

CASE REPORT

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# Primary marginal zone B-cell lymphoma of the cavernous sinus: a case report and review of the literature

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## Abstract

**Background:** Primary lymphoma of the cavernous sinus is a rare form of extranodal non-Hodgkin lymphoma, of which very few cases have been reported in the published literature. This report presents the MRI findings with apparent diffusion coefficient (ADC) value in an exceedingly rare primary marginal zone B-cell lymphoma (MZBCL) of the cavernous sinus.

**Case presentation:** The case in this study is a 59-year-old immunocompetent male patient with a 2-month history of right ptosis and blurred vision. Right third cranial nerve palsy and binocular diplopia were observed upon neurological examination. Preoperative brain CT showed an extra-axial enhancing mass lesion in the right cavernous sinus. On MRI, ipsilateral internal carotid arterial encasement was noted without causing stenosis of the vessel. Isointense signal on T1-weighted and T2-weighted images, homogeneous contrast enhancement, and diffusion restriction were also observed. The mean ADC value of the tumor is  $0.64 \times 10^{-3} \text{ mm}^2/\text{s}$  (b value = 1000 s/mm<sup>2</sup>). Subtotal resection of the tumor was performed, and improvement of clinical symptoms were observed. The pathologic diagnosis of MZBCL was established by immunohistochemical examinations.

**Conclusions:** Primary MZBCL of the cavernous sinus is exceedingly rare, and preoperative confirmation poses a major challenge with CT and conventional MRI only. In this case, preoperative quantitative ADC value is shown to offer valuable additional information in the diagnostic process.

**Keywords:** CNS lymphoma, Marginal zone B-cell lymphoma, Cavernous sinus, MRI, DWI, ADC

## Background

Primary central nervous system lymphoma (PCNSL) is a rare form of extranodal non-Hodgkin lymphoma (NHL) typically limited to the neuroaxis without systemic involvement. It represents approximately 1% of NHLs and 4% of all intracranial neoplasms [1, 2]. The brain parenchyma is the most common site of involvement, followed by the eye, the leptomeninges, and the spinal cord [3]. Most PCNSLs are aggressive lymphomas

that typically affects immunocompromised patients and carry a dismal prognosis [3, 4]. Diffuse large B-cell lymphoma (DLBCL) is the most common histologic type, accounting for 90% of the cases [5]. The PCNSL usually presents as tumor mass located in the periventricular region of the brain parenchyma and exhibits pronounced contrast enhancement. Tumor necrosis with heterogeneous enhancement are more prevalent in the setting of immunocompromise [6]. However, PCNSL arising from the cavernous sinus is an extremely rare condition. The radiologic features of primary cavernous sinus lymphoma remain unclear owing to its rarity. This report details comprehensive preoperative CT and MRI findings with apparent diffusion coefficient (ADC) value in a case of

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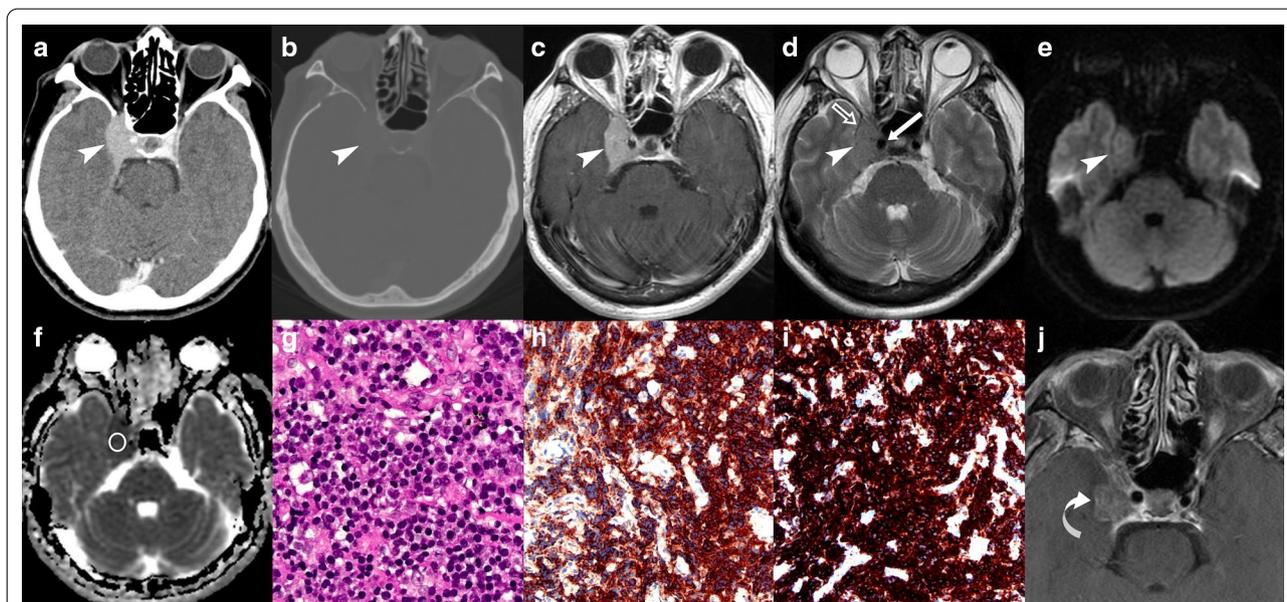
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primary marginal zone B-cell lymphoma (MZBCL) arising from the cavernous sinus. Published works pertaining to primary cavernous sinus lymphoma are also reviewed.

### Case presentation

The case in this study is a 59-year-old male patient with unremarkable medical history and a 2-month duration of right ptosis and blurred vision. No headache, fever, weight loss or nocturnal sweating is documented. Neurological examination revealed palsy of the right third cranial nerve (CN) and binocular diplopia. Pupillary light reflex and corneal reflex were intact. Routine laboratory data including complete blood count and urinalysis are within normal limits. Brain CT revealed an enhancing mass lesion in the right cavernous sinus (Fig. 1a) without surrounding skull bone destruction or hyperostosis (Fig. 1b). On brain MRI, an extra-axial tumor exhibiting isointense signals on T1-weighted and T2-weighted images and homogeneous contrast enhancement is observed (Fig. 1c, d). In addition, diffusion restriction is observed on diffusion-weighted imaging (DWI) with a low ADC value of  $0.64 \times 10^{-3} \text{ mm}^2/\text{s}$  (b value =  $1000 \text{ s}/\text{mm}^2$ ) (Fig. 1e, f). The initial diagnoses made by the reporting neuroradiologist

included meningioma, neurogenic tumor, and PCNSL. The patient underwent subtotal resection of the tumor via a right extended pterion approach. Intraoperatively, a soft and white tumor adhering to the wall of the cavernous sinus was identified, which was then meticulously resected without causing injury to the internal carotid artery (ICA). Histological examination revealed diffuse infiltration of the submitted specimen by small- to medium-sized lymphoid cells mixed with plasma cells (Fig. 1g). The final histopathologic diagnosis is MZBCL by immunohistochemical studies (Fig. 1h, i). A generalized systemic survey consisted of whole-body CT, positron emission tomography (PET) scan, and bone marrow biopsy. The results revealed no evidence of extracranial involvement. Clinical stage I<sub>E</sub> (extranodal disease limited to a single site) was thus designated according to the 2014 Lugano classification [7]. After surgery, the patient experienced relief of right ptosis and blurred vision. Adjuvant radiotherapy and chemotherapy were also implemented for residual tumor. Residual tumor and post-irradiation changes remained stable on follow-up MRI studies for more than 2 years (Fig. 1j).



**Fig. 1** A 59-year-old man with pathologically confirmed primary MZBCL of the right cavernous sinus. **a** Axial contrast-enhanced (CE) brain CT shows a bulging mass lesion (arrowhead) in the right cavernous sinus and measures  $2.0 \times 3.3 \text{ cm}$  in size. **b** Axial bone window CT image revealed no surrounding skull bone destruction or hyperostosis around the tumor (arrowhead). **c** Axial CE T1WI shows homogeneous contrast enhancement of the tumor (arrowhead) after gadolinium administration. **d** The extra-axial origin of the tumor (arrowhead) is identified based on indentation of the right temporal dura (open arrow) on axial T2WI. In addition, encasement of ipsilateral cavernous internal carotid artery is observed without causing narrowing of the vascular lumen (white arrow). **e** Diffusion-weighted image (DWI) shows isointensity in the tumor (arrowhead). **f** The measured apparent diffusion coefficient (ADC) value (circular region of interest) is  $0.64 \times 10^{-3} \text{ mm}^2/\text{s}$  (b value =  $1000 \text{ s}/\text{mm}^2$ ), indicating diffusion restriction as compared with brain white matter. **g** The resected tumor is composed of a diffuse infiltration of small to median-sized lymphocytes mixed with plasma cells (**h, e**,  $\times 200$ ). **h, i** Positive staining for pan B cell markers including CD20 (**h**) and CD79a (**i**) on immunohistochemical examination (original magnification  $\times 400$ ) are observed. **j** A stable residual mass with contrast enhancement (curved arrow) is observed on axial CE T1WI 2 years after surgical resection

## Discussion and conclusions

PCNSL arising from the cavernous sinus is a rare occurrence with only 21 known cases published in available literature in the English language. Amongst these cases, 8 are histologically confirmed MZBCL (Table 1). However, there have so far been no documented studies on preoperative comprehensive MRIs and ADC values in primary MZBCL of the cavernous sinus. The cavernous sinus can be involved by a myriad of diseases including neoplasms, vascular lesions, and infectious or inflammatory processes. In regards to neoplasms, the cavernous sinus is rarely involved by lymphoma, either primary or metastatic. Reported clinical symptoms of cavernous sinus lymphoma include visual disturbance, headache, ophthalmoplegia, cavernous sinus syndrome, or clinical features resembling trigeminal neuralgia and Tolosa–Hunt syndrome (Table 1).

MZBCL, a low-grade non-Hodgkin lymphoma derived from the post-germinal center, is best known for constituting the mucosal associated lymphoid tissue lymphoma (MALT lymphoma or MALToma) of the gastrointestinal tract associated with chronic infection of *Helicobacter pylori* [24]. In addition, recent studies had identified various autoimmune, chromosomal, and genetic factors to also be implicated in the pathogenesis of MZBCL [25]. CNS involvement of extranodal MZBCL is uncommon, and when it occurs, the most commonly involved structure is the dura (80% of the cases), followed by the brain parenchyma and other sites [26]. Radiologically, the disease typically presents as a dural-based mass, a feature rendering it easily mistaken for meningioma [27]. The pathogenesis of primary dural MZBCL is unclear, since the dura is devoid of organized lymphoid tissue. Some authors hypothesized that MZBCL may arise from meningeothelial cells, which are tasked with the immunological protection of the brain from bacterial infection [28, 29]. Likewise, the cavernous sinus also contains dura matter and can, at least theoretically, be involved by MZBCL, as is the case in our report. On the other hand, MZBCL is the most common histologic subtype (up to 75%) in ocular adnexal lymphoma [30].

Common differential diagnoses of cavernous tumors include meningioma, schwannoma, metastasis, Tolosa–Hunt syndrome, and hemangioma. From a radiological point of view, differentiation amongst these lesions can be challenging with conventional MRI only, since all may exhibit similar signal intensities and enhancement patterns. However, ADC values may offer additional diagnostic value in differentiating these lesions. In PCNSLs, diffusion restriction with low ADC values between  $0.63 \times 10^{-3}$  and  $0.71 \times 10^{-3}$  mm<sup>2</sup>/s have been reported [10, 31, 32]. De la Fuente et al. [8] have reported the median ADC value of  $0.598 \times 10^{-3}$  mm<sup>2</sup>/s in six dural

MZBCL cases. Although the final diagnosis of MZBCL of the cavernous sinus needs to be confirmed by immunohistochemistry, the preoperative quantitative low ADC value ( $0.64 \times 10^{-3}$  mm<sup>2</sup>/s) in our case offers valuable additional information in the diagnostic process. On conventional MRI, ICA encasement with vascular stenosis is characteristically present in the case of cavernous sinus meningiomas [33]. In contrast, patent ICA vascular lumen without narrowing is observed in our case. Most meningiomas are benign tumors and typically do not exhibit diffusion restriction on DWI [34]. Although rare high-grade (atypical and malignant) meningiomas may sometimes demonstrate diffusion restriction, higher ADC values of  $0.78 \times 10^{-3}$  mm<sup>2</sup>/s to  $0.8 \times 10^{-3}$  mm<sup>2</sup>/s had been reported in these high-grade meningiomas as compared with our case [35]. Furthermore, occurrence of high-grade meningiomas arising from the cavernous sinus has never been reported. Similarly, most of the nerve sheath tumors arising from the traversing cranial nerves or sympathetic plexus are benign neoplasms that do not exhibit diffusion restriction [36]. Metastases to the cavernous sinus can be more readily recognized based on a known clinical history of cancer, which may occur via direct invasion, perineural spread from the adjacent nasopharynx and bone, or hematogenous spread. Head and neck cancers are the most commonly identified culprits; rare instances of distant metastases from lung, breast and prostate malignancies have also been reported [37]. Tolosa–Hunt syndrome is essentially a clinical diagnosis of exclusion. It describes an idiopathic inflammatory process characterized by painful ophthalmoplegia secondary to inflammation surrounding the cavernous sinus. The usual presentation is that of an enhancing soft tissue lesion involving both the orbital apex and cavernous sinus, features different from those observed in our case [38]. Hemangiomas are rare vascular lesions involving the cavernous sinus which, similar to those occurring elsewhere, exhibit marked hyperintensity on T2WI and progressive contrast filling (centripetal enhancement) on dynamic contrast-enhanced T1WI [39]. In our case, these differential diagnoses can be excluded in sequence by clinical history and MRI findings. Because MZBCL is extremely radiosensitive, regional treatment consisting of focal resection followed by radiotherapy has been shown to achieve complete response in most cases of dural MZBCL [3, 5]. Therefore, preoperative recognition of this rare entity makes it possible to avoid unnecessarily aggressive surgical intervention.

To the best of our knowledge, this report is the first to mention and discuss preoperative ADC values of the primary cavernous sinus MZBCL. This case suggests that the combination of preoperative MRI and ADC values may offer helpful additional information

**Table 1 Primary central nervous system lymphoma of the cavernous sinus in published studies**

| References              | Age/sex | Immune status    | Histologic type                   | Symptoms  | Involvement site                         | Treatment          | CT/MRI | DWI/ADC | Out-come |
|-------------------------|---------|------------------|-----------------------------------|---|--|--------------------|--------|---------|----------|
| de la Fuente et al. [8] | 30 F    | HIV (-)          | MZBCL                             | Facial pain   | CS                                       | Surgery, R/T       | -/-    | N/A     | CR       |
|                         | 51 F    | HIV (-)          | MZBCL                             | Focal paresthesia and numbness  | Left CS                                  | C/T, R/T           | -/-    | N/A     | CR       |
|                         | 48 F    | HIV (-)          | MZBCL                             | Cranial nerve palsy   | Bilateral CS                             | C/T                | -/-    | N/A     | CR       |
|                         | 50 F    | HIV (-)          | MZBCL                             | Cranial nerve palsy   | CS                                       | Surgery, R/T       | -/-    | N/A     | CR       |
| Suresh et al. [9]       | 24 F    | N/A              | MZBCL                             | Right painless vision loss, bitemporal visual field defect              | Left CS, falx, tentorium                 | Surgery, C/T       | -/+    | N/A     | N/A      |
| Dultra et al. [10]      | 63 M    | HIV (-)          | NHK B cell lymphoma               | Frontal headache, right facial pain, diplopia                           | Bilateral CS, sella                      | Surgery, R/T       | -/+    | N/A     | CR       |
| Ko et al. [11]          | 70 F    | N/A              | DLBCL                             | Facial pain, complete right ptosis, diplopia                            | Right CS, right orbit                    | C/T                | -/+    | N/A     | CR       |
| Demirkaya et al. [12]   | 4 M     | N/A              | NHK                               | Right ptosis, pupil dilatation, ophthalmoplegia                         | Right CS                                 | Surgery, C/T       | -/+    | N/A     | CR       |
| Sadrudin et al. [13]    | 17 F    | N/A              | TLBL                              | Rapidly progressive right headache, diplopia, facial numbness           | Right CS                                 | Surgery, C/T, R/T  | -/+    | N/A     | CR       |
| Famoso et al. [14]      | 46 F    | Immuno-competent | MZBCL                             | Right exophthalmos, ptosis, retro-orbital pain                          | Right CS, sella, orbital meninges        | Surgery, rituximab | -/-    | N/A     | PR       |
| Razaq et al. [15]       | 61 F    | HIV (-)          | MZBCL                             | Headache, CN III palsy  | Left CS, left optic nerve                | R/T, rituximab     | -/-    | N/A     | CR       |
| Choi et al. [16]        | 12 M    | N/A              | DLBCL                             | Visual disturbance, periorbital pain                                    | Bilateral CS, dura, sphenoid bone        | C/T                | +/+    | N/A     | CR       |
| Nakamura et al. [17]    | 69 M    | N/A              | *highly malignant B cell lymphoma | Diplopia, left facial numbness, dysarthria, dysphagia (Garcin syndrome) | Left CS, occipital and clival bone       | N/A                | -/+    | N/A     | N/A      |
| Ronson et al. [18]      | 53 F    | N/A              | DLBCL                             | Diplopia, headache, left mouth paresthesia                              | Right CS, right sphenoid sinus extension | Surgery, C/T, R/T  | -/-    | N/A     | N/A      |
| Sanjeevi et al. [19]    | 46 F    | HIV (-)          | MZBCL                             | Left side headache, ophthalmalgia, decreased visual acuity              | Left CS, left orbital apex               | Surgery, R/T       | -/+    | N/A     | CR       |

**Table 1 (continued)**

| References                  | Age/sex | Immune status    | Histologic type                | Symptoms   | Involvement site                 | Treatment         | CT/MRI | DWI/ADC | Out-come         |
|-----------------------------|---------|------------------|--------------------------------|--|----------------------------------|-------------------|--------|---------|------------------|
| Arimoto et al. [20]         | 59 F    | HIV (-)          | *diffuse small B cell lymphoma | Diplopia on right lateral gaze, right facial hypesthesia   | Right CS                         | Surgery, R/T      | -/+    | N/A     | CR               |
| Jaiswal et al. [21]         | 40 M    | HIV (-)          | DLBCL                          | Right sided headache, tinnitus, hearing impairment, ataxia | Right CPA, right CS, right orbit | Surgery, C/T, R/T | +/+    | N/A     | CR               |
| Roman-Goldstein et al. [22] | 37 M    | Immuno-competent | N/A                            | Retro-orbital headache, diplopia                           | Right CS                         | C/T               | -/+    | N/A     | CR               |
|                             | 62 M    | Immuno-competent | N/A                            | Headache, diplopia   | Left CS                          | Surgery, C/T, R/T | -/-    | N/A     | Died at 18 month |
|                             | 51 F    | Immuno-competent | N/A                            | Diplopia   | Left CS                          | Surgery, C/T      | -/-    | N/A     | N/A              |
| Nakatomi et al. [23]        | 77 M    | HIV (-)          | DLBCL                          | Left facial hypesthesia, diplopia                          | Left CS, petro-clival dura       | Surgery, C/T, R/T | -/+    | N/A     | Died at 31 month |

\*Pathologic diagnoses not applicable to WHO 2016 classification, CPA, cerebellopontine angle; CS, cavernous sinus; CR, complete response; C/T, chemotherapy; DLBCL, diffuse large B-cell lymphoma; HIV, human immunodeficiency virus; N/A, not available; NHL, non-Hodgkin lymphoma; PR, partial response; R/T, radiotherapy; TLBL, T-cell acute lymphoblastic lymphoma

regarding to the diagnosis and treatment planning for lymphoma of the cavernous sinus.

#### Abbreviations

ADC: Apparent diffusion coefficient; DLBCL: Diffuse large B-cell lymphoma; DWI: Diffusion-weighted image; MZBCL: Marginal zone B-cell lymphoma; PCNSL: Primary CNS lymphoma; PET: Positron emission tomography; T1WI: T1-weighted image; T2WI: T2-weighted image.

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#### Authors' contributions

Conceived and designed the experiments: CCK. Analyzed the data: CCY YKT CCK. Wrote the paper: CCY CCK. Critically revised the article: TYC CCK. All authors read and approved the final manuscript.

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#### Availability of data and materials

All data generated or analyzed in this study are included in this published article.

#### Ethics approval and consent to participate

This study was approved by the Institutional Review Board (IRB no.: 10902-009) of Chi Mei Medical Center. Written consent was waived because the retrospective nature of this study.

#### Consent for publication

Written consent was waived because the retrospective nature of this study meant that healthcare of included subject was not affected. The personal information was anonymized and de-identified.

#### Competing interests

The authors hereby declare that they have no competing interests.

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