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Spontaneous Oculomotor and Abducens Nerve Palsy as Initial Presentation of Lymphoma of the Cavernous Sinus: Case Report

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ABSTRACT

Primary lymphomas of the skull base are rare (1% of lymphomas in adults); they can originate from the cavernous sinus and the parasellar region. Diffuse large B-cell lymphoma is the most common histologic subtype. Currently, the origin of these lymphomas is controversial, and their clinical characteristics are not very specific. There are various treatments for these lesions with a variable response; therefore, the prognosis of these lesions is variable.

Clinical case: We present the case of a 52-year-old man who spontaneously presented with diplopia. Physical examination revealed a limitation in adduction of the right eye, right palpebral ptosis, and limitation in the abduction of the left eye. Brain magnetic resonance imaging revealed a well-defined and homogeneous extra-axial lesion at the cavernous sinus level. The patient was biopsied and diagnosed with B-cell lymphoma; received chemotherapy and radiotherapy. In this article, we present a clinical case that considers the characteristics of the diagnosis and is the first B-cell lymphoma at the cavernous sinus level reported in Mexico.

Conclusion: Skull base lymphomas have a broad clinical spectrum. Minimally invasive surgery for biopsy purposes is the gold standard for diagnosis, and the treatment with the best results is chemotherapy.

Keywords: lymphoma; skull base; cranial nerves.

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Introduction.

Primary skull base lymphoma (PSBL) is an extranodal non-Hodking lymphoma (NHL) of rare incidence (only 40 cases from 1992 to date) [1,2]. The most common histological type is diffuse large B-cell lymphomas (DLBCL) (30–40%) [2]. The definition and origin of PSBL are controversial, having a broad clinical spectrum. The most compromised regions are the cavernous sinus (CS) and the parasellar region; the biopsy is recommended for diagnosis [3]. In this article, we present a male with a diagnosis of DLBCL involving CS, this being the first case reported in Mexico.

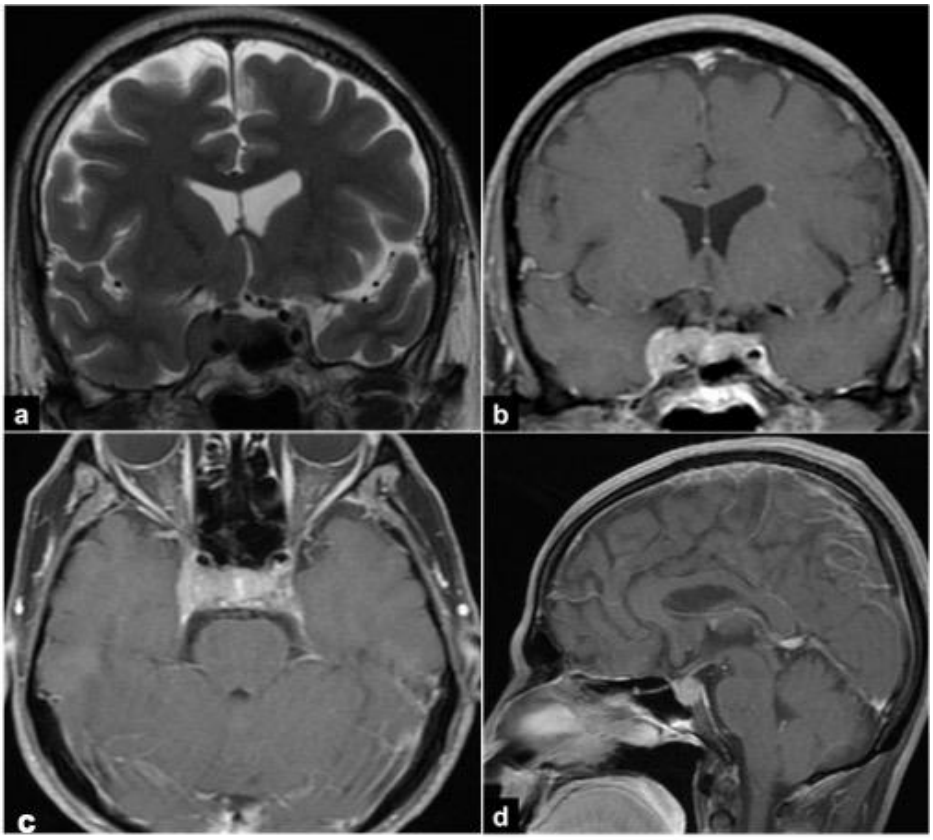

Figure 1. Brain magnetic resonance image. (a) T2-weighted coronal section image, (b) Coronal section image with gadolinium, (c) Image in axial section with gadolinium, (d) Image in sagittal section with gadolinium. A well-defined, homogeneous extra-axial lesion, predominantly on the right side, is shown at the level of the CS, which surrounds the cavernous segment of the ICA, with dimensions of 1.7 cm x 1.2 cm and which has a homogeneous enhancement upon administration of gadolinium.

Clinical case.

We present a 52-year-old male patient, resident of Minatitlán, state of Veracruz, an endemic area of tuberculosis (TB). In February 2019, he presented spontaneous diplopia; the exploration showed a limitation in the adduction of the right eye, right palpebral ptosis, and limitation in the abduction of the left eye. Brain magnetic resonance imaging (MRI) revealed a homogeneous extra-axial lesion at the CS level that predominantly involved the cavernous segment of the right internal carotid artery (ICA), with dimensions 1.7 cm x 1.2 cm, homogeneous isointense in T1 and T2 sequences, and a homogeneous enhancement with gadolinium (Fig. 1).

We have reported TB cases at the CS level in Mexico [4], so our protocol involves first ruling out TB; We performed an IGRA test (Interferon-gamma release assay) [5], which was negative; the next step was the biopsy.

The patient underwent surgery to take a biopsy using an endoscopic transnasal approach. In the sinonasal phase, no macroscopically abnormal mucosa was observed; even so, a sample was taken for histopathological study; during the intracranial phase, we found a lesion of soft, yellowish characteristics, easily aspirated and poorly vascularized. The intraoperative histopathological study reported a lesion compatible with lymphoma; the rest of the sample was sent for a definitive study (Fig. 2a).

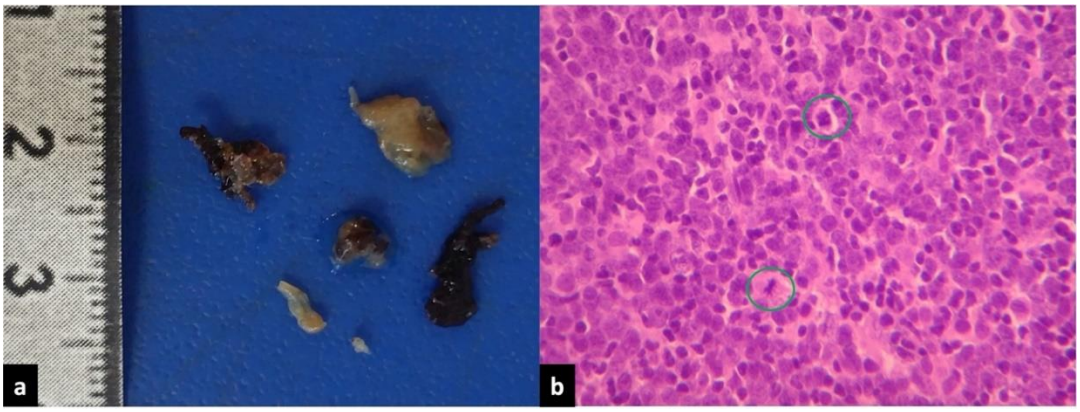

Figure 2. a) Macroscopic image: fragments of the lesion with dimensions smaller than 3 mm. b) Photomicrographs: hematoxylin-eosin staining, 40X, a neoplasm of lymphoid lineage is observed, consisting of large cells with a diffuse growth pattern, which have a vesicular nucleus, evident nucleolus, mitosis figures (circles) and a low amount of cytoplasm, are interspersed with small, mature-looking, reactive lymphocytes.

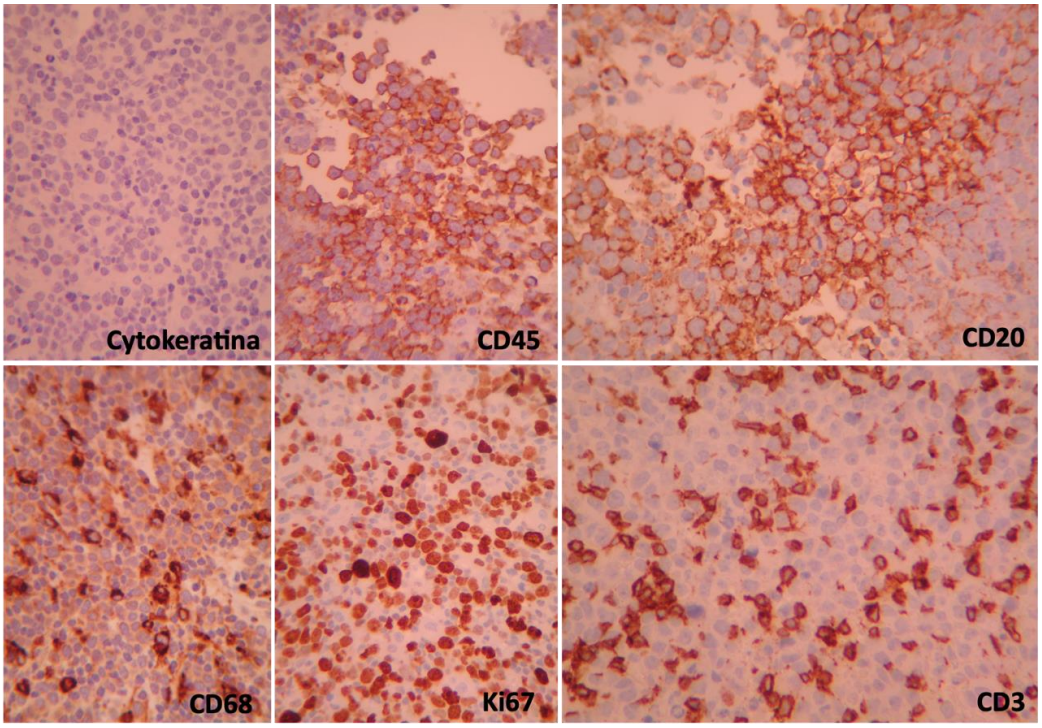

Figure 3. Immunohistochemical markers. They confirm the lymphoid nature of the neoplasm (CD45 positive) and rule out an epithelial tumor (negative cocktail cytokeratin). It is a CD20 positive B

lymphoma rich in T lymphocytes (CD3 positive) and histiocytes (CD68 positive) with a high rate of cell proliferation (Ki 67 positive in 80%).

The definitive histopathological appearance of the sinonasal mucosa was reported normal; On the other hand, the definitive histopathological appearance of the CS lesion showed a neoplasm of lymphoid lineage constituted by large cells, diffuse growth pattern, they had a vesicular nucleus, evident nucleolus, figures of mitosis, scarce amount of cytoplasm, interspersed with small lymphocytes of mature and reactive appearance (Fig. 2b). Immunohistochemical markers confirmed the lymphoid nature of the neoplasm (CD45 positive), and an epithelial tumor (negative cocktail cytokeratin) was ruled out. The final report of the study was a CD20 positive B lymphoma rich in T lymphocytes (CD3 positive) and histiocytes (CD68 positive) with a high rate of cell proliferation (Ki 67 positive in 80%) (Fig. 3).

Postoperatively, the patient continued with the same known neurological deficit. Two weeks later, he received one cycle of Methotrexate; later, he started with six cycles of Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (R-CHOP). Two months after chemotherapy (CT), radiotherapy (RT) was administered to the skull, a total of 25 Gy. Currently, the patient has no recurrence data.

Discussion.

PSBL is a pathology that represents 1 to 2% of lymphomas in adults (around 40 cases and the majority in the Asian population) [1,2]; DLBCL is the most common subtype, accounting for 30-40% of cases. It predominates in males (ratio 1.44); the mean age is 53.6 + 23.3 years [2,6]. We present the first case reported in Mexico, a male in the sixth decade of life with a diagnosis of DLBCL at the CS level.

The duration of symptoms on average is 1.43 + 1.55 months, the onset of symptoms is variable [7,8,9]; in our patient, the onset was spontaneous, and medical attention was provided two weeks after the onset of symptoms. No specific signs or symptoms have been identified; the predominant symptoms are diplopia (52%), trigeminal neuralgia (38%), headache (29%), facial paralysis (25%), and hearing loss (21%). 25% of patients present B symptoms (fever, night sweats and / or weight loss) [2,3,6,7,8,9,10,11]. The involvement of a cranial nerve is common; the abducens nerve is the most affected, the involvement of nerves III, IV, and V have also been reported at the level of the CS (isolated or combined), the involvement of the optic nerve is rare [7]. Ophthalmoplegia can also occur due to the involvement of the sphenoid bone and the orbit [11]. When the sellar region is compromised, it can manifest with a decrease in growth, thyroid-stimulating, gonadotropic, and/or adrenocorticotropic hormones [6]. Our patient presented with spontaneous diplopia, secondary to palsy of the right third cranial nerve and the left sixth cranial nerve, being a classic presentation.

Radiologically, it is characterized by being a hypo-isointense lesion in T1, iso-hyperintense in T2 with a homogeneous enhancement with gadolinium (81.8%) [8]. In the brain MRI of the patient, a homogeneous extra-axial lesion was observed at the level of the CS, predominantly involving the cavernous segment of the right ICA, with dimensions of 1.7 cm x 1.2 cm, homogeneous isointense in the T1 and T2 sequences, and with a homogeneous enhancement with gadolinium (Fig. 1). The most affected regions are the CS, the parasellar region, and the Meckel cavum (72.7-90.9%). In all cases, including ours, involvement of the arteries at the base of the skull is shown 2; but respect its diameter and path; PSBL do not deform, dislocate or infiltrate the arterial wall, unlike other CS lesions (e.g., infiltrating meningiomas); this particular feature can be useful for diagnosis [1,2,10,12].

Differential diagnoses include chordoma, chondrosarcoma, metastatic carcinoma (nasopharynx, breast, lung, or kidney).

Chordoma is a neoplasm of malignant behavior, and it arises from the remains of the fetal notochord within the clivus. Chondrosarcoma, characterized by greater production of cartilage matrix, may resemble chordoma with the difference that the latter has bone destruction [10,12]. In this case, no bone erosion was observed; the lesion predominantly involved the cavernous segment of the right ICA (absence of infiltration, stenosis, deformation, or dislocation), adding radiological evidence for this type of lymphoma.

Minimally invasive biopsy (guided needle, neuronavigation, endoscopy) is considered the diagnostic method of choice. Additionally, we performed a previous IGRA test (Mexico is a TB endemic area, and we have TB cases in CS) [4,5]; Resulting negative, after this we performed an endoscopic transnasal biopsy, the diagnosis of DLBCL in CS was corroborated with histopathology (Fig. 2 and 3).

PSBL is believed to be an atypical subtype of primary central nervous system lymphoma (PCNSL) and may arise from CS. Apart from DLBCL, T-cell and Natural Killer lymphomas have also been reported in the Asian population. There are few reported cases, so the etiology is not yet clear. It is thought that some cases of PSBL come from the NHL of the sinonasal mucosa [1,13]; in our case, the sinonasal mucosa was studied to rule out this possibility.

Immunohistochemistry is vital in the diagnosis; a complete panel is recommended (CD20, CD79a, P53, Ki67) and to study the expressions of BCL6 and BCL2 [11,14]. Diagnostic sensitivity can be increased by using specific antibodies targeting CD5, cyclin D1, CD23, CD10, DBA44, and kappa and lambda light chains [7]. Immunohistochemical markers in our patient confirmed a lymphoid-type neoplasm (CD45 positive), ruling out an epithelial tumor (negative cytokeratin cocktail); leaving a CD20 positive B lymphoma rich in T lymphocytes (CD3 positive) and histiocytes (CD68 positive) with a high rate of cell proliferation (Ki 67 positive in 80%) (Fig. 3).

The treatment strategy for PSBL should include biopsy and CT [1,15]. The standard established CT regimen is six cycles of CHOP therapy (Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone), the addition of Rituximab (R-CHOP) has also been recommended, and it has been documented that in some cases, the initial treatment strategy maybe with a regimen based in Methotrexate. The combination of both CT treatments (Methotrexate and R-CHOP) has reported satisfactory results, with a 1-year survival rate of 87.5% [1,15]. Skull RT after Methotrexate and R-CHOP has been effective as consolidation therapy; isolated RT remains controversial.

Survival has been reported up to 52 months, with a response rate to the treatment of 62.5% [15]. Our patient received one cycle of Methotrexate, then began six cycles of R-CHOP; Two months after CT, he received RT to the skull, a total of 25 Gy; currently, the patient is reported without recurrence.

Conclusions.

PSBL are rare, and this is the first case reported in our country. We consider TB infection within our differential diagnoses; PSBL has a wide clinical spectrum, and they can involve one or more cranial nerves; they may be spontaneous or progressive onset and may or may not be associated with other symptoms. The biopsy is considered the gold standard for diagnosis, preferably minimally invasive surgery, and the treatment of choice suggested is CT with a good response in most cases.

Conflict of interests.

The authors declare that they have no conflict of interest.

Ethical considerations.

The authors confirm that said publication is under the authorization of the patient and that informed consent of the aforementioned is available.

Abbreviations

CHOP Cyclophosphamide, doxorubicin, vincristine, and prednisone

CS Cavernous sinus

CT Chemotherapy

DLBCL Diffuse large B-cell lymphoma

ICA Internal carotid artery

IGRA Interferon-gamma release assay

MRI Magnetic resonance imaging

NHL Non-Hodking lymphoma

PCNSL Primary central nervous system lymphoma

PLSB Primary lymphoma of the skull base

R-CHOP Rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone

RT Radiotherapy

TB Tuberculosis

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