Mucosa-associated lymphoid tissue in the central nervous system presenting as meningioma: A case report

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Abstract. Mucosa-associated lymphoid tissue (MALT) lymphoma involving meningeal tissue is rare condition, easily mistaken for meningiomas upon imaging. In this report, a case of primary left temporal lobe MALT lymphoma that was initially misdiagnosed as temporal meningioma is presented, with subsequent investigation into the mechanism and treatments. Clinically, MALT lymphomas can be easily confused with meningiomas based solely on imaging and clinical manifestations. MALT lymphomas are indolent, localized lesions that can be cured through surgical resection and radiotherapy. Currently, radiotherapy is the most commonly used treatment; however, the patient in the present report did not receive any chemotherapy or radiotherapy after surgery, and recent related examinations revealed a recurrence of lymphomas that had metastasized throughout the body. As a result, future patients may benefit from chemotherapy or radiotherapy, and clinicians should be more meticulous regarding patient follow-up.

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Abbreviations: CLL, chronic lymphocytic leukemia; CT, computerized tomography; LPL, lymphoplasmacytic lymphoma; MALT, mucosa-associated lymphoid tissue; MPO, myeloperoxidase; MRI, magnetic resonance imaging; MZBL, marginal zone B-cell lymphoma; PCNSL, primary central nervous system lymphoma; PET-CT, positron emission tomography computerized tomography

Key words:

Introduction

Primary central nervous system lymphoma (PCNSL) is an extranodal non-Hodgkin lymphoma that primarily affects the brain parenchyma, eyes, cranial nerve and meninges. It is an extremely rare occurrence, accounting for <3% of intracranial tumors in the US (1,2). PCNSL is primarily composed of diffuse large B-cell lymphomas of the activated B-cell subtype (3,4), with a small percentage of these lymphomas being marginal zone B-cell lymphoma (MZBL). MZBL also includes extranodal MZL of mucosa-associated lymphoid tissue (MALT) lymphoma, nodal MZL and splenic MZL (5). MALT lymphoma was initially thought to arise from gastrointestinal lymphoma, which is the most common site; however, it can also occur in other sites, such as the lungs, head and neck, skin, thyroid and breast (5,6). Meningioma, a common tumor of the central nervous system, is easy to diagnose because of its unique imaging features, such as the dural tail sign (7). MALT lymphoma involving meningeal tissue is uncommon and can be easily confused with meningiomas clinically. In the present report, the patient had similar imaging manifestations with meningioma, but was finally diagnosed with MALT lymphoma based on pathologic findings (Fig. 1). MALT lymphoma is rare in clinical practice, therefore, the mechanism and treatments were investigated.

Case report

A 59-year-old female with a history of hypertension, but no other significant medical and surgical history, presented to The Affiliated Huai'an No. 1 People's Hospital of Nanjing Medical University (Huai'an, China) with a 3-day history of dizziness accompanied by bilateral leg weakness after an epileptic seizure with no apparent cause in November 2015. No abnormalities were found after neurological examination or routine laboratory tests. Cranial computerized tomography (CT) revealed a mass lesion in the left temporal lobe surrounded by an edema lesion (Fig. 2A). Enhanced magnetic resonance imaging (MRI) showed a relatively homogeneous enhancing mass measuring 18x43 mm with a dural tail sign under the left frontal-parietal medial plate, which is a typical imaging manifestation of meningioma (Fig. 2B and C). Based

on this information, a diagnosis of meningioma was made on November 11, 2015. The patient subsequently underwent a gross total resection of the tumor. Intraoperatively, a dark red-white 4x5x3 cm-sized tumor based on the dura mater was observed, along with invasion and adhesion of adjacent brain tissue.

For H&E staining, surgical specimens were fixed in 10% neutral formalin at room temperature for 24-48 h, and paraffin-embedded sections were produced (4 μm), stained with H&E at room temperature for 5 min and analyzed under a light microscope. Histological assessment of the tumor revealed a diffuse infiltration containing uniformly sized lymphocytes with atypia (Fig. 3A), consistent with a lymphoma diagnosis, as opposed to a meningioma diagnosis. Generally, most meningiomas are benign, and atypia is rare. The meningothelial meningioma, the most common subtype, is composed of polygonal, ill-defined, arachnoid epithelial cells variable in size, with abundant cytoplasm and large nuclei. The characteristic structure of meningiomas is the arrangement of cells in concentric circles of different sizes, with small blood vessels; the vessel walls can exhibit hyalinization, calcification or psammoma bodies.

Subsequently, H&E staining and immunohistochemistry was performed on the patient's tumor tissues. The primary antibodies used included anti-CD2, anti-CD3, anti-CD5, anti-CD10, anti-CD20, anti-CD21, anti-CD23, anti-CD43, anti-CD68, anti-CD79a, anti-Bcl-2, anti-Bcl-6, anti-MPO, anti-Cyclin D1 and anti-Ki-67 Immunohistochemical findings were as follows: $CD20^{+++}$; $CD79a^{+++}$; CD21+, CD23 $follicle^{+}$; $Ki\text{-}67^{+}$ 5%; $BCL\text{-}2^{++++}$; $CD10^{+}10\%$; $CD3^{+}$, $CD5^{+}$, CD43 $T\text{-}cell^{+}$; Cyclin $D1^{-}$; MPO^{-}; $CD68^{-}$; and $CD10^{+}10\%$ (Fig. 3B shows representative staining for CD20). The characteristics of small B-cell malignant lymphoma were consistent with extranodal MZBL of the MALT type.

Based on the immunohistochemical findings and histological assessment, it was recommended the patient receive chemotherapy or radiation therapy; however, the patients' economic situation led to her decision to be discharged from hospital. Patient follow-up after discharge from hospital continued via telephone and the internet (messaging) for 2 years, during which time the patient experienced no discomfort such as dizziness, headache and weakness. After this 2-year period, the patient began experiencing these symptoms; however, no abnormalities were found upon examination. Unfortunately, a cranial enhancing CT performed in November 2021 revealed a mass lesion in the left temporal lobe, along with left frontotemporal lobe and basal ganglia edema, which could not rule out postoperative recurrence; however, the patient opted out of treatment. The patient developed slurred speech accompanied by intermittent nausea, vomiting, headache and dizziness after 2 months, prompting her to re-evaluate treatment. Given the possibility of lymphoma recurrence, an MRI in January 2022 was performed and subsequently revealed abnormal enhancement of the left frontotemporal lobe along with surrounding edema and multiple enhancements of the intracranial meninges (Fig. 3C-E). Furthermore, a PET-CT scan showed multiple metastases throughout the patient's body. The patient was transferred to the oncology department for antitumor therapy after discharge.

Discussion

Primary central nervous system lymphomas are predominantly aggressive diffuse high-grade B-cell lymphomas of the large B-cell type. MALT lymphomas arise from B-cells in the MALT marginal area and are also known as extranodal marginal area B-cell lymphoma. The majority of MALT lymphomas occur in middle-aged women, and symptoms include epilepsy, headache and visual disturbance (8). The cytologic composition can vary, including small lymphocytic, plasmacytoid and marginal zone type cells; these may have reactive follicles, numerous transformed lymphocytes, plasma cells and other inflammatory cells (9).

Currently, there are a few widely accepted mechanisms for the formation of MALT lymphomas. In embryology, meningothelial cells are concentrated in the arachnoid membrane and dural venous sinuses, similar to epithelial cells in other sites where MALT lymphoma develops (4,10) In addition, dural-based MALT may be caused by the implantation metastasis of undiagnosed or disappearing MALT lymphoma at the meninges (11). Furthermore, the role of chronic inflammatory disease, including hepatitis C (12) and *Helicobacter pylori*-associated gastritis cannot be ruled out (8,9,12,13). Additionally, autoimmune diseases have been reported to be associated with MALT lymphoma, such as Grave's disease (14), Sjögren syndrome (8,14), scleroderma (14) and Hashimoto thyroiditis (9,13). Furthermore, IgG4 expression has been linked to primary intracranial MZBLs (15,16); Venkataraman *et al* (15) demonstrated this association through a series of retrospective analyses. A number of cases from the literature have been collated to further understand the characteristics of MALT lymphomas (Table I). Historically, the majority of cases occur in middle-aged women who primarily present with headaches and seizures, yet other manifestations can include hearing impairment, numbness, visual impairment and dysphasia, depending on the location of the tumor.

Clinically, the differential diagnosis of lymphoma is important; however, due to the dural tail sign, it can be difficult to distinguish it from meningioma based solely on imaging and clinical manifestations. Small lymphocytic lymphoma, chronic lymphocytic leukemia (CLL), lymphoplasmacytic lymphoma (LPL) are other potential diagnoses that require further histological and immunophenotypic analysis for confirmation. Notably, MALT lymphomas express CD20, CD79a and CD38, which can also be seen in LPL (Table II). In addition, CLL expresses CD5 and CD23. In the present case, a 59-year-old woman presented with dizziness and bilateral leg weakness. Immunophenotypically, the patients' lymphoid cells were positive for CD20, CD79a, CD21, CD23, BCL-2, CD3, CD5 and CD43, but were negative for Cylin D1, MPO and CD68. Although the immunohistochemical findings were similar to follicular lymphomas, the cells of follicular lymphoma grew nodular and formed obvious follicular structures at low magnification, which were not observed in the pathological findings of this tumor. Although the specific type of lymphoma cannot be confirmed, MALT lymphoma is more likely based on clinical symptoms, imaging and immunohistochemistry. However, it is unfortunate that genetic analysis of the lesion was not performed to verify and validate the diagnosis and treatments. Additional detection of

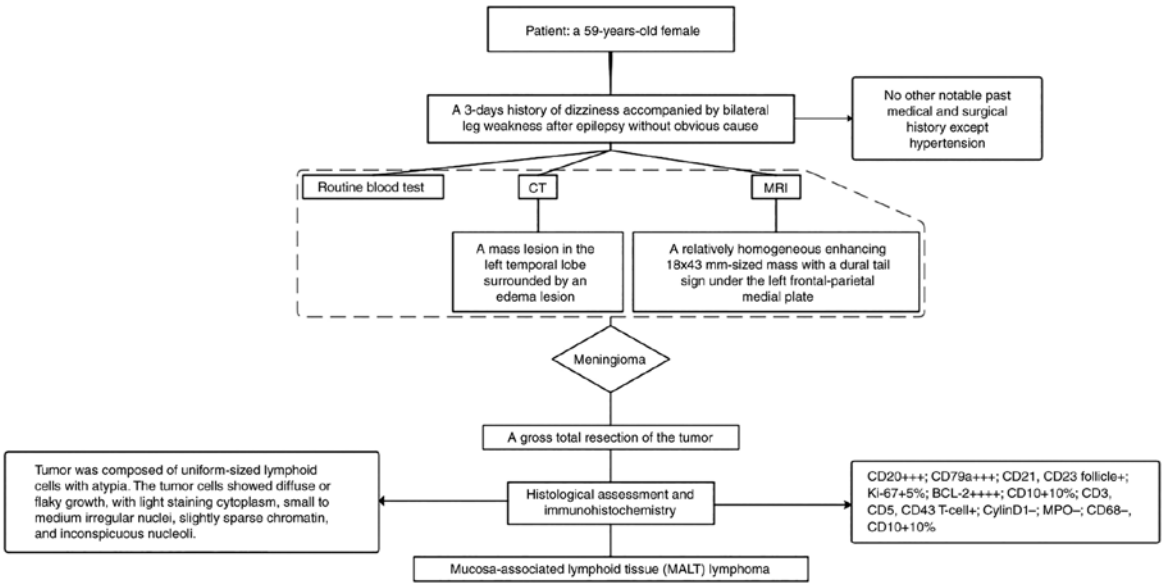

Figure 1. A flow diagram outlining the process of diagnostic examination.

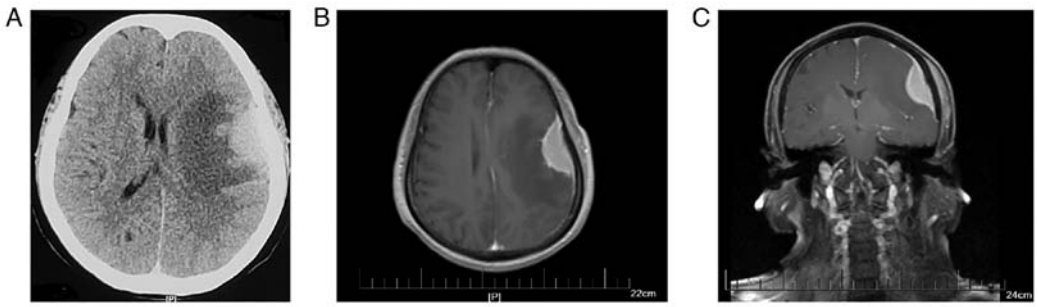

Figure 2. MRI and CT scans of subdural mass before craniotomy. (A) Cranial CT showing a mass lesion in the left temporal lobe with an edema lesion surrounded. (B) Axialand (C) coronal MRI showing a relatively homogeneous enhancing 18x43 mm-sized mass exhibiting dural tail sign under the left frontal parietal medial plate and thickening of the adjacent cranial plate.

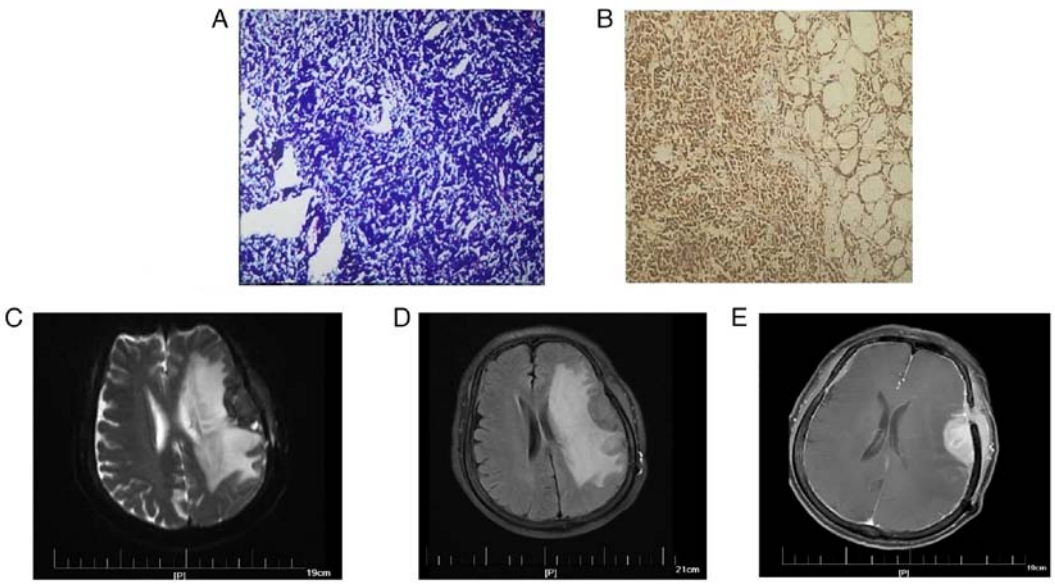

Figure 3. Pathological findings of tumors and the MRI scans of tumor recurrence. (A) H&E staining of the tumor revealed that the tumor was composed of uniform-sized lymphoid cells with atypia. The tumor cells showed diffuse or flaky growth, with light staining of the cytoplasm, small to medium irregular nuclei, slightly sparse chromatin, and inconspicuous nucleoli. (B) Immunohistochemical findings for CD20: The tumors cells highly expressed CD20. (C) T2 phase, (D) T2FLAIR and (E) enhanced MRI scans. Axial MRI showed abnormal enhancement of left frontotemporal lobe with surrounding edema and multiple enhancement of intracranial meninges as well as left frontotemporal subcutaneous and left buccal lesions.

Table I. Summary of patient characteristics with intracranial extranodal marginal zone B-cell lymphomas.

First author/s, year	Case	Age	Sex	Location	Symptoms	Treatment	Remission/ outcome	Immunohistochemistry	(Refs.)
Rottnek *et al*, 2004	1	47	M	Left tentorial	Seizure, visual field defects and memory loss	Subtotal excision and radiation	NED at 8 months	$CD20^+$, $CD79a^+$, $CD43^+$ and kappa LCR	(9)
Kambham *et al*, 1998	2	39	F	Left CP angle (dura)	Hearing loss and facial pain/weakness	Subtotal excision	AWD after 4 years	$CD20^+$, $CD79a^+$, $CD21^+$ germinal centers and kappa LCR	(17)
	3	62	F	Left parietal-occipital area	Headaches	Radiation	AWD after 6 months	$CD20^+$ and $CD79a^+$	
Kumar *et al*, 1997	4	40	F	Right cavernous sinus	Numbness and visual field defects	Radiation	NED at 63 months	$CD20^+$, $CD3^+$ reactive T cells and lambda LCR	(10)
	5	62	F	Biparietal dural	Seizures	Fludarabine	NED at 22 months	$CD20^+$, $CD3^+$ reactive T cells and lambda LCR	
	6	52	F	Left frontal dural	Seizures and numbness	Radiation/ chemotherapy	NED at 9 months	$CD20^+$, $CD3^+$ reactive T cells and kappa LCR	
	7	43	F	Left tentorial	Dizziness, headaches, blurred vision and numbness	Radiation	NED at 7 months	$CD20^+$, $CD3^+$ reactive T cells, $CD43^+$ and lambda LCR	
	8	57	F	Left anterior falx cerebri	Seizures	Radiation	NED at 14 months	$CD20^+$, $CD3^+$ reactive T cells, $CD43^+$ and $CD23^-$	
Itoh *et al*, 2001	9	28	F	CP angle	Tinnitus, nausea, headache and bilateral papilledema	Excision	NED at 2 years	$CD20^+$, $CD10^+$ (follicular center cells), $BCL2^+$ in some follicular centers, $CD43^+$ and $CD3^+$ (50% cells)	(18)
Goetz *et al*, 2002	10	64	F	Right frontoparietal dura	Left hemiparesis and headache	Excision and radiation	NED at 3 months	$IgD^+/CD20^+$ small lymphocytes, $IgD^-/CD20^+$ lymphoplasmacytoid cells, $CD20^-/CD138^+$ plasma cells and kappa LCR	(13)
Ferguson *et al*, 2010	11	29	F	Right frontal dural	Exophthalmos and visual loss	Decompression of the optic nerve, subtotal resection and 30 Gy radiation	NED at 3 years	$CD20^+$, $BCL\text{-}6^-$, kappa LCR and $CD5^-$	(14)

Table I. Continued.

First author/s, year	Case	Age	Sex	Location	Symptoms	Treatment	Remission/ outcome	Immunohistochemistry	(Refs.)
Jesionek-Kupnicka *et al*, 2013	12	60	F	Left parietooccipital dural	Headache, periodic cramp of the right face and numbness of the	Excision and radiotherapy (WS3D 6MV photons)	NED	$CD20^+$, $CD79a^+$, $BCL\text{-}2^+$ (reactive follicles with germinal centers), $CD3^-$, $CD5^-$, $CD23^-$, $CD10^-$, $BCL\text{-}6^-$, Cyclin $D1^-$, $Ki\text{-}67^+$ (10%),	(4)
Kamoshima *et al*, 2011	13	55	F	Left frontal dural	Seizures	Subtotal excision and 40 Gy radiation	NED at 36 months	$CD20^+$, $CD5^-$, $CD23^-$, $CD10^-$, Cyclin $D1^-$, $CD3^+$ (some lymphocytes)	(8)
Shaia *et al*, 2010	14	61	F	Dura of the right posterior fossa	Nausea, vomiting and pain over the top of scalp	Excision and 30 Gy radiation	NED at 6 months	$CD20^+$, $CD79a^+$, $CD5^-$, $CD10^-$, $CD23^-$, $CD43^-$ and kappa LCR	(19)
Tu *et al*, 2005	15	49	M	Frontal	Seizures	Chemotherapy (MTX and fludarabine)	NED at 7.6 years	Not available	(20)
	16	48	F	Dura, tentorium and falx	Headache and ear pain	Chemotherapy (MTX and leucovorin) and radiation	NED at 20 months	Not available	
Lehman *et al*, 2002	17	63	F	Supratentorial and infratentorial dural	Seizure	Excision and 36 Gy radiation	NED	$CD20^+$, $CD45^+$, $CD3^+$ (small population) and $CD138^+$ (small population)	(21)
Venkataraman *et al*, 2011	18	62	F	Bilateral parietal	Unknown	Fludarabine	NED at 22 months	Not available	(15)
Villeneuve *et al*, 2018	19	60	F	Petrous temporal bone	Vertigo and unilateral right mixed hearing loss	Chemotherapy (rituximab and bendamustine)	NED at 2years	$CD20^+$, $CD23^+$, $CD5^-$, $CD10^-$, $BCL\text{-}1^-$ and $BCL\text{-}2^+$	(22)
Park *et al*, 2008	20	18	M	Left basal ganglia	Right-sided central facial nerve palsy, right-sided weakness, dizziness and dysarthria	Radiation	NED at 22 months	$CD20^+$, $CD79a^+$, $CD3^-$, $CD5^-$, $CD10^-$, $BCL\text{-}6^-$, $CD23^-$, MUM1-, $ALK\text{-}1^-$, Cyclin $D1^-$, and negative for kappa and lambda LCR	(12)

Table I. Continued.

First author/s, year	Case	Age	Sex	Location	Symptoms	Treatment	Remission/ outcome	Immunohistochemistry	(Refs.)
Kelley *et al*, 2005	21	53	M	Right lateral ventricle	Headache and seizure	Excision and chemotherapy (liposomal cytarabine)	NED at 14 months	$CD19^+$, $CD20^+$, $CD45^+$, $CD5^-$, $CD10^-$	(23)
Jazy *et al*, 1980	22	59	M	Right temporal	Seizures, visual and hearing impairment	Radiation	NED at 16 months	Not available	(24)
Miranda *et al*, 1996	24	51	F	Right frontal	Major motor seizure	Excision and radiation	NED at 14 months	$CD19^+$, $CD20^+$ and $CD22^+$	(25)
Naberhaus *et al*, 1996	25	48	F	Right temporo-parietal	Headaches	Radiation	NED at 36 months	$CD20^+$	(26)
King *et al*, 1998	26	60	F	Cerebellar vermis and right fronto-parieto-occipital	Seizures and memory loss	Biopsy and chemotherapy	Died 3 months later due to pneumonia	$CD45RB^+$, $CD20^+$, Cyclin D1	(27)
Hodgson *et al*, 1999	27	57	F	Right sphenoid wing	Headache and mild	Excision photophobia	NED at 6 months	$CD20^+$, kappa LCR, BCL-2+	(28)
Freudenstein *et al*, 2000	28	50	F	Parafalcine and bilateral convexity dura	Headache and seizures	Systemic and intrathecal chemotherapy (MTX)	NED at 36 months	$CD20^+$, LCA^+, $Vimentin^+$, $CD3^-$, IgG light $chain^-$ and IgG $heavy\ chain^-$	(29)
Neidert *et al*, 2015	29	44	M	Right fronto-parietal dural	Involuntary muscle movements on the left-side of his body	Excision and 36 Gy radiation	NED at 2 years	$CD20^+$, $CD45^+$, $BCL\text{-}2^+$, $CD79a^+$, EMA^-, $CD34^-$, TDT^-, $CD99^-$, $Ki\text{-}67^+$ (30%), $CD3^+$, $CD5^+$, $CD10^+$, $CD23^+$ (small population)	(30)
Pavlou *et al*, 2006	30	73	F	Left fronto-parietal	Right arm weakness, partial seizures and dysphasia	Excision and chemotherapy (methylpred-nisolone, cytosine and methotrexate, chlorambucil)	Unknown	$CD20^+$, $CD79^+$, $BCL\text{-}2^+$, $CD10^-$, $BCL\text{-}1^-$, $CD5^-$, $MIB\text{-}1^+$ (10%)	(31)

Table I. Continued.

First author/s, year	Case	Age	Sex	Location	Symptoms	Treatment	Remission/ outcome	Immunohistochemistry	(Refs.)
Present study	31	59	F	Left temporal lobe	Dizziness and bilateral leg weakness	Excision	AWD after 6 years	$CD20^+$; $CD79a^+$, $CD21^+$, CD23 follicle$^+$; Ki-67^+ 5%; BCL-2^+; $CD10^+$ 10%; $CD3^+$, $CD5^+$ CD43 T-cell$^+$, Cyclin $D1^-$, MPO^- and $CD6^{8-}$	

AWD, alive with disease; F, female; LCR, light chain restriction; M, male; MPO, myeloperoxidase; NED, no evidence of disease; CP, cerebellopontine; MTX, methotrexate; LCA, leukocyte common antigen; EMA, epithelial membrane antigen; TDT, terminal deoxynucleotide transferase.

Table II. Immunohistochemistry of different types of lymphoma[a].

Types of lymphoma	Immunohistochemistry
MALT lymphoma (extranodal marginal zone lymphoma)	$CD20^+$, $CD79a^+$ and $CD38^+$
Lymphoplasmacytic lymphoma/ Waldenstrom macroglobulinemia	$CD20^+$, $CD79a^+$ and $CD38^+$/IgM^+
Follicular lymphoma	$CD10^+$ and BCL-2^+
Chronic lymphocytic leukemia	$CD5^+$ and $CD2^3$+
Mantle cell lymphoma	$CD5^+$, Cyclin $D1^-$, $CD10^-$ and $CD23^-$
Lymphoblastic lymphoma	TDT^+
Lymphomatoid granulomatosis	EBER *in situ*+

[a]Adapted from Ueba *et al* (16). MALT, mucosa-associated lymphoid tissue; TDT, terminal deoxynucleotide transferase; EBER, EB virus-encoded RNA.

MYD88, IgM and BRAF would aid in differentiating between LPL/Waldenstrom's macroglobulinemia, hairy-cell leukemia and MALT, increasing the accuracy of diagnosis.

In conclusion, MALT lymphomas are often confused with meningioma owing to similarities in imaging and clinical manifestations; thus, clinicians should not jump to conclusions when presented with images that resemble meningiomas, especially containing the dural tail sign. MALT lymphomas are generally indolent, localized lesions that can be cured through surgical resection and radiotherapy. Current evidence suggests that radiotherapy is the most commonly used treatment, and the extent of the dural lesions and leptomeningeal involvement determine the radiation field. As molecular genetic changes are tightly associated with classification, prognosis and treatment of tumors, additional detection of mutated genes is recommended, so as to more effectively treat diseases.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

JBR, LYC, SXL and JHR confirm the authenticity of all the raw data. Study conception and design was performed by LSD and JBR. Material preparation and data collection

were taken by LYC. Analysis and interpretation of data was performed by SXL. Follow-up of the patients was performed by JHR. All authors contributed to manuscript writing. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The report has obtained approval from the Ethics Committee and Institutional Review Board of Huai'an First People's Hospital (Huai'an, China; approval number: KY-2023-035-01).

Patient consent for publication

Written informed consent was obtained from the patient for the publication of the case details and any associated images.

Competing interests

The authors declare that they have no competing interests.

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