

Case Report

Primary marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue type in the brain parenchyma: a case report and literature review

Fan Chen^{1*}, Xiaoliang Liu^{1*}, Ting Lei^{1*}, Xiaoyu Yang^{1*}, Zhen Guo^{2*}, Dongdong Wang^{1*}, Dawei Chen^{1*}

Departments of ¹Neurosurgery, ²Cardiovascular Medicine, First Hospital of Jilin University, Changchun, China.
*Equal contributors.

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Abstract: Primary central nervous system marginal zone B-cell lymphoma (MZBCL) of mucosa-associated lymphoid tissue (MALT) type is extremely rare, and its clinical manifestations, radiological features, histopathological characteristics, and diagnosis have yet to be well elucidated. Herein, we reported a case with MZBCL of MALT type. Additionally, we reviewed the relevant literatures. A 62-year-old male presented with a 10-day history of headache and weakness in the left upper extremity. Brain magnetic resonance imaging (MRI) showed a 2.9 cm nodular lesion involving the right frontal-parietal lobe and centrum semiovale with extensive edema and remarkable enhancement. Surgical resection was performed, and gross total resection was achieved. Pathological examination revealed a MZBCL of MALT type. Immunohistochemical staining showed the lesion was positive to B-cell lymphoma 2 (Bcl-2), CD20, leukocyte common antigen (LCA), vimentin, and CD79a. The MIB-1 staining of the Ki67 antibody showed a labeling index of 30%. Genetic analysis showed immunoglobulin *IGH* and *IGK* gene and B-cell gene rearrangements. No adjuvant radiation or chemotherapy was performed. Six months after operation, brain MRI demonstrated local recurrence. Extranodal marginal zone b-cell lymphoma of mucosa-associated lymphoid tissue type occurring in the brain parenchyma is an exceedingly rare central nervous system tumor. The diagnosis depends on histopathological examinations. Surgical resection with adjuvant radiochemotherapy should be the choice of treatment.

Keywords: Primary central nervous system lymphoma, marginal zone B-cell lymphoma, lymphoma of mucosa-associated lymphoid tissue, case report

Introduction

Primary central nervous system lymphomas are extranodal non-Hodgkin's lymphomas, which can be found in the brain or spinal cord and constitute approximately 3-4% of primary brain tumors [1]. Marginal zone B-cell lymphoma (MZBCL) is a specific subtype of extranodal non-Hodgkin's lymphomas, and is first described as a low-grade lymphoma of mucosa-associated lymphoid tissue (MALT). MZBCL of MALT type occupies about 5% of all non-Hodgkin's lymphomas, and the most common location is the gastrointestinal tract, followed by lung, thyroid, mammary gland, synovial membrane, lacrimal gland and salivary glands, orbital cavity, dura mater, skin and soft tissue [2]. Primary MZBCL of MALT type in the brain is extremely rare, and its clinical manifestations,

radiological features, histopathological characteristics, and diagnosis have not yet been well understood. According to previous case reports, the clinical and radiological presentations might be non-specific, and the preoperative differential diagnosis from meningioma and subdural hematoma is challenging [3-5]. Herein, we reported another case with intracranial primary MZBCL of MALT type. Additionally, we reviewed the relevant literatures.

Case report

A 62-year-old male presented to us with a 10-day history of headache and weakness in the left upper extremity. After admission, brain magnetic resonance imaging (MRI) showed a 0.6 cm × 2.9 cm nodular lesion involving the right frontal-parietal lobe and centrum semi-

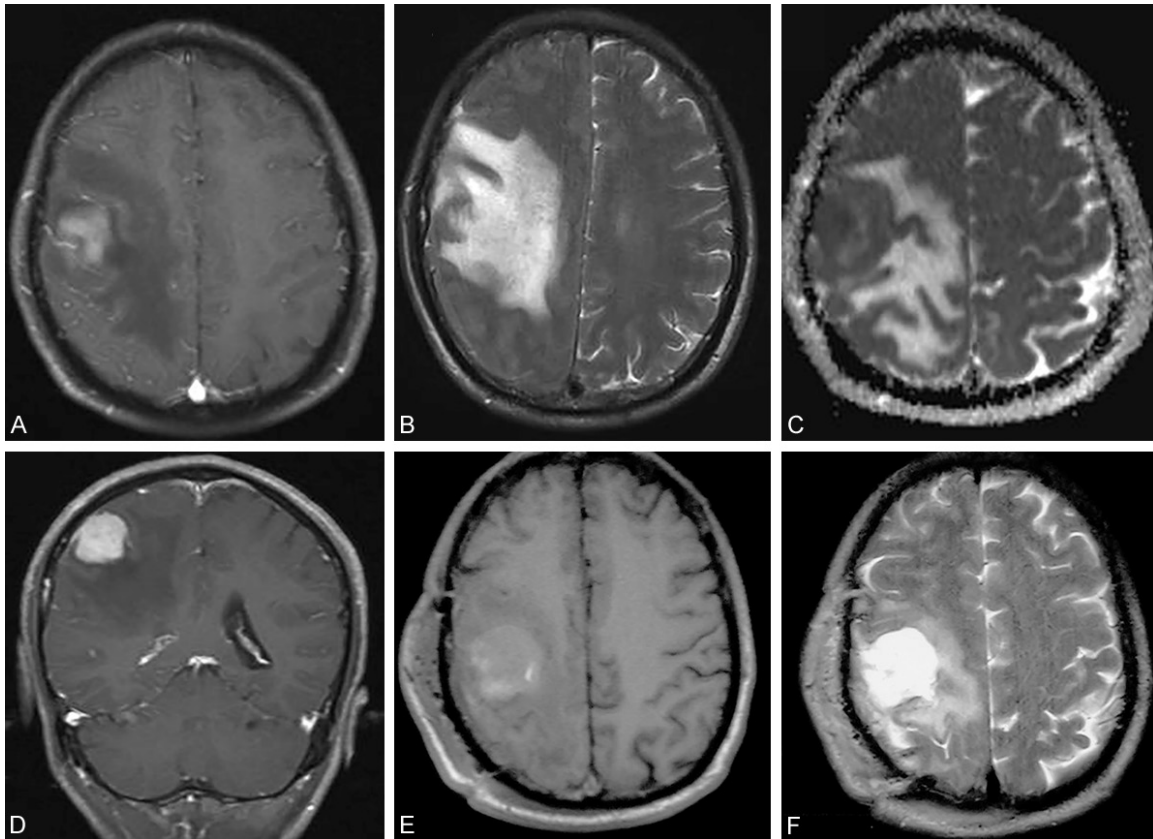


Figure 1. A, E. Axial magnetic resonance T1-weighted imaging showed a heterogeneously hypo- to isointense lesion in the right frontal-parietal lobe and centrum semiovale. B, F. The lesion appeared heterogeneously hyperintense on T2-weighted imaging. C. The lesion appeared heterogeneously hyperintense on diffusion-weighted imaging. D. After the administration of contrasted medium, the lesion was remarkably enhanced.

ovale with extensive perilesional edema and midline shift (**Figure 1**). The lesion appeared heterogeneous hypo- to isointense on T1-weighted imaging, and heterogeneous hyperintense on T2-weighted and diffusion-weighted imaging; after the administration of contrasted medium, the lesion was remarkably enhanced. There was no remarkable finding in the previous medical history. A preliminary diagnosis of high-grade glioma was suspected, and surgical resection was performed. Intraoperatively, the lesion was grayed and hard with rich blood supply and tight attachment with the adjacent parenchyma. Gross total resection was achieved. Pathological examination revealed a MZBCL of MALT type (**Figure 2A**). Immunohistochemical staining showed the lesion was positive to B-cell lymphoma 2 (Bcl-2), CD20, leukocyte common antigen (LCA), vimentin, and CD79a (**Figure 2B-E**). The MIB-1 staining of the Ki67 antibody showed a labeling index of 30%. Genetic analysis showed: 1) *IGH* gene

rearrangements, VH-FR1-JH (-), VH-FR2-JH (+), VH-FR3-JH (-), DH-JH (-), DH7-JH (-); and 2) *IGK* gene rearrangements, VK-JK (+), VK-intron-k de (-) (**Figure 2F, 2G**). No adjuvant radiation or chemotherapy was performed. Six months after operation, brain MRI demonstrated local recurrence.

Discussion

MZBCL includes three specific subtypes: MALT, nodal marginal zone lymphoma, and primary splenic marginal zone lymphoma. MALT is the most common subtype, which was firstly described as a distinct low-grade MZBCL of mucosa-associated lymphoid tissue by Isaacson and Wright in 1983 [6]. MZBCL of MALT can occur in any lymphoid-tissue-lacking extranodal sites including gastrointestinal tract, lung, salivary glands, lacrimal gland and skin; this entity is associated with the chronic antigenic stimulation caused by infectious or autoimmune dis-

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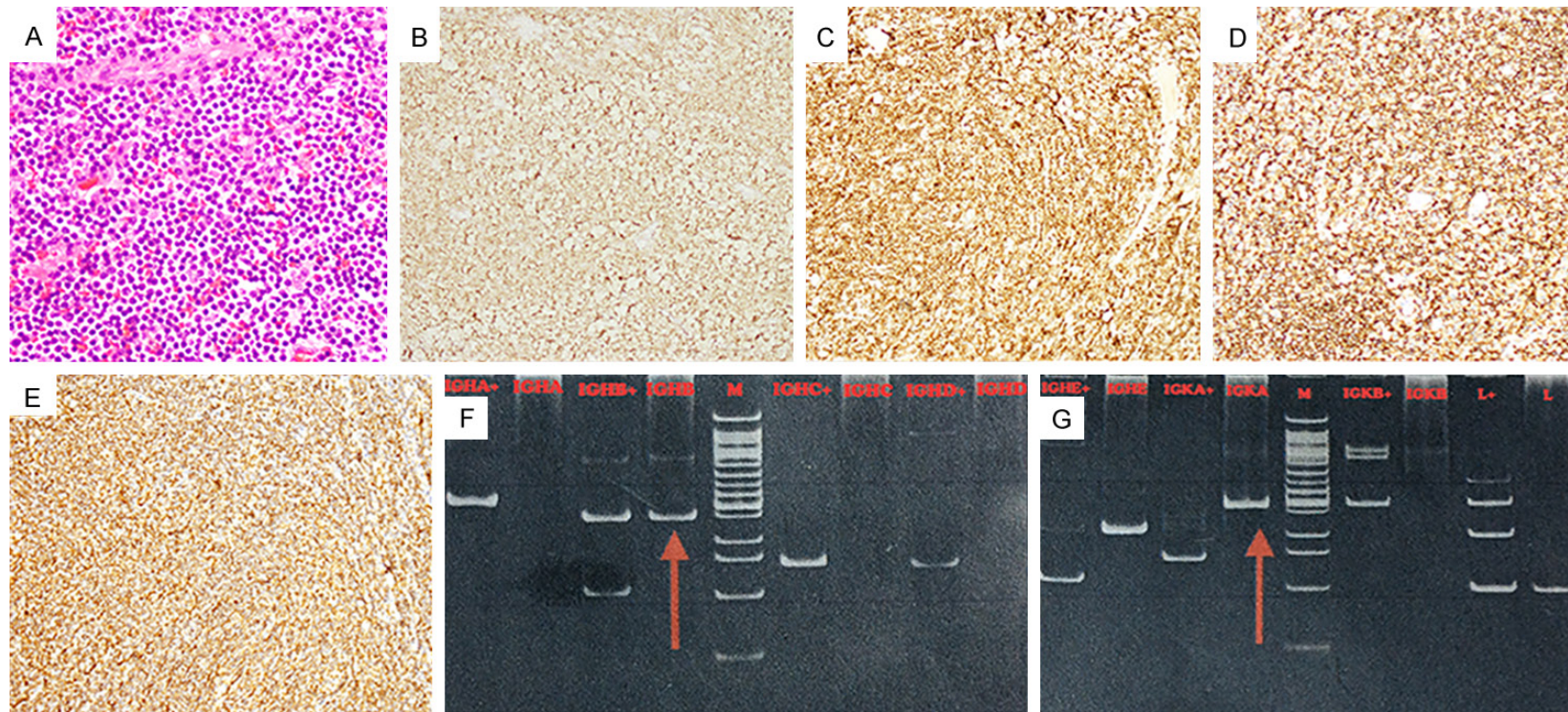


Figure 2. Hematoxylin and eosin staining showed extensive infiltration of small lymphocytes (A, $\times 400$). Immunohistochemical staining showed the lesion was positive to B-cell lymphoma 2 (B), CD20 (C), leukocyte common antigen (D), and vimentin (E). Gel electrophoresis showed monoclonal rearrangements of *IGH* (F) and *IGK* (G) genes.

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eases, such as gastric lymphoma, helicobacter pylori infection, parotidian lymphoma, and Sjogren syndrome. Primary MZBCL of MALT in the central nervous system is extremely rare; the previous literatures were limited to case report. The most common onset age was 40-60 years. The clinical manifestations included epileptic seizure, headache, visual disturbance [7]. This entity could involve the dura matter and the choroid plexus [8]; the former is relatively common, and the latter is infrequent. Previous literature review found 15 of the 17 cases involved the dura matter, and the other 2 cases involved the choroid plexus [7]. Interestingly, primary MZBCL of MALT involving the brain parenchyma is exceedingly rare.

Since there is no mucosa and lymphoid tissue in the intracranial site, the origination of MZBCL of MALT in the central nervous system has been unclear. Some scholars proposed the occurrence of MZBCL of MALT in the central nervous system might be associated with activation of the lymphatic system caused by chronic inflammation or autoimmune diseases [3]. Kumar et al. thought the tumor originated from some specific cells embryologically similar to mucosal epithelial cells, such as meningeothelial cells in the arachnoid and venous sinus [9]. Saggiaro et al. held that MALT in the central nervous system was mostly metastasized from the extracranial sites [10]. The definitive origination still needs further research.

Due to the rarity of MZBCL of MALT in the central nervous system, the radiological features have not yet been well understood. In the previous literatures, the majority of these entities presented as dural space-occupying lesions mimicking meningiomas [2-5, 11-15]. Pavlou et al. found the MALTs arising from meninges had similar intensity as meningiomas, and the differential diagnosis is challenging [4]. However, compared with meningiomas, MALTs are more likely to invade the extracranial region through the basal foramina [3]. Selcuk et al. reported a case with atypical MALT mimicking subdural hematoma [5]. In the current case, the preoperative MRI showed the lesion was heterogeneous hypo- to isointense on T1-weighted imaging, and heterogeneous hyperintense on T2-weighted and diffusion-weighted imaging, with extensive edema and remarkable enhancement, which was consistent with the radiological characteristics of high-grade gliomas.

Pathological and immunohistochemical examination is the gold standard of diagnosis for MZBCL of MALT [3, 6, 11, 13, 14]. Microscopically, MZBCL of MALT presented as extensive infiltration of small to medium sized heterotypic lymphocytes; the tumor cells can appear as centrocyte-like cells, monocytoid cells, or lymphoplasmacytoid cells. In the current study, hematoxylin and eosin staining showed extensive infiltration of small lymphocytes. MZBCL of MALT is positive to B lymphocyte-associated antigens such as CD20 and CD79a, but negative to CD5 and CD23 [16]. MZBCL of MALT has no specific marker, and the main pathological differential diagnoses include small cell lymphoma and lymphadenosis; all these three entities are positive to CD19, CD20 and CD79a, nevertheless MALT is usually negative to CD5 and CD23, follicular lymphoma is positive to CD10, and mantle cell lymphoma is negative to Cyclin D1.

Monoclonal rearrangements of *TCR* and *IGH/IGK* genes are the common genetic characteristics of T/B cell lymphomas [17]. In the current case, we identified monoclonal rearrangements of *IGH/IGK* genes. Additionally, the specimen was negative to Epstein-Barr virus-encoded small RNA (EBER), and the nuclear acid quantification of serum Epstein-Barr virus was negative, consistent with the previous literatures [3, 14, 15]. These findings support that MZBCL of MALT in the central nervous system has no association with Epstein-Barr virus infection.

The treatment of primary MZBCL of MALT in the central nervous system has not been outlined. The previous cases were all diagnosed by postoperative pathology, nevertheless there was no study regarding the relationship between prognosis and different treatment modalities including extent of resection and adjuvant therapy. Considering the potential risk of intraoperative hemorrhage, we recommend an en-bloc resection. According to literature, MALTs in the central nervous system may be sensitive to chemotherapy [13, 18]; the definite role of adjuvant therapy in central nervous system MALTs still needs further research.

In conclusion, primary MZBCL of MALT in the central nervous system is an extremely entity. The radiological features are non-specific and variable. Individual comprehensive treatment should be highlighted for a long-term control.

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Disclosure of conflict of interest

None.

Address correspondence to: Dr. Dawei Chen, Department of Neurosurgery, First Hospital of Jilin University, 71 Xinmin Avenue, Changchun 130021, China. Tel: 0086-43185398815; Fax: 0086-43185398815; E-mail: professorchen@foxmail.com

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