Spinal Neurocysticercosis: A Rare Variant of a Common Parasitic Infection

Neurocisticercose espinhal: uma variante rara de uma infecção parasitária comum

Paulo Moacir Mesquita Filho[1] Nério Dutra Azambuja Junior[1] José Ricardo Vanzin[1] Rafael D'Agostini Annes[1] Daniel Lima Varela[2] Moisés Augusto de Araújo[1] Vanderson Rodrigo de Araújo[1] Candice Ghelen Bregalda[1] Timóteo Abrantes de Lacerda Almeida[3]

[1] Department of Neurosurgery, Passo Fundo City Hospital, Passo Fundo, Rio Grande do Sul, Brazil
[2] Department of Neurology, Passo Fundo City Hospital, Passo Fundo, Rio Grande do Sul, Brazil
[3] Department of Neurosurgery, São Vicente de Paulo Hospital, Rio Grande do Sul, Brazil

Address for correspondence Paulo Moacir Mesquita Filho, MD, Department of Neurosurgery, Neurology and Neurosurgery Service, Passo Fundo City Hospital, Passo Fundo, Brazil, 640 Teixeira Soares Street, ZIP Code 99010-080, Passo Fundo, Brazil (e-mail: pmesquitafilho@hotmail.com).

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Abstract

Neurocysticercosis is the most common parasitic infection affecting the central nervous system, usually involving the brain parenchyma, intracranial subarachnoid space, or ventricular system. In rare cases, there is involvement of the spine (vertebral, epidural, subdural, arachnoid, or intramedullary). Even in endemic regions, this variant is rare, with an incidence below 5% of all patients. The diagnosis is made based on the symptoms, which can be very unspecific, imaging and CSF analysis, with biopsy as a possibility. Treatment is usually curative, but important deficits can develop, due to compression of the spinal cord or nerve roots, arachnoiditis, or meningitis. We present the case of a patient who developed this entity, with poor clinical scenario, and review the literature on the topic.

Keywords
- neurocysticercosis
- spine
- spinal neurocysticercosis

Resumo

Neurocisticercose é a infecção parasitária mais comum afetando o sistema nervoso central, geralmente envolvendo o parênquima cerebral, espaço subaracnóide intracraniano ou sistema ventricular. Em raros casos, há envolvimento da coluna vertebral, espaços epidural e subdural, aracnoide, ou intramedular. Mesmo em áreas endêmicas, esta variante é rara, com incidência abaixo de 5% entre todos os pacientes. O diagnóstico é feito com base nos sintomas, que podem ser bastante inespecíficos, neuroimagem e análise do líquor, sendo a biópsia uma possibilidade. O tratamento geralmente é curativo, porém importantes déficits podem se desenvolver, devido à compressão da medula espinhal ou raízes nervosas, aracnoidite ou meningite. Relatamos o caso de um paciente que desenvolveu esta entidade, com sintomatologia escassa, e revisamos a literatura sobre este tópico.

Palavras-chave
- neurocisticercose
- coluna
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Introduction

Human cysticercosis is a systemic infestation caused by *Cysticercus cellulosae*, the larval form of *Taenia solium*. Neurocysticercosis (NCC) is the most common parasitic infection affecting the central nervous system,[1–4] usually involving the brain parenchyma, intracranial subarachnoid space or ventricular system. In many cases, the infection is self-limited and diagnosed as an incidental finding. The spinal variant, however, even in endemic regions is rare, with an incidence of around 1 to 5%.[1,2,4] Less than 200 cases have been reported so far.[1,3]

We report the case of a patient who developed this rare form of NCC, with unusual clinical findings, and review the literature about this entity.

Case Report

We present the case of a 57-yearold woman, presenting with a 3-week course of headache and posterior neck pain, initially relieved with analgesics, but that have worsened recently. She developed episodes of disorientation and intermittent fever during the evening. The patient also complained about low back pain, irradiated to the right inferior limb. There was no previous history of chronic pathologies, neither cancer nor inflammatory conditions. The physical examination showed only a mild nuchal stiffness, aside from intermittent fever.

The initial CSF evaluation evidenced mild elevation in the leucocytes (11 cells/µL), with 100% of mononuclear cells, extremely low glucose levels (2 mg/dL), and elevated protein levels (100 mg/dL). The CSF culture was negative. The serum examination was uneventful, and the inflammatory tests were negative. Thoracic X-rays were also normal.

We performed a Magnetic Resonance Imaging (MRI) of the brain, which was normal, and of the entire spinal canal, evidencing multiple intradural, extra-spinal cystic lesions from C4-C7 displacing the spine posteriorly, with a weak impregnation by the gadolinium. There were also lesions with the same features at the levels of T12 to L1 and from L1 to S2, surrounding the neural roots (►**Fig. 1–2**).

Empirically, she received treatment for tuberculosis during four weeks, with partial remission of the symptoms. We repeated the neuroimaging of the spine after 30 days of treatment, evidencing that there was no improvement. The new CSF examination revealed persistence of low glucose levels and high protein levels (Cells: 11 cells/µL; monocytes: 95%; neutrophils: 5%; Glucose: 5 mg/dL; Proteins: 60 mg/dL; Lactate: 52 mg/dL), with persistent negative culture. Serum examination evidenced increased inflammatory markers. Thus, we decided to perform a biopsy in one of the lumbar lesions. The biopsy was compatible with spinal neurocysticercosis. The patient received therapy with albendazol plus steroids and is currently recovering very well (►**Fig. 3**).

Discussion

The first case of NCC involving humans was described by Paranoli Rumi in 1550,[1,3] whereas Rockitansky, in 1856, made the first reference of intraspinal cysticercosis. Cysticercosis is widely endemic in Brazil, Peru, Mexico, Tropical Africa, Korea, and India.[2,3,5] As indicated by autopsy findings, the incidence in these regions can be as high as 4% of the general population; in Brazil, recent reports suggest that 7.3% of hospital admissions were related to NCC.[6] In the United States, the first case of NCC was reported by Walter Dandy in 1927, and there have been more frequent reports of

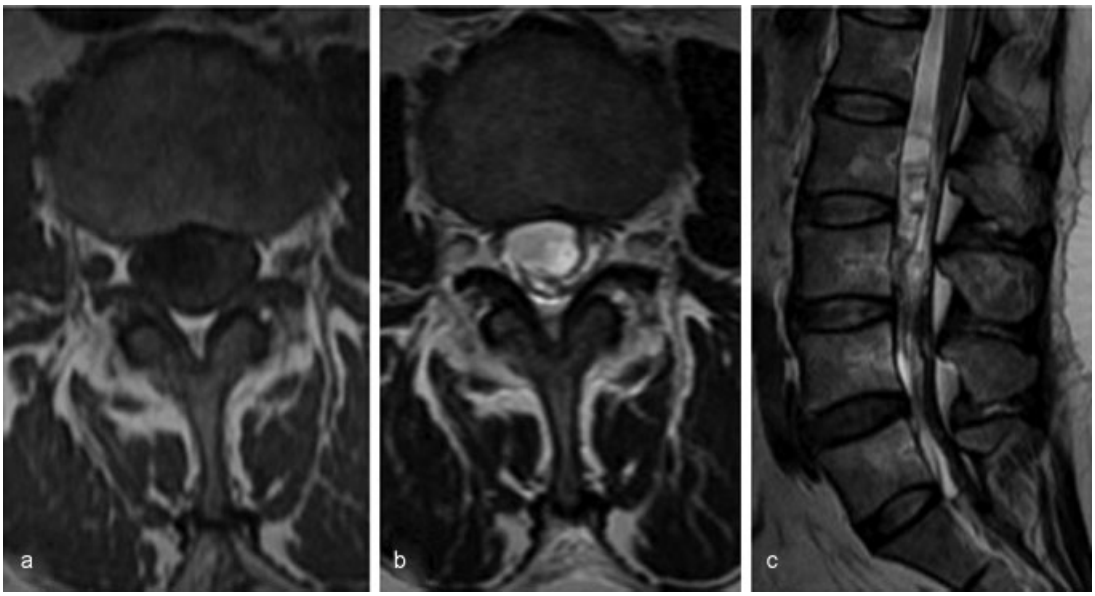

Fig. 1 (a) Axial T1-weighted MRI of the lumbar spine, showing an intradural hypointense mass, distorting the contents of the spinal canal. (b) Axial T2-weighted MRI of the lumbar spine, showing an intradural hyperintense mass and arachnoiditis, with posterior dislocation of the cauda equina. (c) Coronal T2-weighted MRI of the lumbar spine, showing an intradural heterogeneous mass and arachnoiditis, with extensive dislocation of the cauda equina from L2 to L5.

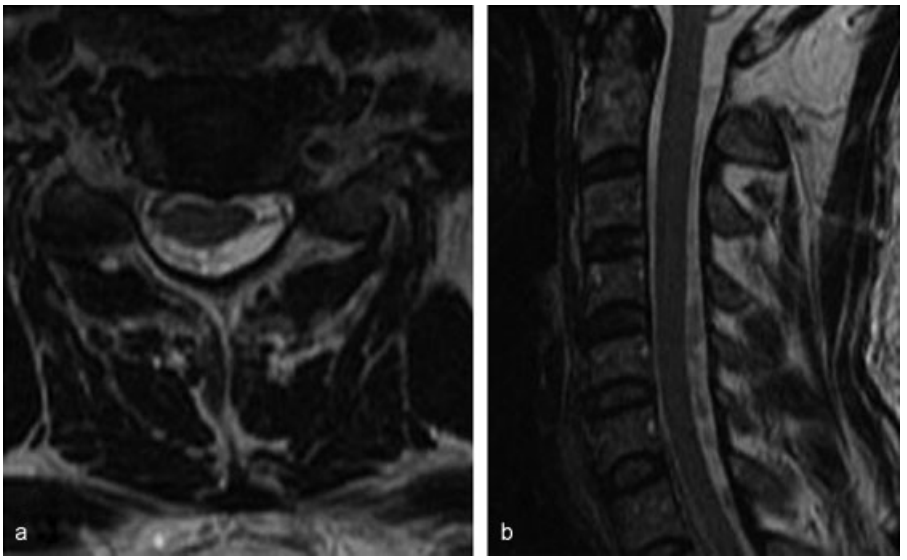

Fig. 2 (a) Axial T2-weighted MRI of the cervical spine, showing an intradural heterogeneous signal intensity, compatible with arachnoiditis, as well as mild dislocation of the spinal cord from the midline. (b) Coronal T2-weighted MRI of the cervical spine, showing an intradural heterogeneous signal intensity, compatible with arachnoiditis.

the disease in the Southwestern United States in recent years, especially among recent immigrants.[3,5]

Human cysticercosis is a systemic infestation caused by *Cysticercus cellulosae*, the larval form of *Taenia solium*.[1] The parasite's life cycle is well known, as pigs are the intermediate host and humans are the definitive (or occasionally intermediate) host. NCC typically results from the ingestion of cysticercal eggs in food contaminated by human or porcine feces. During digestion, gastric acid releases the larvae from the eggs, which penetrate the intestinal mucosa and follow to the bloodstream, where they primarily deposit in muscles, brain, and the eyes.[3,5] Dissemination in the central nervous system (CNS) occurs through small capillaries into the parenchyma or through the choroid plexus into the ventricles, eventually leading to the subarachnoid space.[3]

Spinal neurocysticercosis (SNCC) can be classified according to the anatomical location of the cysticercus in the spine: extra-spinal (vertebral) or intra-spinal (epidural, subdural, arachnoid, or intramedullary).[2] Among these, the most common location of SNNC is the subarachnoid space, in 80% of all cases.[2,7] The intramedullary type is quite rare, accounting for the remaining 20% of cases (only 53 cases have been reported until 2010).[2] Inside the spinal cord, cysticercus usually distributes in the thoracic cord, with a few cases involving the cervical and the lumbar cord.[2] The epidural occurrence of NCC in the spine is exceedingly rare.[8]

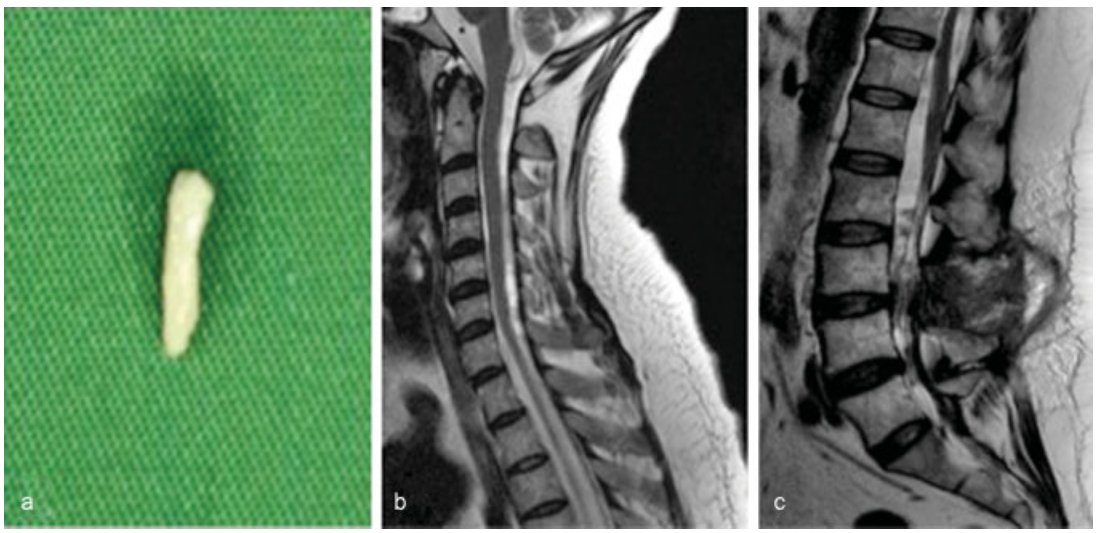

Fig. 3 (a) Intra-operative specimen. (b) Coronal T2-weighted MRI of the cervical spine, evidencing partial remission of the lesions in the cervical subarachnoid space. (c) Coronal T2-weighted MRI of the lumbar spine, evidencing partial remission of the lesions in the cervical subarachnoid space, and post-operative status.

This distributional mode of cysticercus supports the hypothesis that intramedullary cysticercus comes from the blood circulation, because the thoracic cord has a lot more blood supply than other segments of the spinal cord. However, some authors believe that intra-medullary cysticerci could migrate to the spinal cord via the ventriculo-ependymal pathway.[2] Regarding the intradural extra-medullary SNCC, one hypothesis given for *Cysticercus larvae* descending into this space, is the retrograde flow through valveless epidural venous plexus, which may conduct blood in any direction under the influence of intra-abdominal and intra-thoracic pressure variations.[1,7]

Nevertheless, the location of a subarachnoid spinal cysticercal cyst is not necessarily fixed. Studies have demonstrated the migration of the cyst during myelographic procedures, similar to what happens in the ventricular compartments. Thus, the time between neuroimaging and excision should not be long, to ensure that the lesion will be within the planned surgical field.[3]

The reason that the incidence of the disease in the spinal canal is so low when compared with the cranial infection is not clear. Queiroz et al proposed that the CSF reflux at the cranio-vertebral junction can prevent the spinal dissemination by propelling the floating cysts back to intracranial space.[1,3,8] Although the larval migration is prevented by CSF reflux, this portal remains the most important mode of entry for *Cysticercus larvae* to the spinal territory.[1,7]

The clinical scenario varies accordingly to the region affected, as well as the size of the lesion, and, eventually, an inflammatory process due to the cysts degeneration.[1,3] There might be myelopathy or radiculopathy due to mass effect, or arachnoiditis and meningitis, as was the case in our patient.[1,3,5] Extra-medullary disease, especially in the lumbar region, tends to give rise relatively slow and insidious onset of symptoms, whereas an intramedullary lesion in cervical canal produces fast and early deterioration.[1] Most patients experience a progressive worsening course, that can vary in duration from one week up to many years.[2] Common clinical manifestations include pain, paraparesis, spasticity, bowel and bladder incontinence, and sexual dysfunction.[2]

The diagnosis is based on the clinical course, imaging findings, CSF characteristics, and sometimes, biopsy. Since approximately ⅔ cases of SNCC occur in presence of concomitant cranial involvement and more than 50% of patients with intramedullary SNCC have evidence of *T. solium* infection elsewhere, an entire neuro-axis evaluation should be considered.[1,5,8] Nevertheless, isolated cases in the spine have already been reported.[1,5]

The MRI is the best imaging technique to access SNCC. As proposed by Ratnalkar et al,[9] there are 4 different stages of the disease, each with different findings, as follows: (1) Vesicular stage - cystic hypointense lesions in T1 and hyperintense in T2 weighted images, without any surrounding edema; occasionally the scolex can be identified as a mural nodule within the cyst cavity on T1-weighted images. The scolex is isointense to spinal cord parenchyma on T1-weighted acquisitions and does not show on T2-weighted images because it becomes isointense to the surrounding cyst fluid[5]; (2) Colloidal vesicular stage - mild hyperintense in T1 and hyperintense in T2, usually with perilesional edema (inflammatory response to a dying parasite); (3) Granulonodular stage – thickening of the capsule and initial calcification; (4) Calcified nodular stage – dense calcified scolics and cysts, usually difficult to identify in MRI, usually appearing as calcifications in the CT scan.[1,3] All these stages can occur simultaneously.[1]

The use of gadolinium-enhanced MR images usually distinguishes the type of subarachnoid involvement, with a rim enhancement of a discrete intradural-extra-medullary cyst and a homogeneously enhancing sheet-like arachnoiditis.[5] Some associated findings, like syrinx or infectious syringomyelia are caused by a combination of the effects of arachnoiditis, inducing subarachnoid adhesions, parenchymal circulatory insufficiency, and spinal cord atrophy.[5] Myelographic studies, like post-myelography CT may be useful for detecting small subarachnoid SNCC lesions, although bringing risks of arachnoidal scarring and obstruction of CSF pathways.[3] In the case of our patient, the lesions exhibit the characteristics of the vesicular stage, as well as some subarachnoid adhesions.

The CSF findings often show increased protein levels, a low (even undetectable) or normal glucose, moderate lymphocytic pleocytosis, and eosinophilia.[2,4] Cytologic examination may demonstrate high variability and atypia similar to central nervous system lymphoma.[4] Cysticercal antibodies found in CSF by ELISA have a high sensitivity (87%) and specificity (97%), as opposed to sensitivity of 50% and specificity of 70% for serum serological studies, being a mainstay in the diagnosis.[1,2,10] In our patient, the CSF was compatible with an infectious process, initially thought to be tuberculosis.

Sometimes, excision and histopathological examination remains the only definitive method of confirming the diagnosis. The typical histopathological findings of NCC, are the presence of dead or active translucent cysts with eosinophilic lining.[1] The cyst is surrounded by a collagenous capsule that corresponds to the parasite itself. In the form known as cysticerci, an encystment of cysticercus larvae is seen. It is comprised by the tegmentum, the outer layer, covered by fine hairlike projections. Initially the cyst wall contains numerous ellipsoid vesicles and an inner loose fibrillated matrix made up of a network of canaliculi, representing the excretory system of the parasite, along with fascicles of muscle from the parasite, nucleated cells, scattered calcareous corpuscles, and occasional foci of calcification. The cyst's fluid is clear and there is an invagination in its wall corresponding to the scolex of the parasite. The cysts are usually surrounded by clear fluid and chronic inflammatory cells (neutrophils, eosinophils and giant cells), which is mild while the cyst wall remains intact and the organism is alive, but intense after the parasite dies.[5] Calcified cysts can be seen in late and inactive stages. The meningeal thickening and signs of arachnoiditis are also common.[1] Also, clusters of subarachnoid cysts can appear, and are referred to as "cysticercosis racemosus."[5]

The differential diagnosis should include hydatid cysts, tuberculosis, simple/complex arachnoid cysts, dermoid cysts, sarcoidosis, or subarachnoid neoplasm (primary or metastatic).[1,5]

Mohanty et al[11] state that SNCC represents a focal manifestation of a systemic disease, thus recommending medical therapy in all patients. Usually, the treatment is based on the use of albendazole or praziquantel, the former having a superior penetration in the CSF.[1,2] Albendazole is used at doses of 15mg/kg/day for one week, up to a maximal dose of 800mg/day.[12,13] Albendazole has higher parasiticidal effect than praziquantel.[14] Praziquantel is most often used at doses of 50 mg/kg/day for 15 days, or even as a single-day regimen (25–30 mg/kg at 2-hour intervals).[15] Serum concentrations of praziquantel decrease when steroids are also used.[16] Cysticidal drug therapy has been criticized by some clinicians because treatment associated parasite death leads to an acute, severe inflammatory reaction in the surrounding brain tissue, increasing intracranial hypertension and potentially leading to the death of the patient.[17] Simultaneous administration of corticosteroids ameliorates the secondary effects of headache and vomiting that may occur during cysticidal drug therapy, which are associated to the destruction of parasites within the brain and spinal-cord and are reliable indicators of drug efficacy.[18]

Close and frequent neurological assessment is very important due to the possibility of acute neurological deterioration from the inflammatory response as the parasites die.[1,19] If this happens, the neurosurgical team should consider surgical decompression of the spinal canal. The other indications for surgical treatment are severe and progressive symptoms and failure of medical management.[1] Alsina et al, evaluating six cases of SNCC, suggested that medical treatment only appears to be a less viable option, due to the progressive neurological deficits of their patients.[3] Other authors advise that surgery is the procedure of choice only when diagnosis is in doubt, otherwise, medical treatment has its advantages.[2]

The outcomes in patients with SNCC are thought to be related to the location (intramedullary or extra-medullary; cauda equine, or spinal cord levels), severity of inflammation (arachnoid scarring or parenchymal injury), and chronicity of symptoms/time to treatment.[3]

Conclusion

SNCC is very rare compared with intracranial neurocysticercosis, which has a relatively high incidence in endemic regions of the world. Nevertheless, it should always be considered in the differential diagnosis in patients who present with multiple lesions in the spinal canal, as well as in those who have CSF diagnosis of an underlying infection.

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