Neurosarcoidosis Associated with Psychiatric Symptoms: Case Report

Neurossarcoidose associada com sintomas psiquiátricos: relato de caso

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Abstract

Background Sarcoidosis is a granulomatous disease predominant in women and black men that has inflammatory origin of unknown etiology; neurosarcoidosis is a rare and critical presentation of the disease.

Case description A 26-year-old black female presented frontal headache for 1 year, as well as behavioral and mood changes for 15 days. Skull tomography and nuclear magnetic imaging of the skull revealed damaged meninges, a right frontal bone lesion, and an intraparenchymal contrast-enhancing lesion. Screening with computed tomography (CT) scans was performed, and it showed signs of bronchiectasis in the lower third of the right lung, but it was asymptomatic. The biopsy showed signs of reactional lesion with the presence of non-caseating granulomas. After the treatment with corticosteroids, the patient presented progressive improvement.

Conclusions Neurosarcoidosis is a rare and critical pathology of sarcoidosis that presents a lytic bone lesion and clinical psychiatric symptoms; neurosarcoidosis is also rare in the literature.

Keywords
- sarcoidosis
- neurosarcoidosis
- psychiatric manifestations
- pathology

Resumo

Introdução A sarcoidose é uma doença granulomatosa de origem inflamatória de etiologia desconhecida, predominante em mulheres e negros, sendo a neurosarcoidose uma apresentação da doença rara relacionada a gravidade.

Relato de Caso Paciente com 26 anos, negra, apresenta quadro cefaleia frontal ha 1 ano e há 15 dias apresentando sinais de alterações de comportamento e humor.

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Palavras-chave
- sarcoidose
- neurosarcoidose
- manifestações psiquiátricas
- patologia

Tomografia de crânio e Ressonância nucelar magnética de crânio que evidenciaram lesão óssea frontal direita, comprometimento meninges e lesão intraparenquimatosa captante de contraste. Realizado *screening* com tomografias que evidenciaram sinais de bronquiectasia em terço inferior pulmão direito, assintomática. Biopsia indicando sinais de lesão reacional com presenças de granulomas não caseosos, Após a manutenção da corticoterapia, a paciente apresentou melhora progressiva.

Conclusões A neurosarcoidose é uma patologia grave e rara da sarcoidose, nesse caso apresenta uma lesão óssea lítica e sintomas psiquiátricos, apresentação rara na literatura.

Introduction

Sarcoidosis is a multisystem inflammatory disease of unknown etiology in which non-caseating granulomas are found in the affected organs (mainly the lungs, the skin, and the lymph nodes).[1] The incidence of sarcoidosis in Brazil is of 10/100,000 inhabitants, and the worldwide incidence of neurosarcoidosis is estimated to be $\sim$ 0.2/100,000 inhabitants. The incidence of the disease is higher among women and black men aged between 20 and 40 years, and it is rarely seen in children.[1–5]

A genome study has shown that human leukocyte antigens (HLAs) DRB1 and DQB1 are risk factors for the association with sarcoidosis.[6,7] Neurosarcoidosis is rare, and 5–15% of the patients with sarcoidosis will have the central nervous system, brain, and spine cord affected; among these, 50% will present symptoms.[8–10]

Case Report

A 26-year-old black female patient presented frontal headache for 1 year, as well as sadness, tearfulness, and decreased appetite for the previous 15 days. She sought medical attention and was treated with risperidone and clonazepam, but there was no clinical improvement. During the neurological examination, she presented time and space disorientation, so a skull tomography (►**Fig. 1**) was requested, evidencing hypodensity and loss of cortical-subcortical differentiation in the right frontal region. Following the investigation, nuclear magnetic resonance imaging (MRI) was used, which revealed a meningeal lesion with infiltration of the cerebral parenchyma associated with lytic lesions in the cranial calotte (►**Fig. 2**).

Thoracic and total abdominal screening tests were performed, and showed a focal lesion (1.6 cm) in the spleen with late uptake compatible with hemangioma and focal bronchiectasis in the lower lobe of the left lung (►**Fig. 3**), as well as bilateral subsegmental atelectasis. The echocardiogram and cerebrospinal fluid (CSF) examination were normal.

Meningeal and brain tissue biopsies were performed using a surgery approach, with supraorbital access and right supraciliary incision. During this period, the patient was treated with corticoids due to cerebral edema and mass effect; she showed an improvement in the signs and symptoms.

The anatomopathological analysis showed a small amount of granulomas in the bone region and meninges (►**Fig. 4** and **5**). Immunohistochemistry: CD99 negative, BCL6 negative, BCL2 negative, AE1/AE3 negative, CD68 positive, kappa and lambda immunoglobulin chains positive, PAX positivity (25%), KI67 focal positivity (10%), CD1a negative, HHF35 negative, calretinin negative, and S100 with focal positivity $< 2\%$. Thus, the morphological aspects and the immunomarkers showed a limphohistiocytic lesion with a polytypic aspect compatible with a reactional lesion.

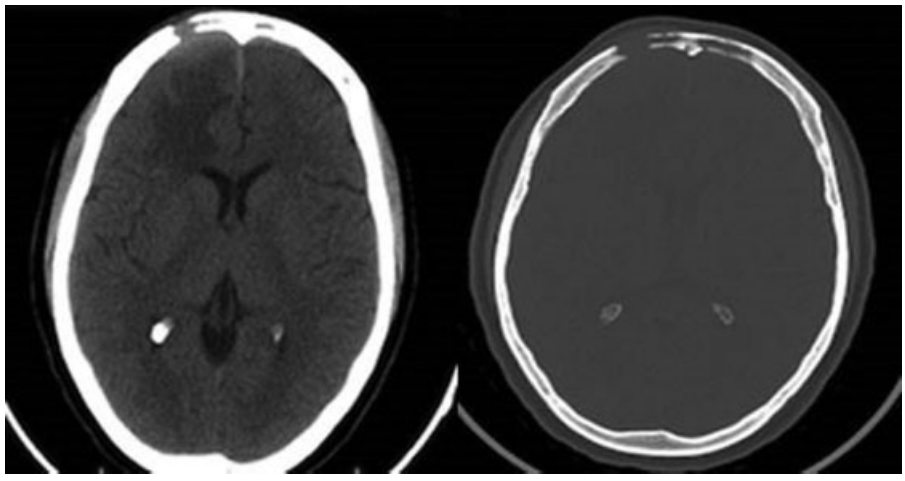

Fig. 1 A Skull CT (axial cut) shows a lytic lesion in the right frontal region and loss of cortical-subcortical differentiation.

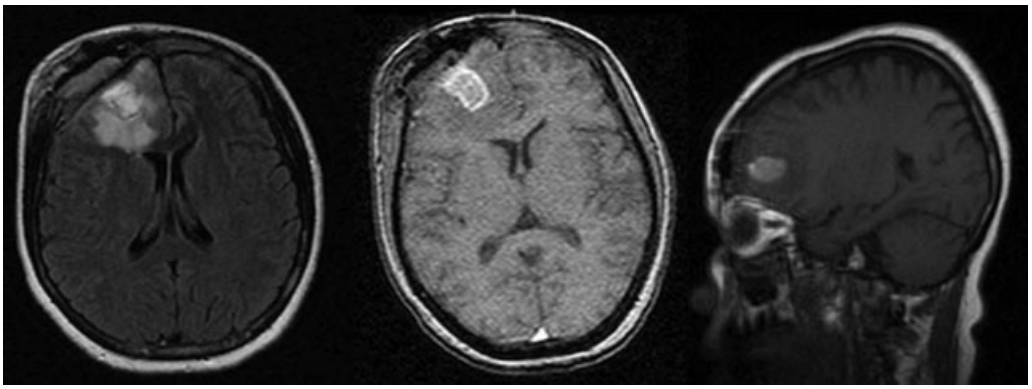

Fig. 2 An MRI shows the frontal and interhemispheric pachymeningeal thickening, which is predominantly right, associated with contrast enhancement. The presence of impairment of the cranial calotte and infiltration of the superior frontal gyrus and frontobasal can be observed.

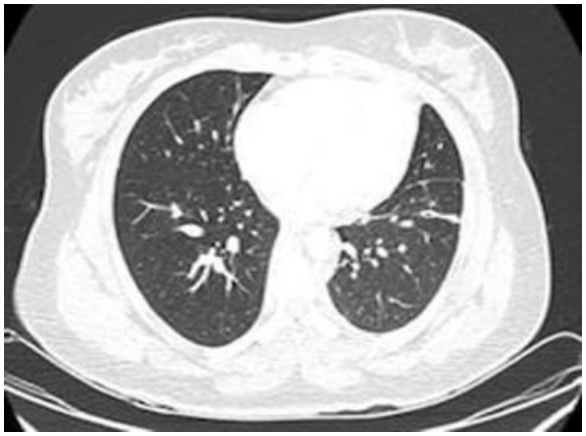

Fig. 3 Thoracic tomography (axial cut).

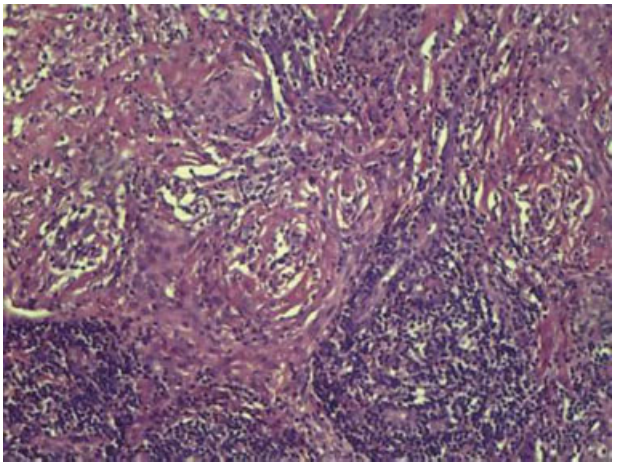

Fig. 4 Multiple non-caseating well-defined granulomas with fibrosis in the skull.

Clinical Manifestations

The symptoms of sarcoidosis depend on the affected organ, and the most nonspecific are fever, weight loss, night sweats, and fatigue. Neurological and cardiac symptoms are rare; however, when they are present, they indicate severe illness.[4] The clinical presentation of neurosarcoidosis is usually optic neuropathy, facial paralysis, meningitis, chronic meningitis, diabetes insipidus, hydrocephalus, elevated intracranial pressure, spinal cord syndromes, vasculitis, cerebral infarction, dysfunctional hypothalamus, myelopathy, myopathy, peripheral neuropathy, and encephalitis (►**Table 1**); the presentation of psychiatric symptoms and osseous involvement is rare.[3,10–14]

Cranial nerve alteration is present in 50–75% of the patients with neurosarcoidosis, and the most common affected nerves are, in descending order, cranial nerves VII, II and VIII. Cranial nerve VII is unilaterally affected in 65% of the cases, and bilaterally affected in 35%;[7,15] cranial nerve II is affected in 5–25% of the patients.[1] Bone involvement of the skull and bone involvement of the spine are rare; however, when the latter exists, it is located in the lower thoracic spine, or in the lumbar spine in most cases.[16]

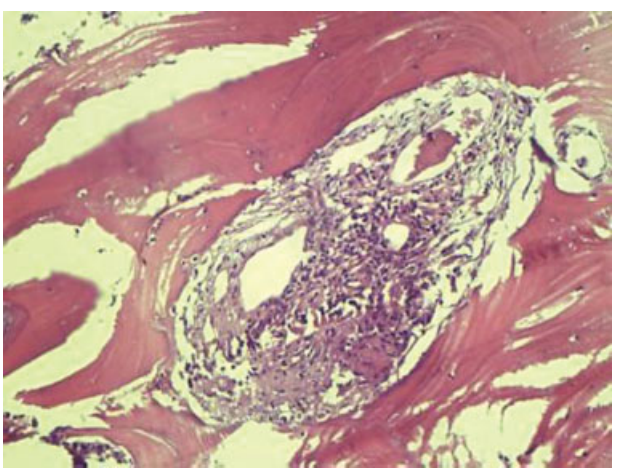

Fig. 5 Decalcified section of involved area of the skull (osseous tissue).

Diagnosis

The diagnosis is based on the clinical condition and radiological presentations; MRI with contrast is the chosen exam, and laboratory tests such as CSF analysis must be evaluated.

Table 1 Percentages of neurological signs and symptoms

Peripheral mononeuropathy	69%
Depression	60–66%
Stress	55%
Cranial nerve	50%
Headache	17–48%
Myelopathy	16–43%
Polyradiculoneuropathy	39%
Hydrocephalus	5–38%
Meningeal disease	10–20%
Seizures	15%
Osseous involvement	13%

However, for the diagnostic confirmation, the exclusion of other inflammatory granulomatous diseases is necessary.[17] The investigation with thorax imaging usually shows strong indications for the diagnosis and helps distinguish it from differential diagnoses (►**Table 2**).[5]

The Japanese Sarcoidosis Society and the Japanese Society of Respiratory Disease presented new diagnostic criteria for neurosarcoidosis that must consider two of six exams: bilateral pillar lymphadenopathy; abnormal uptake of 67Ga scintigraphy; alveolar lavage fluid examination; elevated serum angiotensin-converting enzyme (ACE); negative tuberculin reaction; and elevated serum or urinary calcium level. Besides these exams, there must be a compatible clinical history.[18]

The definitive diagnosis is made by biopsy of brain tissue, evidencing inflammatory tissue associated with non-caseating granuloma and systemic disease compatible with the diagnostic hypothesis; other possible causes must be excluded.[19]

Discussion

Pulmonary manifestations are present in 90% of the patients, but most of them are asymptomatic. Pulmonary involvement tends to be bilateral and asymmetrical, predominating in the upper lobes, and present atypical radiological aspects in 25% of the cases.[20] Bronchiectasis is a typical, uncommon finding, mainly located in the lower lobes and unilateral, as presented in this case report. Pulmonary fibrosis is another finding that is present in bronchiectasis caused by sarcoidosis.

The psychiatric symptoms of apathy, agitation, delirium, hallucinations, irritability, lethargy, and depression improve with the use of corticosteroids.[15] Involvement of the skull is uncommon; when it involves the bone in general, the incidence is between 1–13%,[16] and is usually asymptomatic, as in the case presented here.

Brain parenchyma involvement may present multiple lesions (35%) or single lesions (10%) analyzed in the MRI contrast phase.[19] The MRI is the most sensitive test for the diagnosis of neurosarcoidosis, but a normal examination does not rule out the diagnosis, especially if the patient is under corticosteroid treatment. In MRI with contrast, leptomeningeal involvement is observed in 40% of the cases, and it is more common in the frontobasal and suprasellar regions.[5,19] The CSF may present hyperproteinemia in 73% of the patients and lymphocytosis in 55%; normal CSF is uncommon.[2,5,11]

The non-caseating granuloma of sarcoidosis has immunological origin, and is formed by giant cells and epithelioid cells (consisting of histiocytes modified by T lymphocytes). The presence of giant and epithelioid cells is a sign of high cellular turnover. Granulomas are uniform, and have as their components histiocytes of broad and eosinophilic cytoplasm, oval or twisted vesicular nucleus, and prominent nucleoli.[4,13,21] Fibrinoid necrosis is present in 35% of the cases.[21]

As radiological differential diagnoses we could mention glioblastoma, lymphoma, abscess, metastasis and even variations of multiple sclerosis. Nevertheless, among the lesions that can affect the skull and brain, we can list metastasis, lymphoma; primary skull tumors, such as chondrosarcoma, chordoma, esthesioneuroblastoma and malignant histiocytic tumor; and tumor-like lesions, such as fibrous dysplasia eosinophilic granuloma.[22,23]

The treatment is clinical, with prednisolone 40–80 mg (oral administration) at first; as an alternative for more severe cases, intravenous methylprednisolone can be used.[9] In case of refractoriness, there are options such as: mycophenolate, methotrexate, cyclophosphamide, azathioprine, chloroquine and tumor necrosis factor alpha (TNF-α);[7] another alternative is radiotherapy.[15] In cases of systemic suspicion of neurosarcoidosis, stereotactic biopsy can be used for confirmation.[7]

Table 2 Differential diagnoses

Involvement of brain parenchyma	Meningeal involvement
Multiple sclerosis	Bacterial meningitis
Cerebral metastasis	Tuberculous meningitis
Cerebral lymphoma	Carcinomatous meningitis
Neurotuberculosis	Meningioma
Fungal infections of the brain	Leukemic infiltration
Low- and high-grade glioma	Meningeal plasmacytoma

Conclusion

Neurosarcoidosis is a serious and rare condition. The discussed case presented a single extracranial alteration: asymptomatic pulmonary bronchiectasis located in an atypical region. The intracranial manifestations presented were: lytic bone lesion and psychiatric symptoms (rare occurrence in the literature). Thus, this case may contribute to the diagnosis of other cases with rare presentation.

Disclosure – Conflicts of Interest
Authors declare no conflicts of interest.

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