosomiasis showed expansive lesions with surrounding edema and nodular, ring, or heterogeneous enhancement, and in some cases an arborized appearance. All patients had neurologic manifestations.4,9,13,16,18,19

There are no published reports addressing brain MRI findings in persons with HSM with or without neurologic manifestations. However, many investigations in which brain MRI
findings were obtained were conducted with patients with cirrhosis, including persons with hepatic encephalopathy, and with children with congenital portal-systemic encephalopathy (PSE). The MRI results showed typical neuroradiologic findings of PSE characterized by bilateral and symmetrical T1-weighted hyperintensities, particularly in the basal ganglia of these patients. The exact mechanism of hepatic encephalopathy and abnormal MRI findings is not clear, and the pathogenesis remains unknown. It was initially proposed that these findings were caused by increased levels of serum ammonia.

Presently, the most widely accepted hypothesis for the hyperintensity of the basal ganglia seen on T1-weighted MRI in patients with PSE is deposition of manganese. Manganese is a paramagnetic transitional metal that is able to promote T1 shortening in MRI examinations, and several studies have supported the manganese hypothesis. The T1-weighted high signal intensity of the globus pallidus was
observed in 40% (8 of 20) of the patients with significant brain MRI signal abnormalities in this group and concomitant involvement of the cerebral peduncles was seen in six patients. A variable degree of hyperintensity was detected with higher signal in some cases. There has been a case report of schistosomal PSE in a young woman in Brazil in whom MRI showed high signal on T1WI in the globus pallidus, subthalamic regions, and cerebral peduncles.32

Although the patients described in this series had similar MRI findings, none had any neurologic manifestations and none had abnormal liver function test results. Liver function test results may be almost completely within normal limits or only slightly abnormal despite liver involvement in patients with HSM.35 Thus, based on review of medical literature, it is possible that the same pathogenesis may be implicated in the finding of T1-weighted hyperintensity in the basal ganglia in eight patients in this study, although serum manganese levels were not measured. To support this hypothesis, it would be necessary to include serum manganese levels and/or neuropathologic studies. Proton magnetic resonance spectroscopy could also be useful.

The most frequent MRI findings in the present series were small focal T2 and FLAIR hyperintensities involving the cerebral white matter, predominantly in the frontal lobes. This finding was observed in 60% (12 of 20) of the abnormal MRI results believed to be related to schistosomiasis. These lesions are not specific and can be related to ischemic changes, gliosis, or demyelinating diseases.

There have been few MRI studies describing the occurrence of T2 hyperintensities in the cerebral white matter in patients with chronic hepatic encephalopathy. One study that correlated MRI results with histologic findings in two patients with chronic hepatic encephalopathy showed astrocytic gliosis and perivascular cuffing in the cerebral white matter.

Table 1

<table>
<thead>
<tr>
<th>Image description</th>
<th>No.</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>T1-weighted bilateral and symmetrical hyperintensities</td>
<td>8†</td>
<td>40.0</td>
</tr>
<tr>
<td>Globus pallidus</td>
<td>7/8</td>
<td>87.5</td>
</tr>
<tr>
<td>Cerebral peduncle</td>
<td>7/8</td>
<td>87.5</td>
</tr>
<tr>
<td>Floor of the fourth ventricle</td>
<td>2/8</td>
<td>25.0</td>
</tr>
<tr>
<td>Pituitary gland</td>
<td>1/8</td>
<td>12.5</td>
</tr>
<tr>
<td>Focal T2 and FLAIR hyperintensities</td>
<td>12†</td>
<td>60.0</td>
</tr>
<tr>
<td>Bilateral white matter</td>
<td>6/12</td>
<td>50.0</td>
</tr>
<tr>
<td>Unilateral white matter</td>
<td>6/12</td>
<td>50.0</td>
</tr>
<tr>
<td>Corpus callosum</td>
<td>1/12</td>
<td>8.3</td>
</tr>
<tr>
<td>Oval lesion with high signal on T2 and low signal on T1 and FLAIR involving the corpus callosum</td>
<td>1†</td>
<td>5.0</td>
</tr>
</tbody>
</table>

* FLAIR = fluid attenuated inversion recovery.
† Some patients showed concomitant MRI findings.

Table 2

<table>
<thead>
<tr>
<th>Result</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>9</td>
<td>26.5</td>
</tr>
<tr>
<td>MRI findings that could possibly be related to schistosomiasis</td>
<td>20†</td>
<td>58.8</td>
</tr>
<tr>
<td>Focal T2 and FLAIR hyperintensities involving the cerebral white matter (unilateral or bilateral)</td>
<td>12</td>
<td>60</td>
</tr>
<tr>
<td>T1-weighted bilateral and symmetrical hyperintensities particularly restricted to globus pallidus and cerebral peduncles or both. Oval lesion with high signal on T2 and low signal on T1 and FLAIR involving the corpus callosum</td>
<td>8</td>
<td>40</td>
</tr>
</tbody>
</table>

* MRI = magnetic resonance imaging; FLAIR = fluid attenuated inversion recovery.
† Some patients showed concomitant MRI findings.
autopsy-proven cases of chronic hepatic encephalopathy demonstrated that cortical hyperintensities on T2-weighted images represented pseudolaminar spongy degeneration in the deep layers of the cerebral cortices, and hyperintensities in the cerebral white matter represented tissue rarefaction associated with loss of myelin and axons. 36 It has also been reported that T2 hyperintensities in the cerebral white matter found in patients with liver cirrhosis can normalize after successful liver transplantation, suggesting that they may reflect mild edema. 24,36,37 The hyperintense lesions seen on T2 and FLAIR in these patients could also reflect mild edema or loss of myelin and axons, although the patients were much younger than patients reported in the literature and none of them had clinical signs of hepatic encephalopathy. However, we cannot exclude the possibility that these brain MRI changes may also have been caused by scattered isolated Schistosoma ova in nervous tissue and by the discrete inflammatory reaction surrounding the ova. Although this series included only post-operative patients, it seems less likely that these brain findings could be caused by surgery. All studies were conducted at least one year after surgery and most of them many years after surgery. This surgical approach has been shown to decrease portal hypertension and to maintain the hepatic functional reserve.

An association of schistosomiasis and endomyocardial fibrosis or cardiomyopathy has been suggested. 38,39 It seems less likely that the lesions found in 12 patients in this study could be caused by microembolism related to endomyocardial fibrosis in the context of S. mansoni infestation.

There is a reported case of cerebral schistosomiasis caused by S. hematobium in a man who showed by computer tomodraphy and MRI a cortical oval lesion in the left occipital lobe, which appeared to be a cyst. 18 An oval lesion similar to this description was detected in the corpus callosum in one patient and could also be associated with schistosomiasis mansoni. Cognitive functions were affected in some of these patients, suggesting a possible association with brain MRI changes. However, no conclusions can be drawn from this study because of lack of an age-matched control group and the fact that educational level and nutritional status of the patients could have influenced the results.

There was a high frequency of brain MRI signal abnormalities in young patients with HSM without overt neurologic manifestations. These findings are not commonly seen in healthy young persons, suggesting that there may be a relationship between these abnormalities and schistosomiasis, and that this relationship may be found even in patients without liver dysfunction.

It was not possible to determine if the lesions were the result of hemodynamic disorders, metabolic changes, deposition of eggs, or deposition of immune complexes. Further studies including an age-matched control population are necessary for proper interpretation of the MRI results.

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REFERENCES


