Primary diffuse large B-cell lymphoma of the dura without systemic recurrence four years after diagnosis and successful therapy

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To the Editor,

Central nervous system (CNS) diffuse large B-cell lymphoma (DLBCL) represents $<1\%$ of all non-Hodgkins lymphomas (NHL) and approximately 2–3% of all brain tumors [1]. Some studies suggest an increase in the incidence of CNS DLBCL [2,3], but it is unknown whether this is due to improved diagnostic tools or reflects a real increase.

Approximately 60% of all CNS DLBCL are located supratentorially, and multiple lesions are often present. The leptomeninges are occasionally affected in CNS DLBCL, but isolated leptomeningeal or dural lymphomas are rare. Histologically, primary *leptomeningeal* lymphomas are of the DLBCL type [4,5]. In contrast, primary *dural* lymphomas are usually low grade B-cell lymphomas. Most are of extranodal marginal zone subtype [6–9], while a few low grade follicular lymphomas have been reported on [10,11].

High grade lymphomas arising from the dura is exceptionally rare. To our knowledge only two cases have been described to date [12,13]. We hereby present a case of DLBCL with a component of high grade follicular lymphoma, presenting as a primary lesion of the intracranial dura with extracranial extension, and without leptomeningeal or systemic involvement.

Case report

A 75-year-old woman presented confused after an epileptic seizure. Except for hypertension she was previously healthy. The patient's physical examination demonstrated a palpable occipital mass involving the scalp, and no neurological abnormality. An initial brain computed tomography (CT) scan showed an intracranial occipital tumor with extracranial extension. A few weeks later magnetic resonance imaging (MRI) (Figure 1) revealed a solid lesion ($4.6 \times 2.2 \times 4.2$ cm) with a broad dural base. Surrounding edema and midline shift signalled expansive growth. Preoperative diagnosis was that of a "large meningioma".

A craniotomy with removal of most of the intracranial lesion was performed. The histopathological evaluation was initially, on frozen section, that of a poorly differentiated, pleomorphic tumor. Microscopic examination of formalin-fixed tissue showed a lymphoid tumor with a predominately diffuse and focally follicular growth pattern. The diffuse areas were comprised of large blastic transformed cells (Figure 2a), whereas the follicular areas were comprised of both centrocytes and centroblasts. The tumor cells were immunoreactive for B-lymphocyte marker CD20 (Figure 2b). BCL2+, BCL6+ and CD10+ were also expressed by the tumor cells. Ki67 staining showed a proliferation fraction $>40\%$ (Figure 2c). A multiplex PCR reaction adapted for formalin-fixed paraffin-embedded material using BIOMED-2 primer sets demonstrated clonal rearrangement [14]. These findings were all consistent with a DLBCL with a component of follicular lymphoma grade 3 (A).

Subsequently, staging procedures including CT scans of chest and abdomen and evaluation of cerebrospinal fluid were performed. Bone marrow biopsy and immunophenotyping of bone marrow and blood aspirate were also assessed. All imaging tests and laboratory findings showed no sign of systemic disease.

The patient was treated with systemic chemotherapy, with three cycles of rituximab, cyclophosphamide, adriamycin, vincristin and prednisolone administered every third week (R-CHOP-21). First cycle was supplemented with intrathecal administration of cytarabine, methotrexate and methylprednisolone. Chemotherapy was followed by radiotherapy

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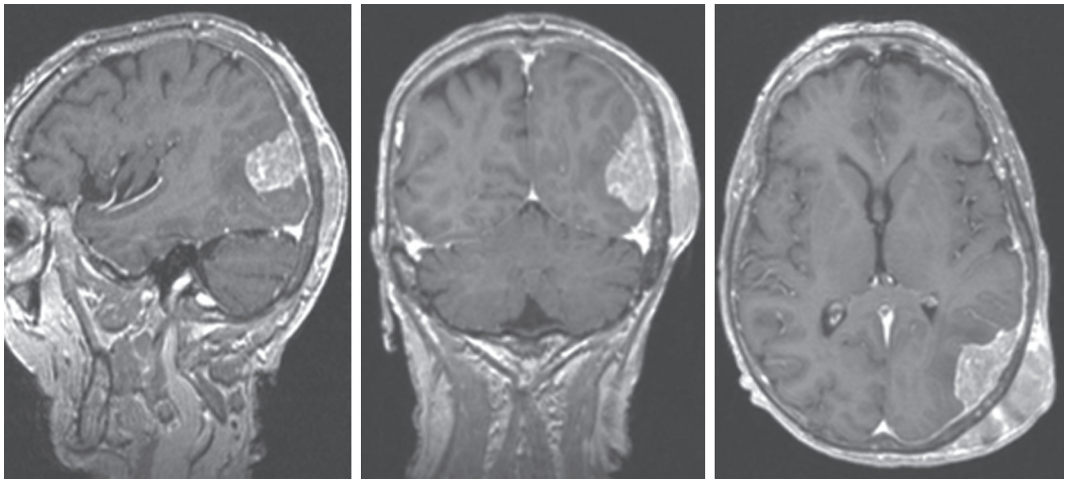

Figure 1. Magnetic resonance imaging showing a dura based solid lesion in the left occipital lobe with extracranial extension.

(4 MV photon irradiation) against the primary tumor area in the occipital region. Twenty fractions of 1.8 Gy each to a total dose 36 Gy were delivered. At follow-up four years after initial diagnosis, she was subjectly well and without recurrence

Discussion

Since leptomeningeal and dural lymphomas are rare, they are not suspected by clinicians or radiologists. Our patient presented clinically with epilepsy. Primary leptomeningeal and dural lymphomas can cause a variety of clinical non-specific symptoms including headaches, altered mental status, seizures, meningism, visual disturbances, cranial nerve palsies and progressive pareses [6,7].

Neuroimaging in cases of leptomeningeal lymphomas is often unremarkable or show non-specific findings such as hydrocephalus. On occasion, significant imaging findings may include widespread meningeal calcification, discrete masses or densities, and faint meningeal enhancement [15,16]. The radiographic presentation of dural lymphomas, however, often suggests a meningioma, which was the preoperative diagnosis in this case [17]. Dural lymphomas may be indistinguishable radiographically from a meningioma, but the presence of vasogenic edema and parenchymal brain invasion with a fuzzy tumor-brain interface do suggest a primary dural lymphoma [6].

The recent literature on CNS lymphoma has focused mainly on primary intraparenchymal lesions [18–21]. Despite the fact that lymphomas of the leptomeninges and dura are located intracranially, they are excluded from the definition of primary CNS lymphoma in the WHO classification [1]. Several other authors also make a distinction between intraparenchymal lymphomas and leptomeningeal and dural lymphomas [4–13].

Due to the few cases described in the literature, there is no standard treatment for primary leptomeningeal or dural lymphomas. Given the known aggressive course of DLBCL in general, our patient was treated with systemic chemotherapy R-CHOP (primary extranodal DLBCL stadium I), supplemented by intrathecal chemotherapy and irradiation treatment. Similar treatment approaches have resulted in positive outcomes. A 61-year-old man

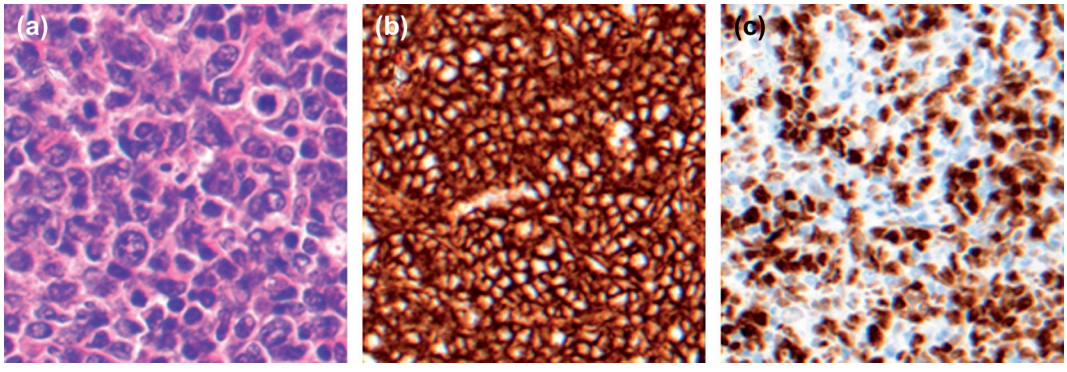

Figure 2. The tumor is histologically composed of large, blastic transformed cells with predominately diffuse growth pattern (a) (HE stain × 40). The neoplastic cells are immunoreactive for B-lymphocyte marker CD20 (b) (× 20). Ki67 staining shows a proliferation fraction > 40% (c) (× 20).

with primary dural DLBCL received a combination of surgery, radiation and CHOP chemotherapy, and no neurological deficits or systemic dissemination of the malignancy was observed after 23 months [12]. Another patient was treated with subtotal resection followed by systemic chemotherapy, consisting of methotrexate, cytarabin, ifosfamide, vincristine and cyclophosphamide. Irradiation was excluded to prevent damage to the optic nerve and chiasma adjacent to the residual tumor. The patient was noted to be without recurrence at 30-months follow-up [13].

The prognosis for dural lymphoma appears to be better than for leptomeningeal lymphomas, but most data behind this assertion is based on the low grade marginal zone lymphoma type [6,8,9]. A cure may be achieved in some patients with low grade dural lymphomas, but the risk of systemic recurrence seems to be high and can occur several years after the initial diagnosis [6]. How this relates to the prognosis of high grade dural lymphomas remains unknown.

In summary, the clinical and radiographic presentation of primary dural lymphomas often suggests a meningioma. Our patient with dural DLBCL and high grade follicular lymphoma type was successfully treated with subtotal resection, postoperative chemotherapy and irradiation. Long-term follow-up and experience with greater number of cases are needed to assess treatment of choice and prognosis.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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