Primary hypothalamic-third ventricle lymphoma. Case report and review of the literature

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Summary

Primary central nervous system lymphomas (PCNSL) are infrequent tumors and their presentation as a solitary hypothalamic-third ventricle mass can be considered exceptional. We report the case of a 57-year-old woman with progressive visual deterioration, diabetes insipidus and mental confusion. She had a diffuse and homogeneous tumoral lesion involving the third ventricle and the adjacent hypothalamic area with marked enhancement after contast administration on both, competed tomography sean and magnetic resonance images. lt was approached and partially resected by the translamina terminalis route. Histological diagnosis proved to be a diffuse non-Hodgkin lymphoma and the patient subsequently was treated with adjuvant radiotherapy and chemotherapy. Followup examination showed visual acuity recover but persistent confesional state. Eight similar well described cases reported in the literature are reviewed with a description of the major diffentiating features of this neurological entity. Treatment of PCNSL remains a challenge, and the topographical location within the hypothalamic-third ventricle area is even more complex.

KEY WORDS : Primary central nervous system lymphoma. Third ventricle tumor. Translamina terminalis approach.

Linfoma primitivo de hipotálamo. Caso clínico y revisión de la literatura

Resumen

Los linfomas primarios del sistema nervioso central son tumores infrecuentes cuya presentación clínica como una lesión aislada a nivel del tercer ventrículo y área hipotalámica puede considerarse excepcional. En este trabajo describimos el caso de una paciente de 57 años que presentaba un cuadro clínico de pérdida de visión, junto a diabetes insípida y confusión mental y que fue diagnosticada mediante tomografía computerizada y resonancia magnética cerebral de una lesión tumoral situada en el tercer ventrículo y área hipotalámica adyacente. En ambas pruebas diagnósticas la tumoración captaba contraste de forma intensa y homogénea. Esta lesión se abordó quirúrgicamente a través de una vía translámina terminalis y fue extirpada parcialmente. El estudio anatomopatológico confirmó el diagnóstico de un linfoma no Hodgkin de tipo difuso y la paciente recibió un tratamiento complementario con quimioterapia y radioterapia. Durante la evolución postquirúrgica la paciente recuperó su agudeza visual pero mantuvo su estado de confusión mental. La revisión exhaustiva de la literatura ha evidenciado la existencia de tan sólo 8 casos similares descritos previamente. El tratamiento de los linfomas primarios del sistema nervioso central sigue constituyendo un desafío médico y quirúrgico, incrementándose en los casos con una localización topográfica en el área hipotalámica y del tercer ventrículo.

PALABRAS CLAVE: Linfoma primario del sistema nervioso central. Tumores del tercer ventrículo. Abordaje translámina terminalis.

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Introduction

Primary central nervous system lymphomas (PCNSL) are uncommon tumors of the CNS that account for less than 2% of primary cerebral neoplasms and 0.7 to 2 % of malignant non-Hodgkin lymphomas[2,7,10,15,19]. However, over the last two decades PCNSL frequency has increased threefold, not only among AIDS patients and others with induced or inherited immunodeficiency, but also among non-immunosupressed patients[7,9,14]. Most PCNSL are diffuse, highly malignant non-Hodgkin lymphomas exhibiting a B-cell immunophenotype[3]. Despite the frequent periventicular location of many PCNSL[19,36], the presence of a solitary primary hypothalamic and/or third ventricle lymphoma may be considered exceptional, with only eight cases previously reported in the english, french and spanish literatures[5,13,18,20,21] (abstracts from the japanesse literature are included; Table 1). We report a case of a diffuse

TABLE 1

Summary of clinical patient data in 9 cases of Primary, solitary hypothalamic-third ventricle lymphoma.

Case No.	Authors & Reference.	Age (yr), Sex	Clinical presentation	Cell type	CT scan / MRI	Treatment	Outcome
1	Lanzieri et al (18) (case 4)	18, M	Headache, diziness, polydypsia.	B-cell type	CT: homogeneous enhancement	?	?
2	Carod et al (5)	58, M	Somnolence, disorientation, memory loss	T-cell type	CT: hyperdense MRI: hyperintense (T2)	Stereotactic biopsy + XRT	Death after 14 months
3	Hirata et al (13)	31, M	Disorientation	?	CT: isodense homogeneous enhancement	Corticoids + Partial removal	?
4	Matsuda et al (21)	27, F	Amenorrhea-Galactorrhea, upper monoparesis	B-cell type	MRI: homogeneous enhancement	Open brain biopsy + XRT + Chemotherapy	Good
5	Lejeune et al (20)	42, M	ICHT, memory loss, behavior change	?	CT: hyperdense homogeneous enhancement	Stereotactic biopsy + XRT + Chemotherapy	Good (survive after 6 years follow-up)
6	Lejeune et al (20)	68, F	ICHT, coma	?	CT: hyperdense	Corticoids + XRT+ Chemotherapy	Death after 2.5 months
7	Lejeune et al (20)	68, F	Neuropsychological disturbances, memory loss	?	CT: hyperdense MRI: hyperintense (T1) homogeneous enhancement	Transfrontal partial removal + Chemotherapy	Death after 2 months
8	Lejeune et al (20)	59, F	Neuropsychological disturbances, memory loss	?	?	Transfrontal partial removal + XRT+ Chemotherapy	Good (survive after 30 months follow-up)
9	Pascual et al	57, F	Visual defect, diabetes insipidus, confusional state	B-cell type	CT: isodense, homogeneous enhancement MRI: isointense(T1) homogeneous enhancement	Translamina-terminalis partial removal + XRT + Chemotherapy	Good (survive after 1 year follow-up)

M= male; F= female; ICHT= intracranial hypertension; CT= computed tomography; MRI= magnetic resonance image; T1= T1-weighted magnetic resonance image; T2= T2-weighted magnetic resonance image; XRT= radiotherapy; ?= data not provided.

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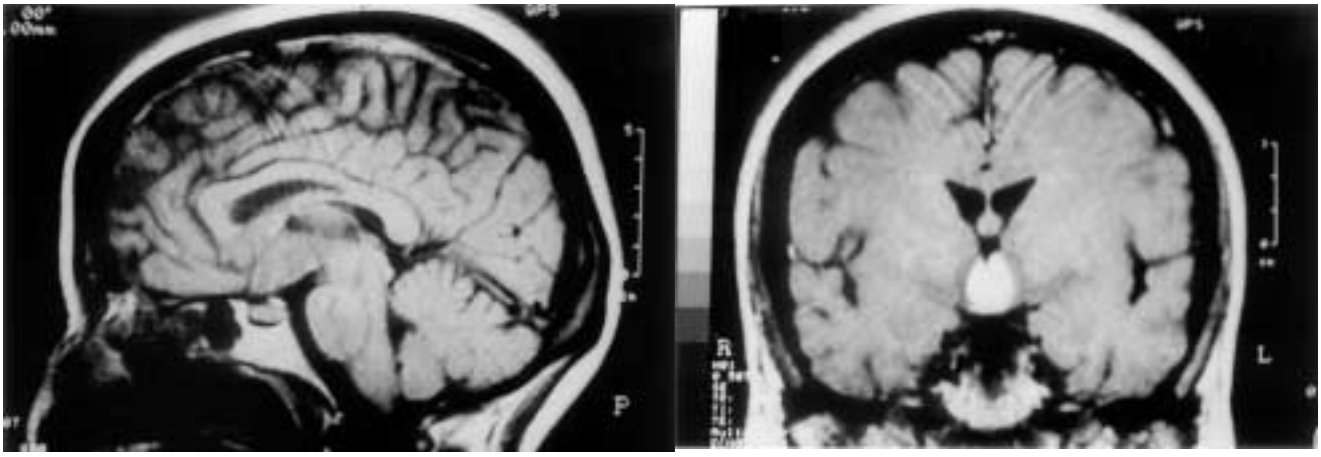

Fig. 1. *Preoperative magnetic resonance imaging. Left: TI -weighted sagittal section showing a homogeneously isointense mass within the hypothalamic-third ventricle region, as well as tumoral invasion of the septal nuclei and paraterminal and subcallosal gyri ; Right: coronal section showing a homogeneously enhanced mass with gadolinium-DTPA in the same region.*

and densely homogeneous tumoral lesion involving the third ventricle and the adjacent hypothalamic area that was approached and partially resected by the translamina terminalis route. Treatment of PCNSL remains a challenge[7,10], and the topographical location within the third ventricle-hypothalamic area is even more complex.

Case Report

This 57 year-old woman was evaluated after a one week history of progressive visual deterioration and some episodes of disorientation as to time and place together with polyuria and polydipsia and general malaise. On admission, her general physical examination was unremarkable. Neurological examination disclosed a disoriented patient as to time and place, a bitemporal hemianopia and right visual acuity loss (30/100). Measurements of 24 hours' urine output and screening of urine density confirmed a diagnosis of diabetes insipidus. Routine serum data and endocrinological investigations for pituitary function were normal.

Cranial computed tomography (CT) performed on admission showed a hyperdense, homogeneously enhancing mass occuppying the third ventricle region. Magnetic resonance images (MRI) disclosed an isointense lesion of 1.5 cm in diameter, which mainly involved the third ventricle walls and floor and which enhanced homogeneously with gadolinium-DTPA. No ventricular dilatation was noted and the chiasmatic cistern was unaffected (Fig. 1).

She was operated through a right pterional craniotomy. After opening the lamina terminalis, a tumoral mass was identified within the third ventricle and biopsied. Intraoperative histological examination of the specimen diagnosed a germinoma and consequently no attempt to achieve total surgical excision was made. Postoperatively, the patient did well and the definitive histological diagnosis proved to be a small-cell brain lymphoma. This was identified as a B-cell phenotype lymphoma by immunohistochemical methods. Looking for systemic extracranial lymphoma involvement, a body CT scan was performed and a bone marrow biopsy taken by aspiration from the iliac crest. Both tests, as well as CSF tumoral cell screening, were negative.

With the diagnosis of a primary hypothalamic-third ventricle lymphoma, the patient received whole brain radiotherapy -4000 cGy fractionated into 20 sessions- plus a booster of 1000 additional cGy over the third ventricle region. Postradiotherapy brain MRI evidenced the disappearance of the hypothalamic lesion without any enhancement after gadolinium administration (Fig. 2). She received adjuvant chemotherapy treatment consisting in 1 g/m^2 of methotrexate. The patient recovered her lost visual acuity, but six months postoperatively she continued to present a confusional state without any neurological deficit, as well as panhypopituitarism and diabetes insipidus requiring hormonal replacement therapy.

Discussion

The diagnosis of a primary brain lymphoma presenting as a unique, solitary mass located at the hypothalamus and/or the antero-inferior third ventricle region is very inusual. An extensive search among series on PCNSLs (906 cases)[1,2,11,12,14,15,22,25,26,28,31,34,36] and third ventricle tumors[4,8,16,20,23,24,27], as well as isolated case reports, yields a total number of eleven well described cases of hypothalamic-third ventricle lymphomas[5,13,18,20,21,29,33]. However, two of these cases corresponded to cerebral extension from

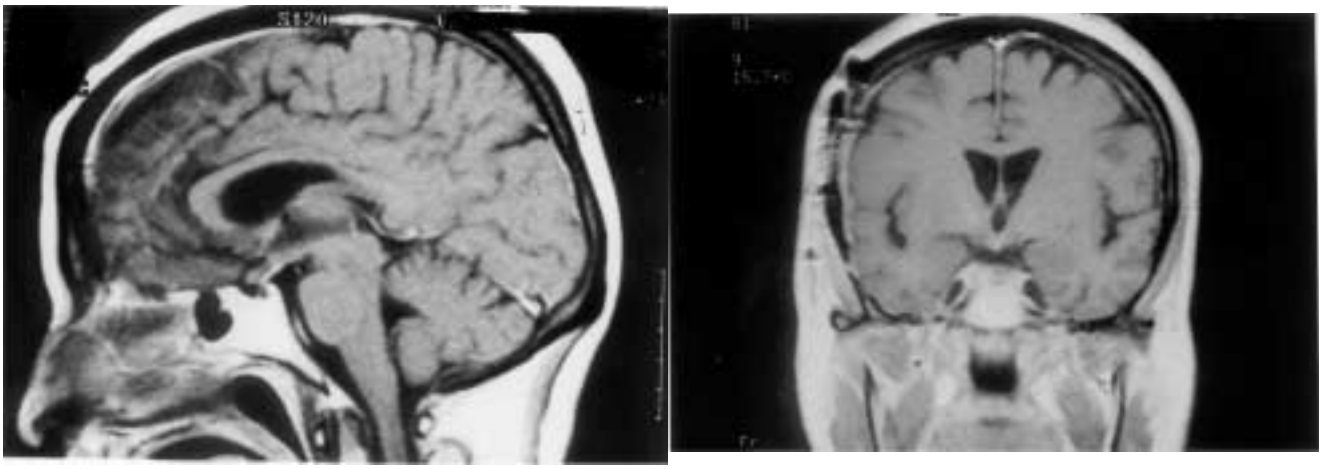

Fig. 2. *Postoperative TI -weighted magnetic resonance imaging after gadoliniumDTPA administration, shows no tumoral mass in the hypothalmic-third ventricle region. Left: sagittal section; Right: coronal section.*

extracranial lymphomas, so they can not be counted as primary third ventricle lymphomas[18,33]. Moreover, there is one case with a double lesion in the hypothalamus-third ventricle region and in the cerebellar hemisphere[29]. In consequence, there are only nine cases of well described solitary primary hypothalamic-third ventricle lymphomas, including ours (Table 1). The recent increase of these lesions could be related to the well-known rise in PCNSL incidence observed in the last two decades, not only among AIDS and immunodeficient patients, but also in the immunocompetent[7,9,14].

As a diffuse, intrinsic tumor that tends to infiltrate or replace the brain tissue rather than displace or compress it, a hypothalamic-third ventricle lymphoma should more accurately be considered a hypothalamic lymphoma that has secondarily invaded the third ventricle cavity[18,25]. This might be due to the preferentially subependymal spreading observed in many deep periventricular lymphomas[3,7,11]. Unfortunately, in many cases neither CT scans nor MRI images can provide an exact delimitation between the tumor and the third ventricle margins and this may lead to topographical misdiagnosis[30,36]. Otherwise, the CT and MRI signal characteristics of third ventricle lymphomas -mainly isodense/isointense masses that enhance homogeneously after contrast administration- are very similar to other tumors commonly encountered in the third ventricle area. Therefore, a biopsy of the lesion is necessary to achieve proper diagnosis. Preoperatively, reduction or even disappearance of the lesion after corticoid treatment may occur and this would lead to suggest primary hypothalamic-third ventricle lymphoma[35].

From the clinical point of view, lesions involving the third ventricle margins and growing within its cavity characteristically provoke mental disturbances and memory defects, as well as hormonal dysfunction. These clinical features have also been related to septal nuclei and basal prosencephalic Meynert's nucleus malfunction and distortion of the fornices and mamillary bodies[6, 17]. In relation to this fact, it must be emphasized that our case had a selective invasion of the paraterminal and subcallosal gyri, including the septal nuclei (c.f. Fig. 1)

Neurosurgeon' role in these cases should be restricted to facilitating a histological diagnosis either by stereotactic or open surgical biopsy, since there is a high rate of tumoral regrowth and a poor outcome after total PCNSL excision[2,7,19]. This is more true in third ventricle lymphomas infiltrating the hypothalamic area, since any risky maneuver can be very dangerous for the patient. In the case that a stereotactic biopsy is not suitable or can not be accomplished, the translamina terminalis approach provides a safe access to the anterior third ventricle region without damaging any functional nervous tissue area and allows visual control of both lateral walls and floor of the third ventricle [32].

Treatment of PCNSL is based on radiotherapy and chemotherapy[7,10,14,33]. However, despite the many different chemotherapy regimens used, overall results continue to be discouraging compared to the good response found in extracranial non-Hodgkin's lymphomas. This difference has been attributed to the difficulty of drugs to cross the blood brain barrier[7]. Two of the five primary hypothalamic-third ventricle lymphoma cases that have reported outcomes have had long survivals without morbidity, whereas the remaining cases died within fourteen months. There is no agreement about the chemotherapyradiotherapy administration sequence in order to achieve optimal results. Regardless of the sequence chosen, it seems to be clear that chemotherapy must be added to radiotherapy in all cases, since the two cases with good outcome received both kinds of treatment.

Conclusions

Diagnosis of a primary Central Nervous System lymphoma presenting as a unique mass involving the hypothalamic-third ventricle region is very rare. Besides hormonal dysfunction, psychiatric and memory disturbances are usual clinical manifestations. A homogeneous isointense mass with marked enhancement after gadolinium administration is the common MRI. Whether the tumor is purely intraventricular or has expanded to the third ventricle from the hypothalamic area is difficult to precise preoperatively. Differential diagnosis from other tumoral lesions of the region is difficult and consequently a histological specimen has to be obtained. Radical excision must be avoided by two reasons: 1) outcome will not be improved, as in the remaining PCNSL; and 2) high risk of hypothalmic injury. Combination of chemotherapy plus radiotherapy is considered the elective treatment.

Acknowledgments

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