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Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue of the dura mimicking meningioma: a case report and literature review

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Abstract

MALT lymphoma of the dura is a very rare type of low-grade B-cell lymphoma. Little more than 100 cases have been reported in the literature to date.

We report a 43-year-old woman who was referred to hospital because of a series of three tonic-clonic seizures on the day of admission. Neurological examination revealed confusion and aphasia. Magnetic resonance imaging (MRI) showed a contrast-enhanced, broad-based lesion along the dura in the left parieto-occipital area. The suspicion of an en plaque meningioma was raised. The tumour invaded the brain parenchyma with visible extension into the brain sulci. There was a marked brain oedema surrounding the lesion and causing the midline shift 8 mm to the right. After stabilization of neurological condition (intravenous diuretics and steroids), the operation was performed. The diagnosis of dural MALT lymphoma was established. During the pathological examination, it was especially problematic to distinguish MALT lymphoma from follicular lymphoma, but the final diagnosis was MALT lymphoma. Surgical partial removal with additional R-CVP immunochemotherapy (rituximab, cyclophosphamide, vincristine and prednisone) resulted in complete remission. The follow-up period is 1 year. Our presented case of a MALT lymphoma highlights the fact that surgical partial removal with additional immunochemotherapy is an available option in these rare intracranial tumours.

Key words: *MALT lymphoma, CNS lymphoma, en plaque meningioma, extranodular marginal zone lymphoma.*

Introduction

Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) is a low-grade mature B-cell neoplasm [12]. The most common location of MALT lymphoma is mucosa of the gastrointestinal tract although some rare locations, such as the lung, salivary glands, breast, thyroid, bladder, kidney, skin and lacrimal glands have been mentioned [12]. An especially rare location is the central nervous system (CNS) and the dura mater. Little more than 100 cases of dural MALT lymphoma have been reported in the past [2,13,16]. Generally, most MALT lymphoma cases occur in adults, with a median patient age in the seventh decade of life. Men and women are about equally affected although there are site-specific sex differenc-

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es, with a female predominance reported for cases in the thyroid, salivary glands and dura mater. There is a clear predominance of younger middle-aged women affected by MALT lymphoma in the dura mater localization [2,3,13,16]. Due to the small number of dural MALT lymphoma cases, which do not belong to immunologically privileged site (of the CNS) lymphomas, there are still no prospective studies and the best treatment is still under consideration [2,13]. Nevertheless, this type of tumour is characterized by slow growth and generally good prognosis. Here, we report a rare case of tumour mimicking a meningioma that was partially removed and pathological diagnosis revealed a dural MALT lymphoma.

A case report

A 43-year-old woman was referred urgently to the Institute of Psychiatry and Neurology in Warsaw because of a series of three tonic-clonic seizures on the day of admission. The patient was confused and presented with mild features of mixed aphasia. No other neurological deficiency was found on physical examination. The patient had no history of comorbidities and was taking only hormonal contraception. Computed tomography (CT) (Fig. 1) in the left parieto-occipital region revealed a 5-cm contrast-enhanced lesion with surrounding oedema in the left parieto-occipital region.

The patient was admitted to the neurological ward for further treatment. The patient received intravenous steroids and antiepileptic drugs with improvement of neurological status. Thereafter, the magnetic resonance imaging (MRI) was done (Fig. 2) showing a contrast-enhanced, broad-based lesion along the dura in the left parieto-occipital area and extending through the sigmoid and transverse sinuses to the posterior cranial fossa. The mass was surrounded by large cerebral oedema of the left hemisphere, with a mass effect on the lateral ventricle and especially left occipital horn. The MRI suggested a plaque meningioma with neuroradiological findings suggestive of malignancy, which included the presence of aggressive infiltration of this tumour on the arachnoid space and visible infiltration of cerebral sulci (Fig. 3). The patient was qualified for surgical resection of the tumour.

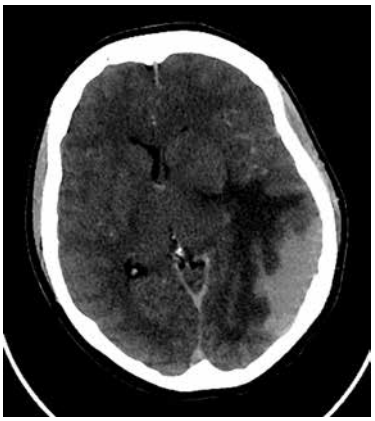

Fig. 1. The computed tomography (CT) examination revealed a contrast-enhancing lesion with surrounding oedema in the left parieto-occipital area adherent to the dura mater suggesting an en plaque meningioma or malignant form of meningioma.

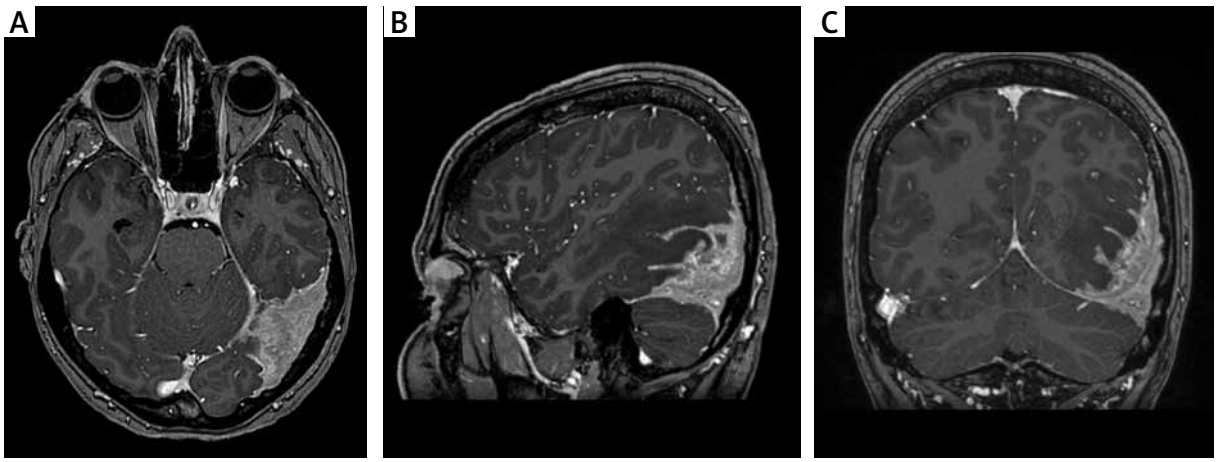

Fig. 2. Axial (**A**), sagittal (**B**) and coronal (**C**) magnetic resonance imaging (MRI) showed a contrast-enhanced, broad-based lesion along the dura in the left parieto-occipital area that extends through the sigmoid and transverse sinuses to the posterior cranial fossa. The suggestive findings of the malignance in sagittal (**B**) MR imaging included the presence of aggressive infiltration of this tumour on the arachnoid space and visible infiltration of cerebral sulci in the left parieto-occipital region.

The partial resection of the tumour was achieved. Complete tumour resection was not possible due to the high risk of cerebral cortex damage because of massive infiltration of venous sinuses. The dural cranioplasty and bone decompression were made due to the massive cerebral oedema. The postoperative CT scan showed the subtotal resection of the tumour with visible resolution of the midline shift and significant reduction of cerebral oedema (Fig. 4).

The postoperative course was uneventful, the neurological deficits completely resolved and the patient was discharged home on the second day after the surgery.

Neuropathological examination

Brain with dura samples for neuropathology studies were formalin-fixed, paraffin-embedded tissue (FFPET) and sections were prepared by routine histopathological (HP) methods. For immunohistochemistry (IHC), tissue sections were incubated with the monoclonal antibodies (MoAbs) specific for: LCA(CD45), CD20, PAX-5, CD10, BCL6, MUM1, FOX-P1, BCL2, CD5, CD43, CD45-RO, kappa, lambda and Ki-67 as previously described [15]. A reaction for CD45, CD20, PAX-5, BCL6, MUM1, FOX-P1, BCL2, CD5, CD43, CD45RO was considered positive if at least 20% of the MALT lymphoma cells or T cells showed staining, while for CD10, if any cell showed staining. For the Ki-67 index assessment, 200 cells were counted under HPF (400×) examination. Microscopic examination showed diffuse proliferation of small neoplastic cells in the parietal and occipital dura (Fig. 5A). These B-cells were immunoreactive for MoAbs: LCA, CD20 and PAX-5 (Fig. 5B), MUM1 (but only 10% of cells were positive), FOX-P1 (Fig. 5C), BCL2 but without restricted expression of either kappa or lambda. The accompanying T cells were characterized by immunoreactivity with LCA, CD5, CD43, FOX-P1, CD45-RO and BCL2. In addition, a few normal B lymphocytes positive for CD10 (< 10%) (Fig. 5D) and BCL6 were found, corresponding to the remains of the reactive lymphoid follicles that were destroyed by MALT lymphoma cell infiltration. The Ki-67 proliferation index was very low, about 1%. Pathological findings were indicative of the diagnosis of MALT lymphoma of the dura.

Postoperative course

Positron emission tomography and computed tomography (PET-CT) exam excluded a disseminated disease and revealed only an increased, pathological uptake of FDG within the posterior wall of the uterus. Furthermore, there were a few small areas of increased FDG accumulation in the thyroid and sacrum area, which could indicate lymphoma infiltration. Due to gynaecological examination with transvaginal ultrasound, hysterectomy and ovariectomy were performed but the histopathological examination revealed non-neoplastic lesions unrelated to MALT lymphoma. Cerebrospinal fluid examination by flow cytometry showed no lymphoma cells. No lymphoma infiltration was found in bone marrow biopsy. The performance status of the patient

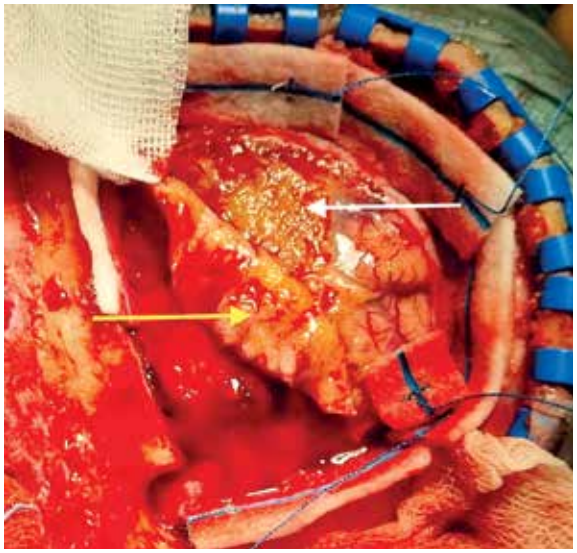

Fig. 3. Intraoperative image. After occipito-parietal craniotomy and durotomy the tumour infiltrating parenchyma was revealed (white arrow). Infiltrated dura mater (yellow arrow).

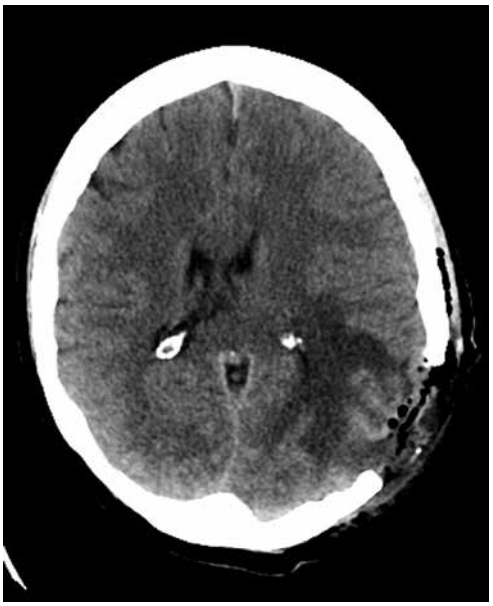

Fig. 4. Postoperative computed tomography (CT) showing subtotal tumour removal with visible reduced mass effect.

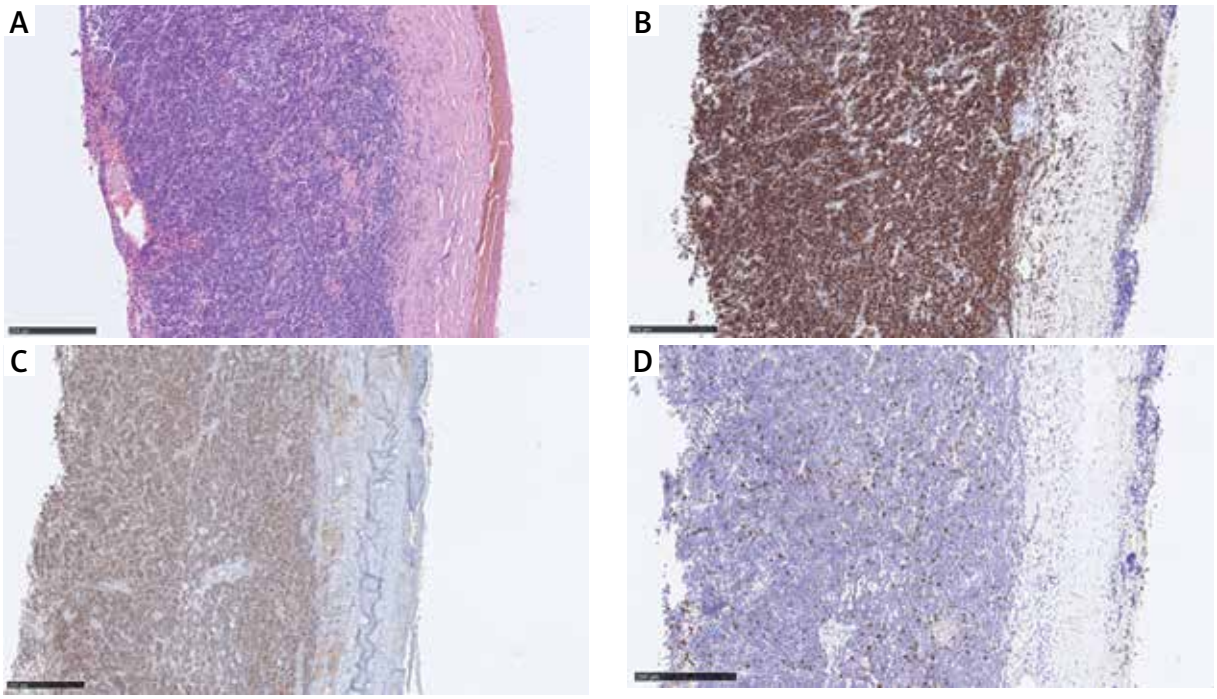

Fig. 5. MALT lymphoma of the dura. **A**) Diffuse proliferation of lymphoid cells in the occipital dura. **B**) Tumour cells express the B-cell marker, PAX-5. **C**) The lymphoma expresses FOX-P1. **D**) CD10 immunohistochemistry showing the remains of the reactive lymphoid follicles CD10(+) that were destroyed by MALT lymphoma cells CD10(–) infiltration (all photos magnified 40×).

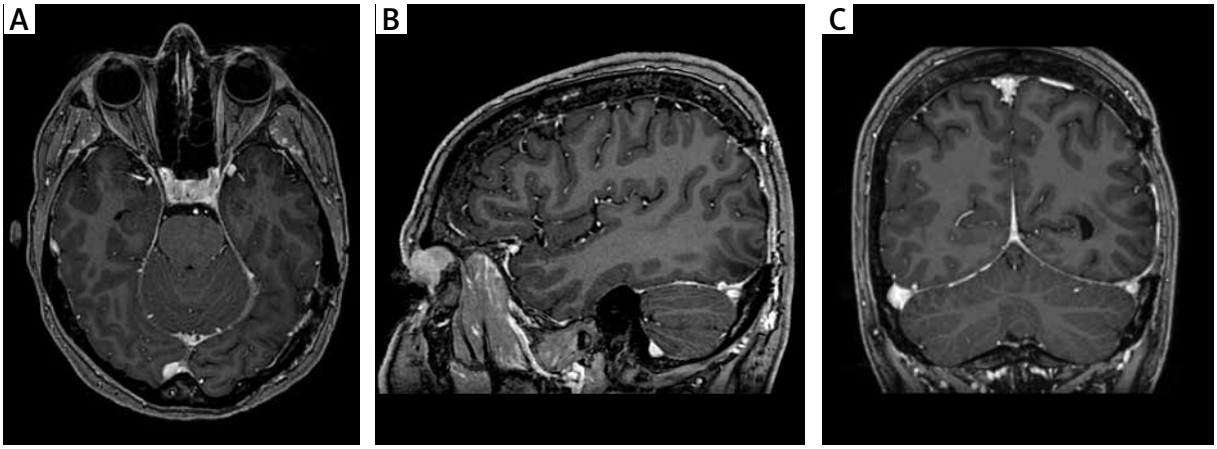

Fig. 6. Postoperative magnetic resonance imaging (MRI) – axial (**A**), sagittal (**B**) and frontal (**C**) images showing the total remission of the MALT lymphoma located in the left parieto-occipital region.

was assessed as fully active, able to carry on all pre-disease performance without restriction (ECOG 0).

Thereafter the patient underwent 8 cycles of immunochemotherapy R-CVP (rituximab, cyclophosphamide, vincristine, prednisone) with 4 intravenous infusions of high-dose methotrexate (HD-MTX) as the prevention of the secondary central nervous system involvement. The immunochemotherapy was well tolerated. Two years of rituximab maintenance is planned. So far she received 2 doses of rituximab in 2 months' interval.

An early postoperative follow-up MRI performed six months after tumour resection showed no residual mass (Fig. 6). The other lesions seen on the PET-CT scan were also in regression. No features of patholog-

ical FDG absorption were also noticed at the operated site. The preoperative neuropsychological assessment due to the neurological status of the patient was not performed. Although, the postoperative neuropsychological examination performed 11 months after surgery revealed proper functioning with slight difficulties with word finding fluency. 13 months after the operation, the patient was further followed in the neurology, neurosurgery and oncology out-patient clinic. The patient is prepared for scheduled cranioplasty.

Discussion

MALT lymphoma of the dura is a very rare type of low-grade lymphoma characterized by the proliferation of mature B-cells [2,3,13,16]. It is more typically associated with the mucosal tissues such as the gastrointestinal tract. The primary location of the dura mater is unusual, however, the dura mater is the most common occurrence of this tumour in the CNS. Diagnosis of MALT lymphoma of the dura is difficult due to the high similarity to meningiomas in the radiological examination [11]. Other rare differential diagnoses include dural metastasis, solitary fibrous tumours, gliosarcomas, and inflammatory pseudotumours. Several cases of lymphomas misdiagnosed as chronic sub- or epidural hematomas have been described [6,8]. The diagnosis of dural MALT lymphoma is confirmed mainly by histopathological and immunohistochemical features. It is difficult to distinguish MALT lymphoma from follicular lymphoma. Follicular lymphoma (FL) of the dura is less common than MALT. They are very similar in clinical and radiological presentation. Altshuler *et al*. reported only 15 FL cases of this tumour [1,7]. In our case, the lack of expression of BCL6 and CD10 and positivity for FOX-P1 on lymphoma cells clearly excluded the diagnosis of FL. In addition, a very low proliferation index of Ki-67 also fits the diagnosis of MALT lymphoma and does not match the diagnosis of FL [12]. However lack of plasmocytic differentiation on lymphoma cells in our case, which is common in MALT lymphoma, prevented confirmation of monoclonality by kappa/lambda IHC estimation.

We report the case of a MALT lymphoma of the dura presenting symptomatically and radiologically as a meningioma. Postoperative PET-CT scan suggested disseminated tumour, but it was not confirmed by HP/IHC examinations. Dural MALT lymphoma is almost always localized disease, without systemic involvement. Only 5 cases have been reported with involvement outside the CNS [10]. Bustoros *et al*. in a retrospective analysis of 105 cases of MALT lymphoma of the dura reported that a mean age at diagnosis was 51 years (range 28-78 years), with a female to male ratio of 3 : 1. The most common symptoms of CNS lymphomas are headaches, convulsions, visual disturbances dizziness, ataxic gait, speech deficits and hearing deficits [2].

A review of previous reports showed that treatment modalities include surgery, radiotherapy and immunochemotherapy alone or in combination [1,6-8]. Surgery is often the primary treatment due to acute symptoms of the disease, as in our case. However, a combination of surgery and additionally radiotherapy is most commonly used. In our case, the patient did not undergo radiotherapy. The decision was made by oncologists due to the neurotoxicity associated with radiation. In the case of our patient, this was associated with a high risk of damage to the eloquent areas of the brain, such as the speech area. The symptoms and preoperative MRI suggested that the tumour was very close to the Wernicke's area. We also wanted to avoid the neurotoxicity of radiotherapy in this young woman with the favourable prognosis of indolent lymphoma. For this reason, the patient received only immunochemotherapy. Dural MALT lymphomas are very radiosensitive, stereotactic radiosurgery can be very useful but requires further research. According to Karschnia *et al*., GammaKnife is safe and effective in the treatment of these types of tumours [9]. Due to the rarity, the clinical features and optimal management of dural MALT are not well defined. Zhao *et al*. used only radiotherapy in a patient with MALT lymphoma of the midbrain [5,16]. On the other hand, Villeneuve *et al*. presented complete remission (CR) for more than 2 years after 6 cycles of rituximab and bendamustine without invasive surgery [14]. Complete total resection is the primary goal of surgical treatment which cannot be achieved in cases when the involvement of dural sinuses by MALT lymphoma is present. Our demonstrated case support the statement that the partial resection is recommended without the need to perform the gross total tumour resection.

De la Fuente *et al*. reported that many of the patients underwent only partial resection, achieving CR with additional treatment [4]. In our case, surgical partial removal with additional R-CVP + HD-MTX immunochemotherapy resulted in complete morphological and metabolic CR. Despite CR, the patient received 2 doses of rituximab maintenance therapy.

The role of PET-CT scan and follow-up MRI are important in the control and detection of other lesions. However, multiple foci of increased FDG absorption may be misdiagnosed as disseminated disease, like in our case. Regardless of the kind of treatment, patients always require long-term follow-up.

Conclusions

In conclusion, MALT lymphoma of the dura is a rare disease. This type of the tumour should be considered as a differential diagnosis of meningioma when the

lesion is non-typical in the radiological scan. Surgical treatment with immunochemotherapy and/or radiotherapy is usually associated with a good prognosis. The decision to choose the method of treatment should be made individually taking into account the location of the lesion, size, age and the past medical history of the patient. Although the current recommendations for the treatment of these tumours are still debatable due to their rarity in clinical practice.

Disclosure

The authors report no conflict of interest.

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