DOI: 10.1590/0004-282X20130157

Mansonic neuroschistosomiasis

Neuroesquistossome mansônica

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ABSTRACT

Mansonic neuroschistosomiasis (MN) is not only the most common but also the most serious ectopic presentation of the infection by *Schistosoma mansoni*. Both, brain and spinal cord can be independently affected by the infection, but the later is more frequently affected. Brain MN by itself is due to the presence of eggs and/or adult worms *in situ* and can be symptomatic or asymptomatic. Unlike the brain MN, spinal cord mansonic neuroschistosomiasis is more frequently symptomatic. In both forms the intensity, the seriousness and also the clinical characteristics of signs and symptoms depend on the amount of eggs in the compromised region and on the intensity of the inflammatory reaction surrounding the eggs. Cerebrospinal fluid examination and magnetic resonance imaging are important diagnostic tools. Both corticosteroids and drugs against *S. mansoni* are used in the treatment. The outcome may largely depend upon the prompt use of these drugs.

Keywords: *Schistosoma mansoni*, neurological involvement, brain, spinal cord, inflammatory reaction.

RESUMO

A neuroesquistossome mansônica (NM) é não apenas a mais comum, mas também a mais grave apresentação da infecção pelo *Schistosoma mansoni*. Tanto o encéfalo quanto a medula podem ser independentemente afetadas pela doença, embora a última o seja de forma mais frequente. A NM encefálica é secundária à presença dos ovos e/ou da forma adulta do verme *in situ*, e pode ser sintomática ou não. Ao contrário da forma encefálica, a NM medular é mais frequentemente sintomática. Em ambas as formas a gravidade dos sintomas dependerá na quantidade de ovos na região comprometida e na intensidade da reação inflamatória ao seu redor. Os exames do líquido cefalorraquiano e de imagem por ressonância magnética são importantes ferramentas diagnósticas. Corticosteróides e drogas parasiticidas são usadas no tratamento desta doença, e seu prognóstico dependerá diretamente do rápido uso destas drogas.

Palavras-Chave: *Schistosoma mansoni*, comprometimento neurológico, encéfalo, medula, reação inflamatória.

Mansonic neuroschistosomiasis (MN) is not only the most common but also the most serious ectopic presentation of the infection by ***Schistosoma mansoni***[1] which is a digenetic trematode and the only natural inhabitant of the mesenteric veins of human beings. Both, brain and spinal cord can be independently affected by the infection. The involvement of the central nervous system (CNS) can occur at any time from the beginning of the egg spawn and can be symptomatic or asymptomatic. The involvement of the spinal cord is more frequent.

In patients with mild forms of the infection by ***S. mansoni***, it means the intestinal and the hepatointestinal forms, the anomalous migration of worms in copula to sites next to the CNS promoting the deposition of many eggs into an restrict area of the CNS, or followed by egg spawn in situ[2] (when the worms themselves reach the CNS), or the occurrence of massive embolization of eggs from the mesenteric portal venous system to the CNS are the most important mechanisms for the establishment of symptomatic MN. In both cases the worms or the eggs reach the CNS through the retrograde venous flux in the Batson's venous plexus, which has no valves and links the portal venous system and the inferior caval vein to the veins of the spinal cord as well as of the brain. Concomitantly or right after the acute or toxemic form of schistosomiasis (Katayama Syndrome), although rarely, encephalitis[3] or encephalomyelitis can occur as part of the acute manifestation of the infection. At this phase, vasculitis of the CNS can also occur.

Brain MN by itself is due to the presence of eggs and/or adult worms in situ. As aforementioned it can be symptomatic or asymptomatic. The presence of clinical symptoms depend upon the amount of eggs in an delimited region of the brain, the intensity of the inflammatory reaction surrounding the eggs and/or worms, the location of the lesion and whether there is mass effect or not. Seizures (partial or generalized), signs and symptoms of intracranial hypertension, focal signs (in the pseudotumoral form), acute headache, visual disturbances, as well as brain and meningeal hemorrhage can also occur. Headache, ataxia, nystagmus, nausea and vomiting are present in the pseudotumoral forms of the cerebellum. The asymptomatic form of brain MN is more frequently

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associated with the more serious forms of schistosomiasis, which are the hepatosplenic and the cardiopulmonary, but mainly with the latest. In these forms of the disease eggs have access to the brain through the arterial system via pulmonary arterial-venous shunts formerly formed or through portal-pulmonary anastomosis via the azygus vein, or through the Batson's venous plexus as described above, adding the fact that the presence of portal venous hypertension facilitates the opening of the anastomosis that link the spinal and cerebral vein to the portal venous system. Portal-pulmonary anastomosis trough the azygus veins allow eggs and adult worms to reach the lungs from where they can via the pulmonary veins reach the CNS as arterial embolus. The scattered distribution of eggs in the brain of these patients shows that the embolization of isolated eggs is the most frequent way of invasion of the CNS by the *S. mansoni* in the serious forms of schistosomiasis. The scattered distribution of eggs, associated to a discrete inflammatory reaction toward them, explain the absence of symptoms, though they can be cause of seizures.

Unlike the brain MN that is usually asymptomatic, spinal cord mansonic neuroschistosomiasis (SCMN) is more frequently symptomatic. At first regarded as a rare condition, SCMN has been increasingly diagnosed in patients from endemic areas for schistosomiasis. Nonetheless, the real epidemiological importance of this disease is still unknown. It is certainly underestimated due to the lack of clinical recognition and diagnostic difficulties. SCMN compromises more frequently male young adults whom have intestinal or hepatointestinal schistosomiasis in their labor phase of life. When it is neither early diagnosed nor properly treated, very likely the patients will develop irreversible sequels that leads to personal, familial as well as social damages, not to mention those damages to the labor force. In terms of frequency, the next groups most affected are male teenagers and male children. Probably the explanation for this fact relies on the greater exposition of young males to water activities and male work characteristics, such as farming, agriculture, husbandry, land cultivation and field work in contact with infected water in the country side.

The intensity, the seriousness and also the clinical characteristics of signs and symptoms in SCMN depend on the amount of eggs in the compromised region of the spinal cord, on the intensity of the inflammatory reaction surrounding the eggs, and on the location in the spinal cord. The clinical spectrum varies from mild to very serious forms and even sub-clinical or asymptomatic ones. Both the intensity and the seriousness of the signs and symptoms can vary in a patient during the evolution of the disease.

According to clinical signs and symptoms SCMN can be classified or divided into three different clinical forms(1): spinal, myeloradiculopathic and conus/cauda equina syndrome. In the spinal form the spinal cord is predominantly compromised. Moreover it is the most serious among the three forms and related to the poorest prognosis. In the myeloradiculopathic form, both spinal and nerve roots manifestations occur in association. In the conus/cauda equina syndrome form the outcome is more favorable. The myeloradiculopathic form is the most frequent whereas the cone cauda equina is the less. The former form can become worse and therefore turn from one form into another (from myeloradiculopathic to spinal).

Unlike the patients who have brain MN, the patients who have SCMN seldom present clinical evidence of abdominal schistosomiasis. Visitors to endemic areas for schistosomiasis considered ***naïve*** may develop SCMN during the acute phase of schistosomiasis when there is massive infection by *S. mansoni*.

SCMN diagnosis is presumptive and relies on epidemiological, clinical, imaging and laboratory grounds. Proof of infection by *S. mansoni* by stool examination and/or rectal biopsy as well as ruling out other possible causes of myeloradiculopathy are necessary. On the other hand it is important to keep in mind that idiopathic compromise of the spinal cord is not infrequent, and therefore any patient who has schistosomiasis can develop such condition. The classical clinical triad of SCMN is composed by lumbar and/or lower limb pain, vesical disfunction and weakness of the legs. Any patient presenting these symptoms must be investigated for SCMN. The installation of the clinical picture can be acute or subacute. Usually the patients present lumbar pain followed by urinary retention and thereafter weakness of the legs. Paresthesias, paraplegia, fecal disfunction, sexual disfunction, exacerbation or diminishment of deep tendinous reflexes may also occur[1,4,5].

CSF examination is important in SCMN for two reasons: at first suggestive alterations although not specific are present in most patients, and secondly it can identify clinical conditions that can mimic SCMN such as HAM/TSP, syphilis, *C. neoformans* myeloradiculopathy, spinal infiltration by leukemias, lymphomas or solid tumors, and bacterial myelitis. Moderate lymphomononuclear pleiocytosis, presence of eosinophils, hyperprotein concentration from discrete to moderate and IgG antibodies against *S. mansoni* are present in the CSF of the majority of patients. Currently there is no commercial test available to confirm SCMN diagnosis[6].

MRI also shows alterations in the majority of these patients. Spinal cord swelling in T1; hyper intensity in T2; heterogeneous captation of the contrast showing small focal areas more intensely contrasted in T1 forming a granular pattern can be observed. The so-called 'characteristic' (but not 100% specific) MRI image of SCMN comprises linear central lesion surrounded by multiple small nodules giving an arboreal appearance though less specific images may also occur[7-10].

Both corticosteroids and drugs against *S. mansoni*, particularly praziquantel, are used in the treatment. As soon as a reasonable suspicion of SCMN is done, the introduction of corticosteroids must be initiated even before CSF and MRI results. The outcome may largely depend upon the prompt use of these drugs because of their antiinflammatory action. The most reasonable scheme is to initiate metilprednisolone (15 mg/Kg/day for 5 days, maximum dose 1 gr/day) divided into 2 doses, followed by prednisone (1,5 to 2,0 mg/Kg/day) divided into 3 doses for 3 to 4 weeks, followed by gradual reduction to one daily dose until completely discontinuing it in 3 to 4 months. Prednisone alone can also be used and it is especially indicated for outpatients. The rationale for this scheme relies on the fact that the life span of the embryo inside the egg is 18 to 20 days at maximum, the peak of inflammatory reaction (characterized by the granuloma maximum volume) around the egg occurs in 4 to 8 days and then diminishes gradually[1]. The complete resolution takes at least 3 months. After the demonstration of *S. mansoni* infection the use of praziquantel is indicated (60 mg/Kg/day during 3 days, divided into 2 daily doses, with a 4 hour interval between them, being 15 g the maximum dose).

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