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Case Report

Primary central nervous system lymphoma: A mirror type presentation in an immunocompetent patient

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ABSTRACT

Background: Primary central nervous system (CNS) lymphoma is a very rare extranodal non-Hodgkin lymphoma. The bilateral pattern, as we call it "mirror type", has been identified in other CNS lesions such as gliomas, metastases, and demyelinating lesions, so the differential diagnosis includes imaging studies such as magnetic resonance imaging contrasted with spectroscopy, ruling out immunodeficiency or metastatic disease.

Case Description: A 65-year-old female presented progressing headache, loss of memory and language alterations, as well as sensory alterations. Neuroimaging showed the presence of two equidistant periventricular lesions at the level of both ventricular atria, a spectroscopy study suggestive of malignancy. Serological studies showed no evidence of immunodeficiency or the presence of positive tumor markers; however, a biopsy was performed, which revealed a histopathological result of primary lymphoma of the CNS.

Conclusion: In neuro-oncology, primary CNS tumors with multiple lesions are rare, even more, the "mirror type" lesions. Lymphomas are lesions that can present in different ways on imaging and clinical presentation. These tumors that present a vector effect due to their size, perilesional edema, or that lead to loss of neurological function are highly discussed in diagnostic and surgical treatment. Due to their prognosis, action on diagnosis and treatment must be taken as quickly as hospital resources allow.

Keywords: Central nervous system-diffuse large B-cell lymphoma (CNS-DLBL), Mirror type tumor, Primary central nervous system lymphoma (PCNSL), Primary lymphoma

INTRODUCTION

Primary central nervous system lymphoma (PCNSL) is a very rare extranodal non-Hodgkin lymphoma that accounts for 2.4–3% of all primary central nervous system (CNS) tumors and 4–6% of all extranodal lymphomas.[31] It is more common in males than females and can occur both in immunocompromised patients and who are immunocompetent.[29] PCNSL is related to human immunodeficiency virus (HIV)-positive, cytomegalovirus (CMV) or Epstein–Barr virus (EBV) infections and cancer.[25] These patients are more likely to have multiple lesions, hemorrhage, and peripheral rim enhancement on images than HIV-negative patients.[7] Its diagnosis, guided by clinical signs and imaging studies, is complex; other inflammatory pathologies, demyelinating

diseases, and malignant tumors (including glioblastomas and metastatic tumors) can also be difficult to distinguish from PCNSL.[13] The predilection sites for this lesion are the periventricular white matter, the corpus callosum, and the basal nuclei.[6] Cases of bilateral lymphomas have been reported both at the basal nuclei, hypothalamus and even extra-axially in the cerebellopontine angle, unrelated to HIV and other EBV and CMV infections.[6,19,24] Mirror pattern CNS lesions have even been reported.[2]

Due to the poor prognosis of PCNSL, management protocols with biopsy without prior use of steroids, chemotherapy with methotrexate, and sometimes immunotherapy with anti-CD20 rituximab or radiotherapy are the indicated standard.[4,8,10,12] The role of the neurosurgeon facing a high burden of diagnostic suspicion of PCNSL has been discussed between biopsy versus cytoreduction surgery. In recent years, cytoreductive surgery has been considered a reasonable initial treatment strategy for selected patients;[5,8,12,18,28] however, no clear conclusion is drawn about the advantages of a greater reduction over biopsy in relation to patient survival. The following case report is made of an atypical "mirror type" presentation of a patient with PCNSL.

CASE DESCRIPTION

A 65-year-old female with a history of type 2 diabetes mellitus, systemic arterial hypertension and long-standing right hearing loss. She began his condition 21 days before his initial evaluation in July 2023, presenting with moderate to intense holocranial headache that partially subsided with the use of non-steroidal anti-inflammatory drugs. She had previously been diagnosed with dementia due to retrograde memory and language disorders. In the neurological examination with Glasgow 13 points (O:4, V:3, M:6), mental functions with global aphasia, isocoria of 3 mm, preserving photomotor and consensual reflexes, right side conduction hearing loss, preserved motor function, sensitive without response to pain in the right hemibody. No evidence of intracranial hypertension or history of seizures. A simple and contrasted tomography was performed, showing the presence of two lesions at the level of both ventricular trigone each one apparently, which were confirmed by magnetic resonance imaging (MRI) scan indicating periventricular lesions with extension to the white matter of the temporal and parietal lobes, a clear reduction of the ventricular space of both atrium was observed, no communication between these lesions through fibers of the corpus callosum, with mostly uniform enhancement at gadolinium contrast [Figure 1], and restriction to diffusion. Metastasis, high-grade glioma, and lymphoma were considered as a differential diagnosis, which was complemented by a thoracic and abdominal tomography without evidence of systemic lesions. Serological studies were performed [Table 1], viral profiles for EBV, CMV, and HIV, as well as tumor markers, which were all negative. Subsequently, a spectroscopy study was performed [Figure 2] 8 days before treatment with dexamethasone, where peaks of choline and creatine were observed, a high choline/creatine (Cho/Cr) ratio, with peaks of lipids and lactate, as well as a decrease in N-acetyl aspartate (NAA), suggestive of malignancy and presence of areas of necrosis.

A temporal craniotomy with a transulcal T2–T3 approach guided by a neuronavigation system was performed. Biopsy samples were taken. The tumor was identified as infiltrative and diffused in the white matter, with gray color, soft consistency, and necrotic core. The ventricle was not opened. No complications were presented.

Histopathology revealed diffuse large B-cell lymphoma with an angiocentric pattern with positive immunohistochemical staining for CD20 and Ki67 in 70% [Figure 3].

The patient had a complicated course due to pneumonia, was discharged from the hospital 15 days after surgery, and was referred to an oncology center.

DISCUSSION

The latest World Health Organization 2021 update classifies the main CNS lymphomas as primary diffuse large B-cell lymphoma of the CNS (CNS-DLBL), immunodeficiency-associated CNS lymphomas, lymphomatoid granulomatosis, and intravascular large B-cell lymphoma. CNS-DLBL is solitary lesions in 65% of cases, located in the cerebral hemispheres 38%, thalami and basal nuclei 16%, corpus callosum 14%, periventricular 12%, or cerebellum 9%.[31] It is attributed to being initially inflammatory and demyelinating lesions.[21,26] It occurs mainly in the immunocompromised population, and within the immunocompetent population, those>60 years are the most affected,[22,23] with similar clinical manifestations as in young patients. This case had an atypical presentation, correlating the clinical data with the imaging studies: an immunocompetent elderly patient without EBV or CMV infection. However, the presence of two periventricular lesions is a presentation more commonly seen in HIV-positive patients with EBV infection.[9,14] MRI study with bilateral lesions that, at first glance, occupy almost the entire of both ventricular atria, with mostly homogeneous contrast enhancement, heterogeneous appearance in T2, annular diffusion restriction, and abundant perilesional edema. Differential diagnoses are meningioma of the ventricular atrium, high-grade glioma, PCNSL, and metastasis of unknown origin, including choroid plexus carcinoma (although, due to age, it was unlikely). In the absence of hydrocephalus or ventricular deformation of both atria remained the diagnostic possibility of high-grade glioma, metastasis, or lymphoma. Due to the suspicion of metastasis, we decided to perform a contrast-enhanced computed

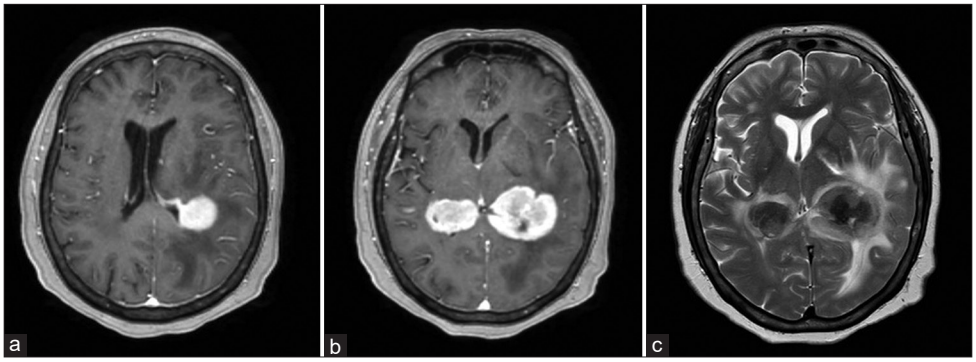

Figure 1: (a) T1-weighted axial-enhanced magnetic resonance imaging sequence, a periventricular lesion is observed on the left lateral ventricle with extension to the white matter of the parietal lobe, the right lateral ventricle is observed without alterations. (b) Two well-defined lesions are observed at the level of the ventricular atrium, and a slightly heterogeneous center is observed. (c) Moderate perilesional edema was observed on the T2 sequence with predominance in the left lesion and with an evident hypointense center. No communication of both lesions through the corpus callosum was identified.

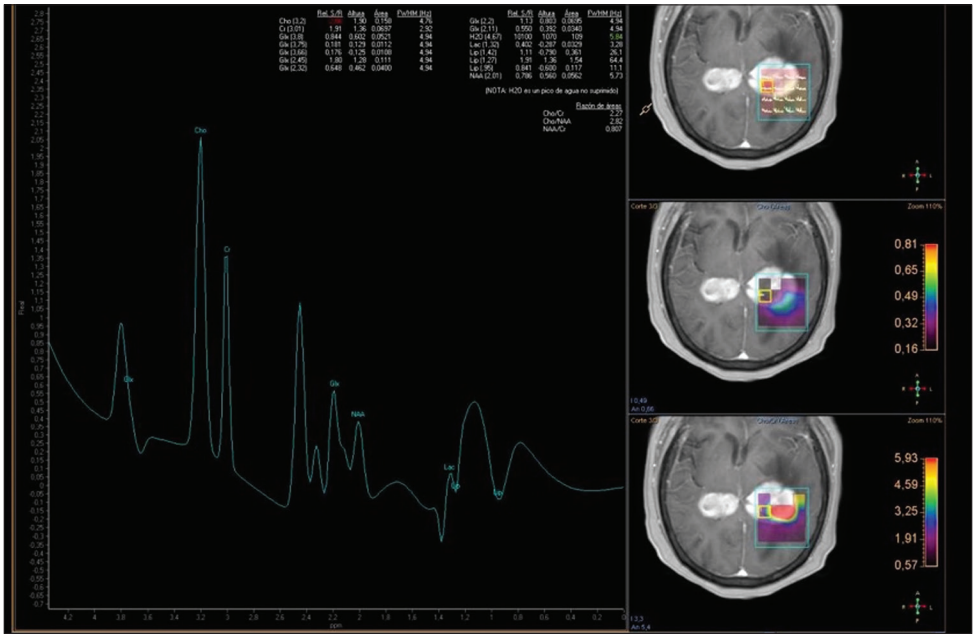

Figure 2: A T1-weighted gadolinium-enhanced magnetic resonance imaging spectroscopy with voxel within the enhancement center of the lesion, at the level of the left ventricular atrium, with the signal of an elevated choline peak, as well as creatine and a reduced N-acetyl aspartate peak. There is an elevated choline/creatine ratio of 2.27 and elevated lipids/lactate consistent with areas of necrosis.

tomography scan of the chest and abdomen with no evidence of lesions, negative tumor markers, no history of weight loss, or palpable lymphadenopathy on examination. Due to the suspicion of high-grade glioma versus lymphoma, a spectroscopy study and viral panel were requested. It should be noted that steroids (dexamethasone 16 mg/day) were previously started due to the large presence of edema eight days before the spectroscopy study; there were no resonance studies before treatment with steroids for comparison.

High-grade glioma is a malignant infiltrative lesion of the white matter that may have image similarities to the case presented, such as multicentric glioma, which represents <2% of patients with malignant gliomas, are periventricular and does not involve the corpus callosum.[20] The general characteristics that high-grade glioma shares with PCNSL are the presence of thick enhancement, periventricular locations, and vasogenic edema; however, most are heterogeneous, with irregular borders, and have a necrotic center and a hemorrhagic component.[1,13,30,32]

Table 1: Laboratories showed an absence of active HIV, EBV, and CMV infection.

Laboratory screening	Result
Epstein–Barr	Anti-Epstein–Barr nuclear IgG (EBNA IgG): Intermediate Anti-Epstein–Barr nuclear IgM (EBNA IgM): Negative Anti-VCA IgG: Positive EA-D IgG: Negative
Cytomegalovirus	Anti-CMV IgG: Negative Anti-CMV IgM: Negative
HIV	Negative
CA-15.3	9.60 U/mL: Negative
Alpha-fetoprotein	1.92 UI/mL: Negative
CEA	2.80 ng/mL: Negative
hCG	0.530 mUI/mL: Negative
CA 19–9	17.74 U/mL: Negative
CA 125	7.15 U/mL: Negative
LDH	427.3 U/L: Negative

Tumor markers in negative ranges. Elevated LDH is present in acute tissue damage. HIV: Human immunodeficiency virus, EBV: Epstein–Barr virus, CMV: Cytomegalovirus, LDH: Lactate dehydrogenase, CEA: Carcinoembryonic antigen, hCG: Human chorionic gonadotropin, EBNA: Anti-Epstein–Barr nuclear, IgG: immunoglobulin G, IgM: immunoglobulin M, VCA: Viral capsid antigen, CA: Carbohydrate antigen.

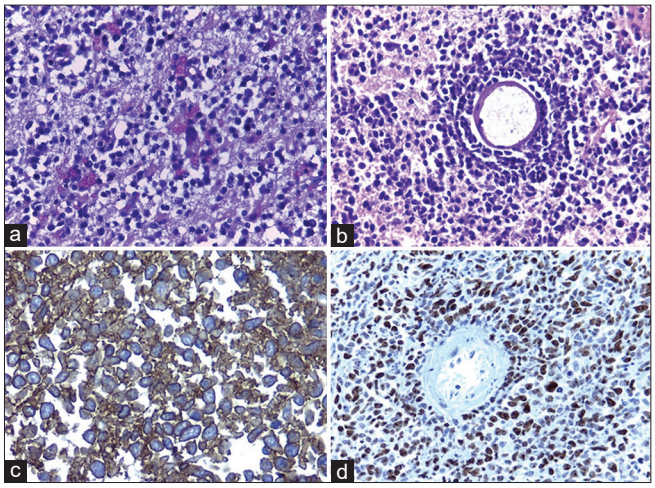

Figure 3: (a) Diffuse proliferation of mature lymphocytes infiltrating the brain tissue is observed. (b) Typical angiocentric arrangement. (c) Intense positive immunoreaction for CD20 in the membrane and cytoplasm. (d) Positive immunochemical expression for Ki-67:70%, related to a high proliferation index.

PCNSL are characteristically iso-hyperdense on non-contrast tomography, with hypointense iso-a enhancement on T2. In immunocompetent patients, when contrast is passed, a marked and homogeneous enhancement is observed due to the alteration of the blood-brain barrier; hemorrhage, calcification, necrosis, and cyst formation are unusual.[9] In immunocompromised patients, lesions with irregular margins, heterogeneity, annular enhancement, and heterogeneous peripheral areas with a center of low attenuation due to necrosis tend to be more multifocal and are also surrounded by a greater degree of vasogenic edema occur.[14,17] In diffusion studies, it presents an evident diffusion restriction and has lower ADC values than gliomas. The MRI spectral pattern in PCNSL shows a decrease in the NAA/Cho and NAA/Cr ratios and an increase in the Cho/Cr ratios, Cho/NAA, as well as the presence of lactate and lipid peaks.[15] With this information, we were more inclined to a probable case of PCNSL.

Regarding the viral panel for EBV, the values of anti-Epstein–Barr nuclear immunoglobulin G (IgG) were observed as intermediate values according to our laboratory parameters, as well as anti-Epstein–Barr viral capsid antigen IgG (anti- VCA IgG) with positive values, which indicate a history of infection, ruling out active infection [Table 1]. EBV has an infection rate of 95% and persists after the acute phase, so reactivation occurs in periods of immunocompetence, including aging, psychological stress, anxiety, and loneliness and even after 5–7 days in intensive care units, it is possible.[11,16]

Current international guidelines[4,8,10,12] have considered that resection of the lesion may provide therapeutic benefit in selected patients. In a meta-analysis, it was observed that the cases that benefit from surgical resection were patients over 70 years of age, multiple lesions, deep lesions, and Karnofsky Performance Status Scale (KPS) <70. Patients over 70 years of age who may benefit are those with superficial and single lesions. Although the authors concluded there were no differences in complications between biopsy and surgery, the complication rate is comparable with other intracranial neoplasms.[5] Other authors have developed a surgical risk category including aspects of daily life functionality, chronic degenerative diseases, cognitive impairment, cerebrovascular disease, age, and deep location of the lesions, demonstrating a high surgical risk for resection.[27] We decided to perform a biopsy due to comorbidities, neurological status, age, presence of multiple periventricular lesions, and preoperative KPS of 40. Another important preoperative consideration that affects the histopathological analysis is treatment with steroids; in this case, it was administered for eight days and was suspended seven days before taking the biopsy for a greater suspicion of PCNSL diagnosis. In the literature, steroid administration is justified in cases of intracranial hypertension, herniation and cerebral edema,[3] and it is suggested to suspend the steroids at least two weeks before surgery because they induce lymphocytic apoptosis, making it difficult for the pathologist to make an accurate diagnosis[4,12] and the requirement of a new biopsy with a longer steroid suspension.[3] Fortunately, a second surgery was not necessary for a definitive result in our case.

CONCLUSION

In neuro-oncology, primary CNS tumors with multiple lesions are rare, even more, the "mirror type" lesions. Lymphomas are lesions that can present in different ways on imaging and clinical presentation. These tumors that present a vector effect due to their size, perilesional edema or that lead to loss of neurological function are highly discussed in the diagnostic and surgical treatment. Due to their prognosis, action on diagnosis and treatment must be taken as quickly as hospital resources allow.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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