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PRIMARY CEREBRAL MALT LYMPHOMA. FIRST REPORT IN LATIN AMERICA

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Abstract

Introduction: B-cell marginal zone lymphomas consisting of the association of extranodal or mucosa-associated lymphoid tissue "MALT" is a rare type of low-grade lymphoma, usually mistaken for a meningioma; there is a small series presenting mostly dural involvement; excluding the latter, primary low-grade lymphomas of the central nervous system are extremely rare pathologies.

Methods: Case report describing the clinic, diagnosis and management of the first case of primary cerebral MALT lymphoma in the region.

Result: Report of the first case of primary cerebral MALT lymphoma in the region, diagnosed with immunohistochemistry.

Discussion: Primary cerebral MALT lymphoma is infrequent; only 5 cases have been reported worldwide. Among the differential diagnoses of primary CNS lymphomas are secondary lymphomas, cerebral toxoplasmosis, glioblastoma multiforme (butterfly glioma), brain abscess, neurosarcoidosis and cerebral tuberculoma.

Conclusion: This pathology should be included in the differential diagnosis of dural and intraparenchymal masses in immunocompetent patients.

Keywords: *Marginal Zone B-cell Lymphoma, Encephalic Neoplasms, Surgical Oncology (DeCS).*

Background

Central nervous system (CNS) lymphomas account for less than 3% of all brain tumors[1]. A variety of them, Primary CNS Lymphoma (PCNSL) constitutes 2.5% of all primary brain tumors; its diagnosis is based mainly on not finding coexistence of systemic pathology at the time of diagnosis, distinguishing it from Secondary Lymphoma [2,3]. According to the World Health Organization (WHO), diffuse extensive B-cell lymphoma is the most frequent subtype of PCNSL, leaving low-grade B-cell lymphoma, extensive anaplastic lymphoma and T-cell PCNSL as extremely rare cases[1,2]. Marginal zone B-cell lymphoma (MZML) consisting of association with extranodal tissue or mucosa-associated lymphoid tissue (MALT) is a very rare type of indolent low-grade lymphoma usually confused with meningiomas; there are small case series with mostly dural involvement; excluding these dural lymphomas, low-grade PCNSLs are extremely rare entities[2,4]. In the present report we present the clinical, surgical, histopathologic and immunohistochemical findings of intraparenchymal MALT-type LPSNC. The study has the patient's consent and the approval of the ethics committee of our institution; also, the CARE guidelines for case reports were followed.

Case Presentation

25-year-old male patient, university student from Lima; with a history of cerebral tuberculoma and seizures, diagnosed 2 years before admission (without bacteriological isolation, only imaging and therapeutic test) in another institution for which he received antituberculosis treatment with sensitive scheme, in addition to corticotherapy and valproic acid. He presents a current illness of 5 months, after a decrease of anticonvulsants he presented with generalized tonic-clonic seizure (GTCS) 2-3 times per week; therefore he went to a

neurologist who indicated dexamethasone by oral route with clinical improvement. 1 day before admission the patient presented with GTCS associated with headache. On admission examination, the patient was cooperative and oriented with no neurological deficit, reporting only headache; it was decided to start corticotherapy with clinical and imaging improvement in the following days (Figure 1). Blood tests showed leukocytosis (reactive to corticoid), negative serology for HIV, AgHBs, HCV and VDRL; at the request of pulmonology a lumbar puncture was performed obtaining GeneXpert, negative PCR (CSF), as well as sputum BK and normal chest X-ray; with this evidence, pulmonology suggested ruling out cerebral tuberculoma as a diagnosis. On admission imaging, encephalic MRI showed in T1 sequence a homogeneous contrast enhancement at the level of the left superior frontal parasagittal gyrus and without apparent involvement of the dura mater, in FLAIR moderate perilesional vasogenic edema and no restriction to diffusion in DWI sequence (Figure 1); also, a pan CT and thoraco-abdomino-pelvic MRI ruled out signs of lesion in other parts of the body. In a clinical meeting and in the face of diagnostic doubt, it was agreed to discharge the patient and to progressively suspend corticotherapy in order to better observe the tumor lesion for biopsy. 2 months later the patient came to the clinic for headache and with the result of the encephalic MRI requested in which a considerable increase of vasogenic edema was observed in FLAIR sequence (Figure 1, 2nd row), so it was decided to hospitalize the patient as an emergency and perform a brain biopsy. As an initial therapeutic intervention, stereotactic-guided tumor resection was performed. Intraoperative findings showed a fibrous, hypovascularized left frontal subcortical tumor, fibrous arachnoid and hypervascularized dura mater, and the patient was discharged on the 5th postoperative day. Pathological anatomy was received (Figure 2) which was described as a low grade B lymphoproliferative process with plasmocytic differentiation consistent with Mucosal Associated Lymphoid Tissue Lymphoma (MALT); with this result he was evaluated by the oncology service who started chemotherapy with Rituximab complemented with radiotherapy. The patient was followed up by phone calls and outpatient consultation. At present the patient is asymptomatic with functional independence following oncologic treatment. MRI at 6 months postoperative period showed no signs of recurrence of the lesion.

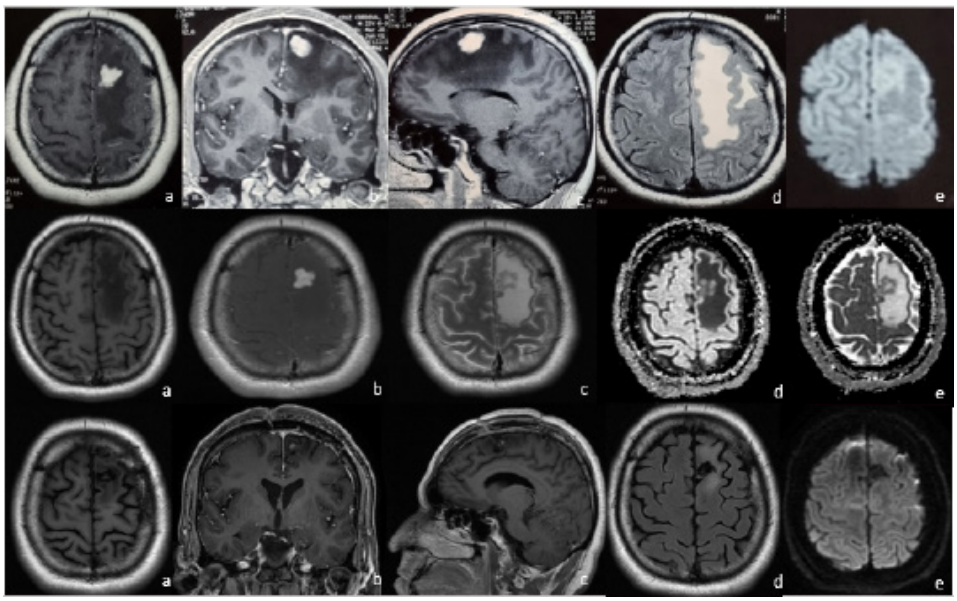

Figure 1. Encephalic MRI at admission, preoperative and 6 months postoperative (1st, 2nd and 3rd row respectively). In the 1st row (a,b,c) contrasted T1 image, a left frontal homogeneous enhancement is seen in coronal and sagittal axial section; (d) with associated edema in FLAIR and (e) without apparent diffusion restriction. 2nd row: image in T1, T1 with contrast and FLAIR (a,b,c); Diffusion and ADC without apparent restriction (d,e). 3rd row: left frontal hypointensity in relation to tumor mass resection; no contrast enhancement (b,c), slight perilesional edema in FLAIR (d).

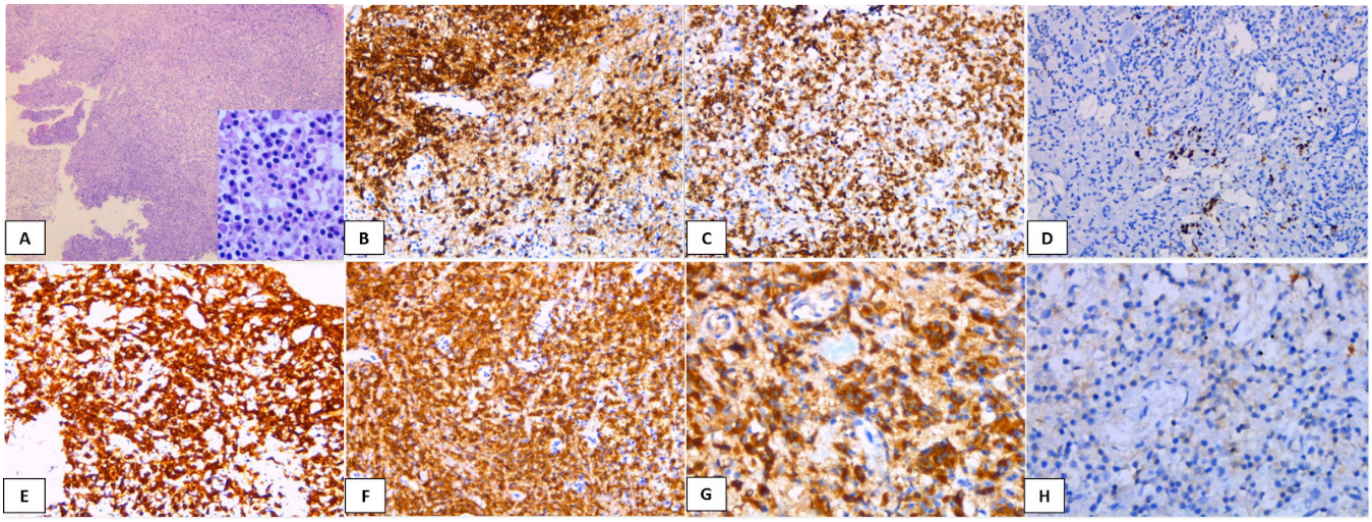

Figure 2. Fig. 1 Brain tumor biopsy (A) Brain parenchyma diffusely infiltrated by small, mature lymphocytes with plasmacytoid (H&E) features. Immunohistochemical staining highlights the positivity of the neoplastic cells for B lineage markers, such as CD20 (B) and PAX-5 (not shown); they are accompanied by a population of CD3-positive mature T lymphocytes (C); and they have a low mitotic index, as shown by Ki-67 staining (D). The neoplastic cells also express markers of plasmacytoid differentiation such as CD138 (E) and CD38 (F), with light chain restriction, a diagnostic aid. Kappa (G) and Lambda (H) immunohistochemical staining.

Discussion and Conclusion

MALT lymphoma was first described in 1983 by Isaacson. These PCNSLs are rare and carry a poor prognosis for the patient due to the aggressive nature of the lymphoma; however, cerebral MALT lymphomas have a good prognosis due to their indolent nature[5]. Only a few cases of low-grade MALT PCNSL have been described throughout history, almost entirely located extraaxially in the dura mater, predominantly in women and simulating intracranial meningioma[2,4,6]. Itoh et al. reported in their case series a total of 9 patients with B-cell MZL, 100% female, mostly supratentorial, and with an initial diagnosis of cerebral meningioma[6]. Likewise, as Park refers in his 2013 report, up to that date 35 cases of B-cell MZL were reported in the English language literature. 85.7% of them were female, with a mean age of 56 years; the site of insertion was at the dural level, mostly at the convexity, except in 3 cases that showed its origin in brain parenchyma[4,6,7]. We conducted our search using the Pubmed Mesh database with the descriptor ("Lymphoma, B-Cell, Marginal Zone" [Mesh]) AND "Brain" [Mesh], also in Latin America with the Scielo database and found a total of 5 cases of intraparenchymal MALT type PCNSL (also called extranodal B-cell MZL), including ours (Table 1); it should be noted that in Latin America no results were obtained in the search for this pathology. In Peru only 2 studies have been found in reference to PCNSL, however, the diffuse type of B cells (more frequent) were the findings in one of them, while in the other study the typification was not performed; the lack of immunohistochemistry and molecular biology inputs in our country weakens the ability to obtain accurate diagnoses[8].

In our study extranodal B-cell MZL was found at the intraparenchymal level; a very infrequent location. Most MALT-type PCNSLs are located at the dural level. It is worth mentioning that there are no MALT cells at the CNS level, which is why one conjecture is that the meningothelial cells of the arachnoid membrane are analogous to the epithelial cells of other organs where MALT lymphoma can originate[6,9]. Another hypothesis is that MALT-like tissue is formed under inflammatory conditions in the CNS, conditioning the pathway for MALT lymphoma formation[2]. In general, cerebral MALT lymphomas have a chronic, indolent presentation; they mainly affect middle-aged women and predominantly present as a dural mass, radiologically indistinguishable from a meningioma[7,10]. Among the differential diagnoses of PCNSL are secondary lymphomas, cerebral toxoplasmosis, glioblastoma multiforme (butterfly glioma), brain abscess, neurosarcoidosis and cerebral tuberculoma [3].

Table 1. Case reports of intraparenchymal extranodal Marginal Zone B-cell Lymphomas (MALT)

Case nº.	Reference	Age	Location	Clinical diagnoses	treatment
1	7	66a	frontal right	unavailable	QT
2	6	28a	PCA right	schwannoma	surgery
3	4	18a	BG left	high grade glioma	RT
4	5	45a	Right palietal	linfoma	RT
5	Current care	27 a	frontal left	tuberculoma	surgery + QT +RT
PCA: Pontocerebellar angle; GB: Basal ganglia					

In our patient we found positivity for CD38, IgG, CD20, CD 138 and PAX-5; also CD3, CD23, and S100 negative. The Ki-67 index DEL 5% and Kappa chain restriction (Kappa/ Lambda). The histology and immunophenotype are similar to MALT lymphomas found elsewhere in the body; the lymphomas are composed of small lymphocytes, marginal zone cells with slight irregularity, as well as pale cytoplasm, a few elongated cells and many plasma cells and rarely with foci of amyloidosis. Neoplastic cells without CD5 negative and CD10 negative B cells, usually with monotypic plasma cells, indicative of plasma differentiation. IgG4-positive plasma cells in some cases without evidence of systemic disease. Trisomy 3 is possible to detect in these patients and translocations are rare[1]. In dural MALT lymphoma the proliferation index (Ki67) is usually <5%; however, higher grade dural MALT lymphomas have been described at the cerebral and spinal levels[11].

MALT lymphoma presents a slow development and can be treated with local therapy such as surgery and radiotherapy, although due to the rarity of its presentation an optimal treatment has not yet been established[3,6,11]. Some literature mentions a better prognosis with respect to surgery in association with adjuvant radiotherapy[12]. In fact, primary radiotherapy is recommended in patients with slow tumor growth and little neurological deterioration[13,14]. Likewise, George *et al*. mention chemotherapy as the only management with a long-term follow-up of survival with Methotrexate[15]. In our case, the patient underwent surgery followed by chemotherapy with Rituximab and radiotherapy of 2600 cGy in 13 sessions. MALT-type PCNSL of intraparenchymal origin is a relatively benign disease that can be treated with surgery, chemotherapy and/or radiotherapy. Corticosteroid therapy can dramatically decrease the volume of PCNSLs due to the combination of its anti-edema and cytotoxic effects[3]. A probable cause of failure in the initial diagnosis in our case could be due to the reduction of the neoplasm when starting dexamethasone as antiedema; and therefore, it was decided to suspend corticotherapy to appreciate the real magnitude of the lesion and proceed with the excision of the same with the best margins.

Intraparenchymal CNS MALT lymphoma (also called extranodal B-cell MALT) should be included in the differential diagnosis of dural and intraparenchymal masses in immunocompetent patients. Additional reports may contribute to clarify its etiology and improve the therapeutic approach. Within the limitations such as the lack of budget within the health system that prevent performing complementary studies (neuropsychology studies and functional evaluation) and anatomopathological diagnoses with immunohistochemical profiles early, this could lead to the loss of cases with this same etiology; added to this, the low diagnostic suspicion and its lack of intentional search as differential diagnosis hinders its finding.

Financial and Conflict of Interest Disclosure

The report was funded by the authors; they declare that there is no conflict of interest.

Author contributions

JLLP worked on conceptualization and field research, writing the original draft, and editing the final version of the document. SCZ participated in the literature search, writing the original draft, and reviewing and editing the final version of the document. GBL participated in the field research and literature search and review of the final version of the document.

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