



Case Report

Intramedullary histoplasmosis lesion in children: A case report

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ABSTRACT

Background: Histoplasmosis is a fungal disease endemic in some regions of the United States of America, Canada, and Latin America. The geographic characteristics, humidity, soil, and climate are responsible for such distribution. In Brazil, there are case reports of histoplasmosis throughout its territory, being considered an endemic region. It is considered an opportunistic disease, affecting mostly immunocompromised patients. To the present date, scientific publications dealing with pediatric cases of histoplasmosis are restricted to case series. Spinal cord injuries caused by histoplasmosis are rare, even in the adult population, being described in few studies.

Case Description: The present report deals with a 4-year-old patient, from the southeast region of Brazil, who started a condition of fever, weight loss, cervicobrachialgia, and symmetrical tetraparesis, with evolution over 2 months. In the diagnostic investigation, she was found to have primary immunodeficiency and neuroimaging examinations showed a cervical spinal cord lesion at the level of C4-C6. The anatomopathological diagnosis of histoplasmosis was possible after surgery for decompression and biopsy of the lesion.

Conclusion: According to our research, there are no reports in the literature that address the situation of spinal cord compression syndrome due to histoplasmosis in the pediatric population.

Keywords: Histoplasmosis, Neuroinfection, Neurosurgery, Pediatrics, Spinal cord lesion.

INTRODUCTION

Histoplasmosis is a fungal disease endemic in some regions of the United States of America, Canada, and Latin America. The geographic characteristics, humidity, soil, and climate are responsible for such distribution.^[6,11,21] In Brazil, there are case reports of histoplasmosis throughout its territory, being considered an endemic region.^[3,5] It is considered an opportunistic disease, affecting mostly immunocompromised patients. The central nervous system (CNS) infection occurs in 5–10% of cases that develop the disseminated form of histoplasmosis.^[19]

Dissemination occurs mainly through hematogenous or contiguity. The most common neurological symptoms are chronic meningitis, hydrocephalus, and encephalitis, in addition to focal lesions in the brain and spinal cord.^[20] Despite its higher prevalence in immunocompromised

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patients, approximately 1/3 of neurohistoplasmosis cases occur in immunocompetent individuals. There are data in the literature reporting 62% of CNS involvement in pediatric patients with disseminated histoplasmosis.^[10]

Spinal cord injuries caused by histoplasmosis are rare, even in the adult population, being described in few studies.^[7,8] In the renowned study by Wheat *et al.*, restricted to adult patients, of the 77 individuals affected by neurohistoplasmosis, only 7.7% of them had spinal cord injuries.^[22] Among adults, some case reports present intramedullary lesion due to histoplasmosis.^[2,9,16,18] However, in the pediatric population, such presentation is even rarer, even in series that studied larger groups of children diagnosed with histoplasmosis.^[4,13]

The present report deals with a 4-year-old patient, from the southeast region of Brazil, she was found to have primary immunodeficiency and neuroimaging examinations showed a cervical spinal cord lesion at the level of C4-C6. The anatomopathological diagnosis of histoplasmosis was possible after surgery for decompression and biopsy of the lesion. So far, according to our research, there are no reports in the literature that address the situation of spinal cord compression syndrome due to histoplasmosis in the pediatric population.

CASE DESCRIPTION

A 4-year-old girl with no previous comorbidities is admitted to the emergency room for 2 months, presenting with asthenia, weight loss, neck pain, difficulty in walking, and frequent falls for 2 months, evolving for 1 week with fever and progressive tetraparesis in all four limbs. On neurological examination, the patient had Glasgow 15, isochoric and photoreactive pupils, dysbasia, axial and appendicular ataxia, as well as alterations of the upper motor neuron syndrome (spastic tetraparesis, bilateral Hoffmann and Babinski signs, and global hyperreflexia).

In the diagnostic investigation, neuroaxis magnetic resonance imaging (MRI) was performed, which showed multiple intramedullary expansile formations with diffuse leptomeningeal enhancement of the structures and spinal cord, as well as intraparenchymal enhancement in the brainstem, suggesting areas of cerebritis [Figure 1]. Given the lack of specificity of the imaging examination in defining the etiology of the lesion, several diagnostic possibilities arise, such as infectious, inflammatory, and neoplastic causes. Therefore, to define the type of injury, the patient in question had, surgical treatment was proposed with the aim of decompressing the spinal cord and biopsying the injury.

On the 11th day of hospitalization, the patient underwent microsurgery for the resection of an expansive intramedullary lesion by C4-C6 posterior laminectomy, a procedure that occurred uneventfully. However, on the 6th

postoperative day, the child evolved with a worsening level of consciousness, vomiting, and prostration. An urgent cranial computed tomography was performed, which showed acute hydrocephalus, and an external ventricular drainage (EVD) was then indicated for resolution of the condition. After the EVD procedure, the patient showed a significant improvement of the sensorium and the intraoperative cerebrospinal fluid (CSF) analysis showed erythrocytes 220, leukocytes 12.5 (72% lymphocytes; monocytes 3%; and neutrophils 25%), glucose 58, and proteins 29.

On the 20th day of hospitalization, the anatomopathological result of the spinal cord lesion compatible with histoplasmosis was obtained [Figure 2]. In view of this diagnosis, we started treatment with liposomal amphotericin 50 mg/day for 42 days. After clinical and laboratory improvement, ventriculoperitoneal shunt was performed for definitive treatment of hydrocephalus. The patient was discharged using fluconazole 100 mg/day in maintenance treatment for another 12 months.

An outpatient investigation for immunodeficiencies was carried out. The HIV test was negative, but the measurement of immunoglobulin A, complement, and CD4/CD8 suggested a probable diagnosis of primary immunodeficiency [Table 1]. After 2 years of the surgical procedure, the patient presents neurological evolution, maintaining Grade 4 tetraparesis,

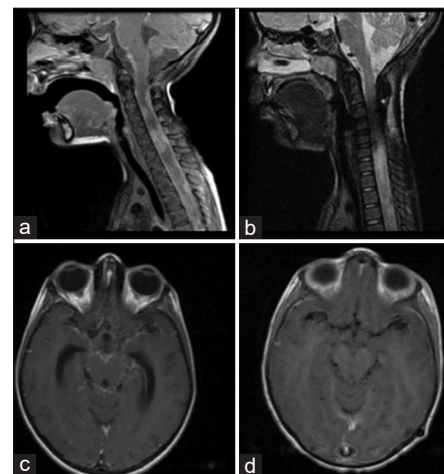


Figure 1: (a) Pretreatment T1-weighted magnetic resonance imaging (MRI) of cervical spine, sagittal view, showing multiple contrast-enhancing solid intramedullary expansive formations. The intramedullary lesion between C4 and C6 stands out, with dimensions: 14 mm in diameter caudal, 7 mm anteroposterior, and 8.2 mm laterolateral, as well as leptomeningeal enhancement. (b) T2-weighted posttreatment MRI with significant reduction in meningeal enhancement, denoting the resolution of the infectious process after the implemented therapy; (c) pretreatment T1-weighted axial MRI of the brain showing the important diffuse leptomeningeal enhancement in the basal region of the brain, typical of granulomatous diseases. (d) MRI after 42 days of T1-weighted treatment showing the important reduction in meningeal enhancement.

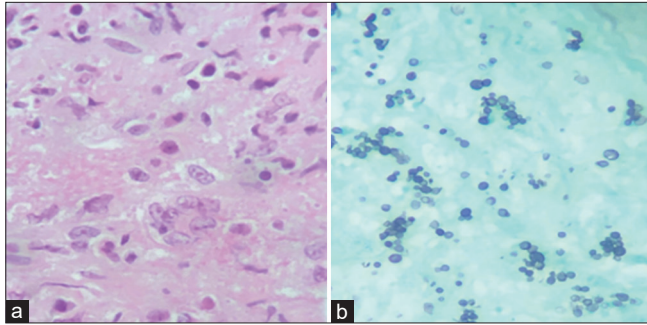


Figure 2: Photomicroscopy of spinal cord lesion (a) – Detail of the inflammatory process, where epithelioid macrophages, lymphocytes, and a multinucleated giant cell are observed (hematoxylin-eosin, ×400). (b) Detail of fungal structures, which do not present budding (Gomori-Grocott, ×100).

Test	Value	Reference value
C4	17 mg/dl	19 - 52 mg/dl
C3	141 mg/dl	90 - 180 mg/dl
IgA	100 mg/dl	27 - 195 mg/dl
CD4	26.39%	23% - 48%
CD8	41.56%	14% - 33%
CD4/CD8	0.64	0.9 - 2.0

improvement in spasticity, and motor coordination, being able to walk with support. Neuroaxis MRI after 6 months of treatment does not show evidence of residual damage.

DISCUSSION

Histoplasmosis is considered an opportunistic disease and affects mainly immunocompromised patients who are also the most susceptible to disseminated forms of the disease, including among pediatric patients.^[4] CNS infection occurs in 5–10% of cases that develop the disseminated form of histoplasmosis.^[19] Specifically, in the pediatric population, there are few data in the literature, but there are cases that report up to 62% of CNS involvement in patients with disseminated histoplasmosis.^[10]

The most common neurological symptoms are chronic meningitis, hydrocephalus, and encephalitis, in addition to focal deficits caused by brain and spinal cord injuries.^[20] Due to the expressive variety of clinical manifestations related to histoplasmosis, especially of the CNS, its diagnosis is challenging and generally late.^[12] Studies show that in 60% of cases, the average time of 30 days is needed to diagnose meningitis by histoplasmosis. Furthermore, the diagnosis is not rarely obtained only after performing autopsies.^[1]

Diagnostic tests include analysis of serum, urine, cerebrospinal fluid, with testing for antigens and antibodies,

as well as culture for fungi.^[15] The low suspicion of fungal etiology, together with the nonspecificity of imaging tests and findings in laboratory tests, including the CSF (up to half of the cases do not have lymphocytic pleocytosis) contribute to the diagnostic challenge of cases of histoplasmosis of the CNS.^[15,22] However, when testing for histoplasma antigen or anti-histoplasma antibodies in the CSF, sensitivity can reach 78% and specificity 97%.^[17]

In critically ill patients, biopsy of lesions identified on imaging studies may be preferred to repeated assessment of the CSF to obtain a more rapid definitive diagnosis or when the CSF cannot be reliably obtained.^[15] In the series by Wheat *et al.*, a sensitivity of 55% was found in histopathological examinations for diagnosis.^[22]

A recent report evaluated spinal cord involvement in histoplasmosis in adults and showed that four out of eight cases had isolated CNS involvement in the spinal cord and all of them were treated with amphotericin.^[14] Assessing in detail the publications that address histoplasmosis in the pediatric population, there is little information about intramedullary lesions, and according to our research, there is no report described in the present literature, corroborating the rarity of this presentation.^[4,13] In the case described here, the surgical procedure with biopsy was essential for the etiological definition of the disease. Similar to the case reported by Manning *et al.* of a 27-year-old patient with a history of progressive paraparesis, whose diagnosis of neurohistoplasmosis was made after a biopsy with posterior access through laminectomy of C7-T12, an intramedullary cervicothoracic lesion.^[9]

Despite having other complications resulting from histoplasmosis (hydrocephaly), the patient in the present report evolved with significant clinical improvement after the institution of treatment with liposomal amphotericin B followed by outpatient treatment with fluconazole. After 2 years of follow-up, the patient is stable, with the previous motor sequelae and in constant rehabilitation with physiotherapy, without cognitive limitations, and with good school performance.

The differential diagnosis of patients who progress with progressive limb paresis is broad and encompasses several etiologies, including infectious causes (syphilis, fungal infections, tuberculosis, and other mycobacteria), demyelinating (acute demyelinating encephalomyelitis – ADEM), and neoplastic causes.^[17]

The treatment recommendation for histoplasmosis in its disseminated form is different when there is involvement of the CNS. While patients without neurological involvement can be treated on an outpatient basis with itraconazole as the drug of choice, patients with neurohistoplasmosis require hospitalization and should be treated with liposomal

amphotericin for 2–6 weeks, to drastically reduce fungemia followed by treatment with oral antifungal agents such as itraconazole.^[15,22]

CONCLUSION

According to our research, there are no reports in the literature that address the situation of spinal cord compression syndrome due to histoplasmosis in the pediatric population.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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