

SPINAL CORD SCHISTOSOMIASIS IN CHILDREN

Analysis of seven cases

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ABSTRACT - We describe seven cases of children (ages 2 to 14 years) with myeloradiculopathy caused by infection with *S. mansoni*. None of them presented hepatosplenic involvement and one presented an intestinal picture. The myeloradicular and pseudotumoral forms were observed in four and three patients, respectively. Comparing the reports in the literature, we found that the pseudotumoral form is more similar frequent among children than in adults, while the myelitic and myeloradicular forms are the most frequent and distributed across all age groups. Diagnosis is based on clinical and epidemiological findings in association with laboratory tests. The diagnosis was confirmed by the presence of *S. mansoni* eggs in feces (5 cases) and / or the positivity in specific immunological tests (5 cases) associated with a cerebrospinal fluid inflammatory pattern with presence of eosinophils (between 1 and 24%). Magnetic resonance image, although it does not enable an etiological diagnosis, helped to confirm the form and spinal cord level of the lesion.

KEY WORDS: schistosoma mansoni, spinal cord schistosomiasis, schistosomal myelopathy, myelitis, spinal-cord pseudotumor, child.

Esquistossomose medular em crianças: análise de sete casos

RESUMO - Relatamos sete crianças com mielorradiculopatia devida a infecção pelo *S. mansoni*, com idade entre 2 e 14 anos. Nenhuma apresentou acometimento hepatoesplênico e uma apresentou quadro intestinal. A forma mielorradicular foi observada em quatro pacientes e a pseudotumoral em três. Revendo os achados da literatura, encontramos que a forma pseudotumoral é mais frequente nas crianças que nos adultos, apesar das formas mielíticas e mielorradiculares serem ainda as mais frequentes em todas as idades. O diagnóstico baseou-se nos achados clínicos e epidemiológicos, associados aos laboratoriais. A presença de ovos de *S. mansoni* nas fezes (5 casos) e/ou a positividade de testes imunológicos específicos no líquido cefalorraquidiano (5 casos), com padrão inflamatório e eosinofilia (entre 1 e 24%) confirmou o diagnóstico. O estudo da imagem de ressonância magnética, apesar de não permitir o diagnóstico etiológico, ajudou a confirmar a forma e o nível medular da lesão.

PALAVRAS-CHAVE: esquistossomose mansoni, esquistossomose medular, mielopatia esquistossomótica, mielite, pseudotumor medular, criança.

Schistosomiasis mansoni (SM) is endemic in several areas of Brazil, affecting about 3 million people and exposing another 25 million to risk, characterizing the country as the main epidemic area of the Americas and one of the main epidemic regions in the world^{1,2}. The prevalence of oviposition in the central nervous system (CNS) varies among studies from 0.3 to 30 percent of infected individuals³⁻⁵. It is generally myeloradicular and occasionally encephalitic, as opposed to *Schistosomiasis japonica* in which encephalitic involvement is more frequent. Many patients remain asymptomatic. Spinal cord schisto-

somiasis (SCS) is one of the most frequent causes of non-traumatic myelopathies, responsible for 6% of these in endemic areas⁶.

Vascular lesions caused by SM appear to be responsible for the neurological sequels. Vascular obstruction in the spinal cord (SC) is secondary to the formation of a granuloma, with an intense inflammatory reaction and ischemic necrosis, even in some cases where eggs are not found in the nervous system⁷.

Two mechanisms have been proposed to explain the involvement of the nervous system by SM: a)

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increase in the intraabdominal pressure allows a retrograde venous flow through a venous plexus, leaving the SM eggs. This venous plexus, Batson system, is a valve-free venous system connecting intraabdominal and spinal veins. As this system only links the drainage of the lower SC, it could explain the predilection of myelitis for the lower levels⁸; b) elimination of eggs directly inside the vessels, due to the anomalous migration of adult worms; this hypothesis is strengthened by the occasional finding of adult worms and eggs in a row inside vertebral vessels^{9,10}. The extension of the lesions depends on the degree of infestation and the host's immunologic response. The interval between the supposed infestation and onset of the spinal cord picture varies from several days up to 6 years¹¹.

Muller and Stender in 1930¹², described the first case of SCS related to SM in a patient, with clinical manifestations of transverse myelitis that had lived some years in Brazil. The first report of SCS in Brazil was made by Gama and Sá in 1945¹³ and to date no more than 200 cases have been described, it is believed that this is an under-diagnosed condition. As a rule, most of the series show prevalence in adults ranging from 24 to 40 years¹⁴.

SCS in children is more rarely referred and the first description dates back to 1957¹⁵. We report on seven cases of SCS in children.

METHOD

Seven patients with diagnosis of SCS at the Instituto da Criança, Hospital das Clínicas, São Paulo University, between 1981 and 2000 were studied. Data regarding the laboratorial aspects are presented in Table 1.

A current revision of the Brazilian and international

literature, by Index-Medicus and Latin-American Index-Medicus, found 50 cases of SCS in children^{7,14-33} and the adult patients series by Galvão¹¹ and Peregrino et al²⁶ were compared with the authors' findings.

Case 1. (PAS). A female patient, three years old, born and resident in the rural zone of Teixeira de Freitas, Bahia State, presented a picture which began suddenly with fever, diarrhea, abdominal colic and pain in the lower right member, coursing to difficulty in walking and within several days she was completely non-ambulatory. The patient was transferred to the Instituto da Criança after three months evolution. The pre and perinatal antecedents showed no pathological data; her parents and brother were healthy and she had an uncle with a history of tuberculosis. Physical examination revealed: weight 11 kg, regular general state, discolored mucous membranes, afebrile and without visceromegaly. On neurological exam, the patient was conscious, well in-touch with her surroundings although not very collaborative; she presented asymmetrical crural paraparesis, with right-side prevalence of the deficit, exacerbation of myotatic reflexes, clonus of feet and bilateral Babinski's sign. Radicular signs were present with positive Lasègue's sign and sensitivity apparently preserved. The patient was medicated with oxaminiquine (20mg/kg) and prednisone (2 mg/kg/day), remaining hospitalized for 27 days. She coursed with partial improvement of the deficit, however we have no data for subsequent follow up.

Case 2. (ASS). A male patient, aged 6 years, coming from the rural area of Jequié, Bahia State. The neurological picture which began 15 days before internment in the Instituto da Criança, was characterized initially by pain in the legs that made walking difficult and progressed to complete walking incapacity on the 7th day and onset of sphincter incontinence on the 10th day. The pre-and

Table 1. Diagnostic tests.

Case	1	2	3	4	5	6	7
Blood							
Eosinophils	1%	12%	11%	1%	3%	1%	9%
IF	+	+
ELISA	...	+	-	+	+
Fecal exam	+	+	-	+	-	+	+
CSF							
Leukocytes (cell/mm ³)	265		90	40	50	638	37
Lymphocytes (%)	69		92	42	95	70	78
Neutrophils (%)	30		3	34	1	16	12
Eosinophils (%)	1		1	24	4	14	-
Protein (mg/dl)	140		230	40	106	78	43
ELISA	...	+	+	+	...	+	+
IF	+
ID	...	+
MRI	Enlarged spinal-cord, T12-L1, contrast enhancement	...	Spinal-cord tumor, T11-L1, contrast enhancement; hydromyelia	Enlargement conus, contrast enhancement; hydromyelia	Spinal-cord tumor, T10-L3.	Normal	Enlarged spinal-cord (T-L)

CSF, cerebral spinal fluid; MRI, magnetic resonance imaging; ELISA, enzyme-linked immunosorbent assay; IF, Immunofluorescence-reaction; ID, intradermic-reaction; T, thoracic; L, lumbar; +positive, - negative; ... not performed

perinatal conditions as well as the neuropsychomotor development were normal and both parents and two siblings were healthy. Physical exam showed patient weighting 20 kg, in good state. Abdominal palpation revealed the presence of distended urinary bladder and in the sacrolumbar area there was paravertebral tumor to the right, with cystic consistence, 2 by 5 centimeters in diameter, painless and without signs of inflammation. At the neurological exam, the patient was conscious, in good contact and collaborative during the exam. The exam showed presence of symmetric flaccid crural paraparesis, with areflexia, and he only just managed to overcome gravity. No pyramidal release signs were detected. The exam revealed a sensibility level between D12-L1. The patient was medicated with oxaminiquine (20 mg/kg) and prednisone (2 mg/kg/day), remaining hospitalized for 26 days and then returning to his city of origin. No data is available regarding his progress.

Case 3. (DVNS). A male, 12 years old, born in the rural area of Ubaitaba, Bahia State and living in São Paulo for one year. The patient was healthy with adequate neuropsychomotor development and without relevant data in the family history. The neurological picture had a sudden onset, 3 weeks before hospitalization, with a loss of strength in the lower members and urinary retention. He presented at a hospital service, where after cerebral spinal fluid (CSF) exam he was medicated with oral dexamethasone for one week with improvement of the picture. After suspension of the medication he presented motor difficulties again and was then hospitalized in the Instituto da Criança. Physical exam showed: 33.8 kg weight, patient in good general state, normal complexion, hydrated and without visceromegaly. At neurological exam he was conscious, active and cooperative. The exam revealed a flaccid crural paraparesis with distal prevalence, asymmetrical and the most important deficit to the left, with abolished Achilles tendon reflexes and hypoactive patellar reflexes. The presence of radicular signs and retained sensibility were also observed. During the evolution he presented signs of neurogenic bladder. Due to the tumorous aspect shown by magnetic resonance imaging (MRI), laminectomy was performed with biopsy of nervous roots showing a chronic granulomatous inflammatory process and the presence of *S. mansoni* eggs. He was then medicated with oxaminiquine (20 mg/kg single dose) associated with dexamethasone initially and later prednisone. He progressed well with complete functional recovery and at the 7th month of follow-up he still maintains the Achilles tendon reflex abolished to the left.

Case 4. (LFAS). A male, 11 years old, born and resident in São Paulo, São Paulo State but had lived in Recife, Pernambuco State, for 2 years. The patient initially presented difficulty in walking with urinary and fecal incontinence 10 days before hospitalization in the Instituto da Criança. The personal, pathological and familial anteced-

ents did not show any relevant data. Physical exam showed an adolescent in good state, normal complexion, 23.6 kg weight, without visceromegaly. At neurological exam the patient was conscious, in good contact and collaborative. The exam revealed flaccid areflexic crural paraparesis, discreetly asymmetrical, with the most important deficit on the right. There was a radicular picture with bilateral Lasègue's sign. The sensibility exam was normal. The patient was medicated with oxaminiquine and prednisone with progressive improvement of the neurological picture. In the 3rd month after treatment the patient was shown to be functionally normal and with normal neurological exam.

Case 5. (HRCF). A male, 2.5 years old, born and resident in the rural area of Inhapim, Minas Gerais State. The neurological picture had begun 30 days before hospitalization with pain in the right lower member, accompanied with urinary and fecal sphincter disturbance developing with ambulatory stoppage in 7 days. No relevant data was found in the pre- and perinatal antecedents, neuropsychomotor development and family history. Physical exam showed 16.5 kg weight, good general state, normal complexion and without visceromegaly. On neurological exam the patient was conscious with good contact and collaborative. The exam detected flaccid areflexic crural symmetric paraparesis, without pyramidal and / or radicular signs. The sensitivity exam showed complete anesthesia below D10. He presented neurogenic bladder and fecal incontinence. Due to a possible neoplasia, laminectomy was performed on the 13th day of hospitalization and the biopsy showed granulomatous tissue and *S. mansoni* eggs. He was then medicated with oxaminiquine (20 mg/kg single dose) and dexamethasone during several months. Six months after the onset of the picture, he presented independent walk, although with claudication and still maintains the sphincter disturbance.

Case 6. (TAF). A male, aged 14 years, born in Londrina, Parana State, and resident in São Paulo, São Paulo State. He presented a clinical picture that had a sudden onset with pain and loss of strength in the left lower member and 3 days later he presented urinary retention. The pre- and perinatal antecedents and neuropsychomotor development were normal. Both parents and sister were healthy and the patient had traveled to an endemic area of schistosomiasis 10 months before the beginning of the picture. The physical exam showed the patient with 45.8 kg, good general state, normal complexion, afebrile and without visceromegaly. The neurological exam showed a conscious and collaborative adolescent. The exam detected flaccid distal right crural monoparesis and with Achillean areflexia, without pyramidal and / or radicular signs. The sensitivity exam did not reveal any alterations. He presented neurogenic bladder but without fecal incontinence. He was medicated with oxaminiquine (20 mg/kg, single dose) and prednisone for 85 days, with clinical improvement. The

neurological evaluation 2.5 months later showed him to be functionally normal and with a normal neurological exam.

Case 7. (FS). A male, aged 10 years, born and resident in the rural area of Divisa Alegre, Minas Gerais State. He presented an acute onset of pain and loss of strength in the legs, more intense on the right side, associated with urinary retention. No relevant data was found in the pre- and perinatal antecedents, neuropsychomotor development and family history. Physical exam showed 31.7 kg weight, good general state, normal complexion and without visceromegaly. On neurological exam the patient was conscious with good contact and collaborative. The exam detected flaccid areflexic crural asymmetric paraparesis (more intense on the right), with radicular signs and without pyramidal signs or sensitive level. He presented neurogenic bladder but without fecal incontinence. He was medicated with oxaminiquine (20 mg/Kg, single dose) and prednisone for 54 days, with clinical improvement. The neurological evaluation 2 months later showed him to be functionally normal afterwards he still maintained the Achilles tendon reflex abolished to the right.

DISCUSSION

SCS presents in three clinic forms: myelitic form, which is the most frequent; granulomatous or pseudotumoral form; and radicular or myeloradicular form^{8,11}. It is also accepted the occurrence of asymptomatic forms of SCS, the diagnosis of which has been realized through necropsy studies, are 3 to 4 times more common than the symptomatic form^{3,14}. On our review of the literature, we found 25 cases in children with the myelitic or myeloradicular form (67.6%) and 12 cases of the tumoral form (32.4%). This ratio was similar to our cases, where four patients (57.1%) presented the myelitic form (Cases 1,2,4 and 6) and three (42.9%) the pseudotumoral form (Cases 3, 5 and 7). In an adult series, Galvão et al⁵. found a higher predominance of the myelitic form (20 cases out of 32; 62.5%) and myeloradicular forms (18 cases; 56.25%) against the pseudotumoral (3 cases; 9.37%) and radicular (1 case; 3.12%) forms. Salomão et al. in 1987³⁴, reviewing 30 cases of pseudotumoral form found that 10 cases occurred in patients under the age of 20 years. These data could indicate a predominance of the pseudotumoral form in children, possibly related to the immunological state of the host.

Most patients have no clinical evidence of hepatosplenic schistosomiasis and the diagnosis is often made following SC damage. In adult series we found

different results. Peregrino et al.²⁶, in an endemic area, found only 1 case in 21 patients as opposed to 10 cases in 32 patients, at a reference hospital, described by Galvão et al.⁵. Hepatosplenic involvement was referred in just 4 children in the literature^{14,28} and was not observed in our patients, however one case (Case 1) presented intestinal disturbances and fever at the beginning of the picture, enabling the intestinal form of schistosomiasis.

The most frequently affected SC levels are the lower thoracic / sacrolumbar, conus medullaris, and cauda equina. Among children, the topography of the lesion was thoracic in 12, thoracic-lumbar in 5, lumbar in 10 and cauda equina in 2. Among our patients, although only using neurological exam, 2 patients presented evident signs of sensibility level (Cases 2, 5 and 7). MRI study allowed localization of injury in the thoracic-lumbar area in 5 cases (Cases 1,2,3,5 and 7) and in the cauda equina in 1 (Case 4).

Affected patients present acute or subacute onset (3 and 4 of our patients, respectively). Of the 50 cases of SCS in the pediatric age group we found reports of the clinical course in 45 patients and of these, 35 presented partial or total improvement; in 11 patients the neurological picture remained unchanged and one patient died from the condition. Among our patients, the clinical course was favorable, with re-establishment of total functional in 2/6 patients (cases 4 and 6); 4/6 patients (cases 1,3, 5 and 7) presented a partial re-establishment. In one case (patient 2), we have no follow-up data. Among our cases we observed a tendency for a worse prognostic in those with the pseudotumoral form (3/3) when compared with the myelitic and myeloradicular forms (0/2).

The diagnosis of SCS in the present series of patients was suspected through the clinical picture associated to a positive epidemiological history. The presence of elevated number of eosinophiles in peripheral blood and CSF associated with increased protein, mainly gammaglobulin were the central feature of these cases, but those findings are not specific and can be presented in many other inflammatory and neoplastic conditions as in other helminthic infections. A positive test for serum anti-schistosomal antibodies proves only that the patient has been exposed to schistosomes. The CSF immunological tests and detection of SM eggs in stool enabled confirmation of the diagnosis in all patients^{20,35,36}.

Fecal smear examination, including quantitative Kato-Katz oogram, should be performed in all pa-

tients suspected of SCS. A single examination has a sensitivity of only about 50 percent¹⁴, but repeated examinations can improve the sensitivity. Stool examinations for SM eggs accomplished in all patients of our series were positive in 5 patients (cases 1, 2, 4, 6 and 7). Among the children described in the literature review, it was described in 28 patients and was negative in 6 patients, similar results were found in adult series (12 positive results in 21 patients according to Peregrino et al.²⁶ and 13 positive results in 32 patients according to Galvão et al.⁵). Thus, the absence of SM eggs in stool does not exclude a SCS diagnosis. Rectal biopsy for eggs is more sensitive (14 positive results in 15 exams according to Galvão et al.⁵ and 10 positive results in 11 exams according to Peregrino et al.²⁶), and should be performed when the stool examinations are negative.

Livramento et al.²⁰ described a CSF pattern in SCS, with a mild lymphocytic pleocytosis with eosinophiles, elevated protein level, and low or normal glucose level. Among the pediatric SCS cases in the literature, we found description of CSF in 44 cases, and in none of these the CSF findings were absolutely normal. Pleocytosis was found in 39 cases, varying between 6 and 1,000 cells/mm³, being mild (between 4 and 10 cells/mm³) in 4, moderate (between 10 and 50 cells/mm³) in 13, intense (between 50 and 200 cells/mm³) in 12 and severe (above 200) in 8 cases. Eosinophiles in CSF were observed in 20 cases, and this value varied between 1 and 56% of the leukocytes. Elevated CSF protein level was the most frequent abnormality, absent in three cases, varying between 50 and 4,600 mg/dl, could be classified as mild (up to 50 mg/dl) in 6 cases, moderate (between 51-200 mg/dl) in 24 and severe (above 200 mg/dl) in 11. Protein electrophoresis in CSF was accomplished in just 8 cases and increased gammaglobulin was observed in 5, with values between 19.1 and 21.2%. Among our patients, only Case 2 did not undergo this exam and in all cases CSF abnormalities were found. We found pleocytosis in all cases, and it varied between 37 and 638 leukocytes/mm³ (moderate in 3, intense in 1 and severe in 2), and eosinophiles were present in 6 cases, with values from 1 to 24%. Increase in the CSF protein content was observed in all cases, varying between 40 and 230 mg/dl (mild in 2, moderate in 3, and severe in 1), and elevated levels of gammaglobulin on protein electrophoresis, was observed in 3 patients. Many immunological assays have been used to evaluate the reactivity to *Schistosoma* antigens in the serum as in the CSF, but with limited specificity. The enzyme-linked immunosorbent assay (ELISA) and

immunoblot assays however have a high sensitivity and more elevated titers in CSF than serum suggest an involvement of CNS^{14,21,23,35,36}. According to the literature, the immunological tests were positive in 15 of 20 cases (precipitin reaction in 1 case, ELISA in 7 cases, immunofluorescence-reaction positive in 8 cases). All the patients of our series had a positive test in CSF (ELISA in 5 cases, immunoblot assay in 2).

The image exams have a great value in the diagnosis, although they are not specific and even when normal do not exclude the diagnosis. The SC MRI is more sensitive and offers fewer risks when compared with computadorized tomography myelographic examination. Only a few reports in the literature described the MRI findings^{23,29,30} showing in all the cases enlarged conus medullaris on T1-weighted images, signal hyperintensity on T2-weighted images, and a heterogeneous pattern of enhancement with contrast material. The MRI in five patients of our series (Cases 1, 3, 4, 5 and 7) revealed enlargement of the SC with contrast enhancement (Fig 1 and 2) but it was normal in one (Case 6), on which



Fig 1. Patient 4. Spinal-cord MRI, (A) T1, sagittal view showing enlargement of conus, with contrast (B) enhancement and hydromyelia.

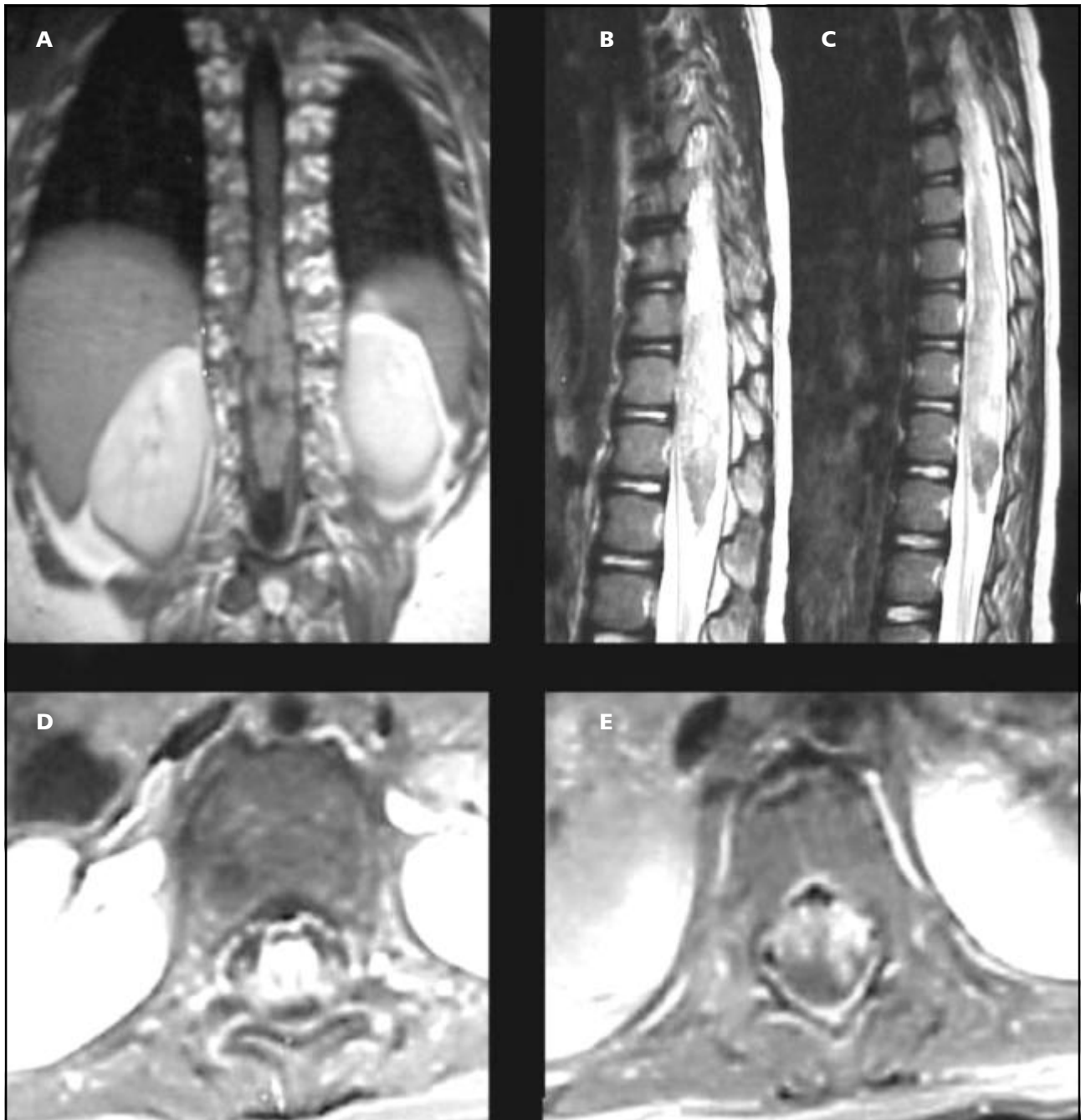


Fig 2. Patient 5. Spinal-cord MRI showing tumour aspect T10-L3, with irregular aspect and contrast enhancement. A: T1- coronal view; B, C: T2 saggital view; D: T1 axial view with normal aspect; E: T2 axial view with abnormal aspect.

the exam was realized after treatment when the patient had a normalization of the neurological examination.

The SCS treatment is eminently clinical and is made with schistosomicides (praziquantel or oxaminiquine) associated with corticosteroids, the latter counters the granulomatous inflammation and can result in rapid improvement, as in Case 3. Some authors suggest corticosteroids should be main-

tained until CSF normalization, but this is controversial²³. Praziquantel is administered at the dose of 20-35 mg per kilogram of body weight in two doses, during one week and oxaminiquine at a dose of 15-30 mg per kilogram of body weight in two doses, in a single day. Approximately 80% of the cases are cured after a single course but more than one course may be necessary. Laminectomy and intraoperative biopsy is indicated for doubtful cases and SC de-

compression in patients with pseudotumoral forms; as in 2 cases of our series (Cases 3 and 5) and in the literature it was realized in 14 cases.

In conclusion, SCS should be considered in pediatric patients with myeloradiculopathy, mainly those with positive epidemic evidence. As SCS presents a specific treatment, the ready diagnosis through the association of clinical and laboratory evidence can guarantee a better prognosis and avoid the occurrence of serious sequels. Precocious diagnosis of this condition will be achieved as a result of improved awareness and knowledge of this disorder among both pediatricians and neurologists.

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