



Marginal Zone B-cell Lymphoma of the Gasserian Ganglion: Case Report and Review of the Literature

Linfoma de células B da zona marginal do gânglio de Gasser: Relato de caso e revisão da literatura

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Abstract

Primary central nervous system lymphoma (PCNSL) is a rare subtype of extranodal non-Hodgkin's lymphoma that accounts for 4% of newly diagnosed central nervous system (CNS) tumors. Most primary lymphomas of the central nervous system are of the subtype of diffuse large B-cell lymphomas, which have highly aggressive behavior and may involve the brain, leptomeninges, eyes or spinal cord without evidence of systemic disease. Primary CNS lymphomas are very rare in immunocompetent patients, but their rates are increasing. So far, only 11 primary Gasser ganglion lymphomas have been reported, with an incidence of 2.5 cases per 30,000,000 inhabitants. However, B cell lymphomas of the marginal zone of the Gasserian ganglion have been very rarely reported. We report here a clinical presentation characteristic of B cell lymphoma of the marginal zone of the Gasser ganglion in an immunocompetent patient who was treated with surgery and radiotherapy, evolving with improvement of symptoms and without recurrence in 3 months of follow-up.

Keywords

- ▶ facial pain
- ▶ primary lymphoma of the central nervous system
- ▶ trigeminal neuropathy

Resumo

O linfoma primário do sistema nervoso central (PCNSL, na sigla em inglês) é um subtipo raro de linfoma não-Hodgkin extranodal que representa 4% dos tumores recém-diagnosticados do sistema nervoso central (SNC). A maioria dos linfomas primários do sistema nervoso central é do subtipo dos linfomas difusos de grandes células B, que tem comportamento altamente agressivo e pode envolver cérebro, as leptomeninges, os olhos ou a medula espinhal sem evidências de doença sistêmica. Os linfomas primários do SNC são muito raros em pacientes imunocompetentes, mas suas taxas estão aumentando. Até o momento, apenas 11 linfomas primários do gânglio de

Palavras-chave

- ▶ dor facial
- ▶ linfoma primário do sistema nervoso central
- ▶ neuropatia trigeminal

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Gasser foram relatados, com uma incidência de 2,5 casos por 30.000.000 de habitantes. No entanto, linfomas de células B da zona marginal do gânglio de Gasserian foram muito raramente relatados. Relatamos aqui uma apresentação clínica característica de um linfoma de células B da zona marginal do gânglio de Gasser em um paciente imunocompetente que foi tratado com cirurgia e radioterapia, evoluindo com melhora dos sintomas e sem recorrência em três meses de acompanhamento.

Case Report

A 29-year-old previously healthy male presented with lancinating left facial pain and paresthesia. The pain involved all divisions of the trigeminal nerve and was worse in the mandibular division. He received a daily dose of 1,200 mg of carbamazepine without improvement. The patient was then seen by a dentist and underwent repeated molar extractions; however, his facial pain became worse. He also suffered from severe symptomatic diplopia, which was evident on lateral gaze to the left. Clinical examination revealed an intact corneal reflex with abducent nerve palsy on the left side. There was hypoesthesia to all sensory modalities, involving the maxillary and mandibular divisions; however, there were no trigger points. There was no evidence of weakness of the muscles of mastication on the left side, but the examination showed atrophy of the temporalis muscle.

Brain magnetic resonance imaging (MRI) revealed a globular lesion straddling the posterior and middle fossae, which caused uniform enlargement of the trigeminal nerve from its root at the prepontine cistern until the gasserian ganglion at the Meckel cave on the left side, and extending to the left cavernous sinus without encasement of the carotid artery (► **Fig. 1**). It measured $3 \times 1.8 \times 2.8$ cm, showing intermediate T1 and T2 signal intensity, and intense enhancement with gadolinium without a dural tail. The preoperative diagnostic hypothesis was schwannoma, based on the site and imaging characteristics. Routine laboratory investigations were within normal values.

Operative Procedure and Findings

The patient was operated by an anterior petrosal approach. The approach was performed through a frontotemporal osteomuscular craniotomy. The details of anesthesia, positioning and craniotomy, drilling of the apex of the petrous bone, dural opening, and division of the tentorium have been described elsewhere.¹ The tumor was evident after exposure of the gasserian ganglion. However, the posterior fossa part of the tumor was only seen after opening of the dura and division of the tentorium. At this point, the whole trigeminal nerve was evident from the root entry zone and all the way until the division of the gasserian ganglion.

The tumor was greyish-brown in color, quite firm in consistency, and adhesive. It was arising within the plexiform part of the Gasserian ganglion. It was dissected using

sharp dissection from within the Gasserian ganglion and, with difficulty, a plane of dissection could be established from the medial aspect of the ganglion. At this point, the sixth nerve became visible and was preserved. We found that the tumor did not encircle the carotid artery. It was completely resected along with the trigeminal nerve root due to its complete infiltration by the tumor. Hemostasis was achieved and the wound was closed in layers.

Postoperatively, the patient was in an excellent condition. The wound was clean and without cerebrospinal fluid (CSF) collection. The sixth cranial nerve started to regain function and the diplopia improved considerably, but did not go back to normal. The trigeminal pain disappeared completely, and the patient stopped taking carbamazepine. However, there was a persistent hypoesthesia involving all division of the trigeminal nerve on the left side, but it was not incapacitating. A follow-up brain MRI with contrast revealed complete excision of the tumor.

Histopathological examination of the excised tumor by light microscopy after hematoxylin and eosin (H&E) staining revealed mildly fibrotic tissue showing moderate lymphoplasmacytic infiltrate with moderate lymphoid hyperplasia.

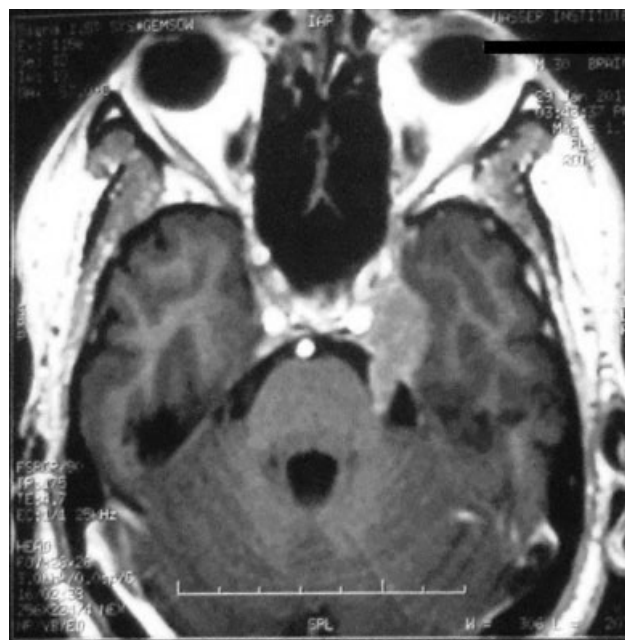


Fig. 1 After discussing the advantages and disadvantages of the available treatment options with the patient, surgery was decided. The other possible treatment was stereotactic radiosurgery (SRS) with serial imaging follow-up.

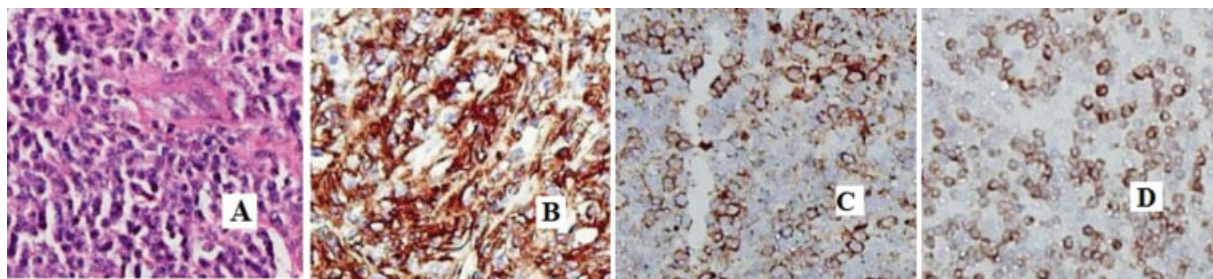


Fig. 2 (A) Histopathology by light microscopy after hematoxylin and eosin (H&E) staining showing moderate lymphoplasmacytic infiltrate with moderate lymphoid hyperplasia. Figure 2 B,C,D: Immunohistochemistry revealed neoplastic cells to be moderately positive for CD20, CD138 and BCL2 in B, C and D, respectively.

The preliminary diagnosis was of an inflammatory process, but immunohistochemistry revealed neoplastic cells that were moderately positive for CD20, CD138 and BCL2, and many scattered non-neoplastic cells positive for CD3. The Ki-67 stain was positive in between 30 and 35% of the neoplastic cells. Accordingly, the findings were compatible with low grade marginal zone B cell lymphoma (►Fig. 2).

Systemic involvement was excluded by whole body positron emission tomography (PET) scan, and laboratory investigations including CSF cytology and bone marrow biopsy. The patient received localized intensity modulated radiation therapy (IMRT) on the tumor bed with a dose of 36 Gy divided over 20 sessions in 4 weeks. After a 3-month follow-up interval, there was no recurrence, and the patient was pain-free.

Discussion

The trigeminal nerve is a rare site for primary CNS lymphomas (►Table 1).²⁻¹² The first case was reported in 1996 by Nakatomi et al.² The reported cases were in patients with ages ranging from 40 to 77 years old, with a mean age of 56 years old. The male to female ratio was 2.67: 1. Our male patient was 29 years old at the time of presentation. In previous reports, the main presenting symptoms were facial pain followed by diplopia and facial numbness. Our patient also presented with left-sided facial pain that was more severe in the distribution of the mandibular division. This was also associated with numbness and diplopia due to paralysis of the 6th nerve.

As in all the available reports, preoperative diagnosis was not possible. Our proposed preoperative diagnostic hypothesis was schwannoma. Differential diagnosis of lesions involving the trigeminal nerve and extending into the cavernous sinus include: schwannoma of the trigeminal nerve, meningioma, lymphoma, and inflammatory lesions (herpes neuritis of the trigeminal nerve, idiopathic trigeminal neuropathy, and chronic granulomatous neuritis).¹¹ It is difficult to distinguish these lesions on pure clinical or radiological basis alone, but trigeminal lymphoma may be suggested by the short duration of symptoms.⁶ The duration of symptoms in our case was only 3 months. Our patient had rapidly progressing abducens palsy. This is rare in trigeminal schwannomas or meningiomas. As in reported cases, the laboratory investigations were all within the normal parameters.

Eight reported cases involved location in the Meckel cave. In our case, the lesion spanned the whole trigeminal nerve, starting from its root until the Gasserian ganglion at the Meckel cave.

The treatment choices for these cases include surgical excision and stereotactic radiosurgery (SRS). SRS is widely used for lesions of this size. Stereotactic radiosurgery has the advantage of being a noninvasive modality to achieve control or even resolution of the lesion. Nevertheless, pain may not be relieved in cases of trigeminal neuralgia due to tumors.¹³ It is risky to perform SRS without definite histopathological diagnosis in trigeminal lymphomas, as in the case reported by Nakatomi et al. Their preliminary diagnosis was meningioma of the cavernous sinus. The patient received Gamma knife radiosurgery leading to improvement of ptosis but not of the facial pain. The imaging obtained 1 year after SRS showed resolution of the cavernous sinus lesion; however, enlargement of the lesion in the prepontine cistern compressing the brain stem was evident, requiring surgical excision.² Additionally, early empirical radiotherapy of lymphomas can render biopsies obtained at a later stage non-diagnostic.⁹ In our case, after discussing the available options of treatment, we opted to operate on the patient. The pain was unbearable despite receiving maximum carbamazepine dosage, and he already had neurological deficits at presentation. Surgery had several advantages over SRS, including: obtaining a histopathological diagnosis, relieving the diplopia caused by the compression of the 6th nerve and achieving immediate pain relief. Moreover, surgery was a better option in younger patients, and SRS is a better option in elderly patients.

The surgical approaches performed in the reported literature include: lateral suboccipital, subtemporal, transphenoidal followed by pterional, anterior petrosectomy through frontotemporal craniotomy, and combined lateral suboccipital and subtemporal. The most common approach used was the lateral suboccipital. The surgical approach should be tailored according to the location, to the extent of the lesion, and to the comfort level of the surgeon. The approach used in our case was anterior petrosectomy through a frontotemporal craniotomy. This approach allowed radical excision of the tumor.

The most common histopathological variant of primary lymphoma of the trigeminal nerve reported in the literature is diffuse large B-cell lymphoma. Our case is distinct, as the

Table 1 Reports of Trigeminal Nerve Lymphoma

Authors	Age and gender	Presentation	Site	Preliminary diagnosis	Approach	Histopathology	Fate
Nakatomi 1996(2)	77 Male	Facial hypoesthesia	Lt prepontine cistern-cavernous sinus	Schwannoma or meningioma	Lateral suboccipital	Diffuse large B cell	Death
Abdel Aziz 1999(3)	40 Female	Facial pain, hypoesthesia	Lt Meckel's cave-cavernous sinus	Schwannoma	Frontotemporal craniotomy with orbit zygomatic osteotomy with anterior petrosectomy.	Monocytoid malignant B cell lymphoma	N.A.
Kinoshita 2003(4)	55 Male	Facial pain, diplopia	Lt Meckel's cave-infratemporal fossa	N.A.	Lateral suboccipital	Diffuse large B cell lymphoma Biopsy	Death
Bulsara 2005(5)	52 Female	Facial pain	Lt Meckel's cave-foramen rotundum	N.A.	Subtemporal	Non-Hodgkin lymphoma	N.A.
Ipilkioglu 2006(6)	50 Male	Facial pain, diplopia	Rt prepontine cistern-cavernous sinus	N.A.	Lateral sub occipital	B cell malignant lymphoma	Complete recovery
Akaza 2009(7)	60 Male	Facial pain	Lt prepontine cistern-Meckel's cave	Schwannoma or sarcoidosis	Biopsy from another lesion	Diffuse large B cell lymphoma	Complete recovery
Yamahata 2012(8)	68 Male	Facial pain and numbness	Distal trigeminal root -Lt Meckel's cave	Schwannoma, meningioma, malignant lymphoma, metastasis, or inflammatory disease	Anterior petrosal approach	T cell/histiocyte-rich B cell lymphoma	Complete recovery
Perera 2014(9)	55 Female	Diplopia	Rt cavernous sinus-pterygopalatine fossa	Meningioma	Transsphenoidal and pterional	Non-Hodgkin small B cell lymphoma with plasmacytoid differentiation	N.A.
Jack 2014(10)	57 Male	Facial pain	Lt prepontine cistern-Meckel's cave	N.A.	Lateral suboccipital	Diffuse large B cell lymphoma	Complete recovery
Ogiwara 2015(11)	47 Male	Facial pain, diplopia	Lt prepontine cistern-infratemporal fossa	Schwannoma or neuritis	Lateral suboccipital and subtemporal	Diffuse large B cell lymphomas, nongerminal center B type	Complete recovery
J.W.J 2015(12)	55 Male	Facial pain	Rt cavernous sinus-RtMeckel's cave-infratemporal fossa	Schwannoma or meningioma	Right temporal	Diffuse large B cell lymphoma	Complete recovery
Present case	29 Male	Facial pain	Lt Meckel's Cave - lt cavernous sinus	Schwannoma	Anterior petrosectomy through frontotemporal craniotomy	Low grade marginal zone B cell lymphoma	

pathological type of the lymphoma was marginal zone B-cell lymphoma (MZBL). To our best knowledge, this is the first case of this variant to be reported. Primary marginal zone lymphomas have been reported elsewhere in other intraparenchymal sites only six times in the literature.^{14–19} Marginal zone B-cell lymphomas usually give rise to dural based lymphomas. Marginal zone lymphoma is a non-Hodgkin lymphoma that occurs more commonly in the gastrointestinal tract. So, it is sometimes called the “mucosa-associated lymphoid tissue” (MALT) lymphoma. Patients with marginal zone lymphomas have a more promising outcome, with a 5-year overall survival rate exceeding 86%.²⁰

Chemotherapy regimens incorporating high-dose methotrexate (HD-MTX) are considered the standard of care as induction therapy for newly-diagnosed PCNSLs.²¹ Following introduction of HD-MTX-based chemotherapy, whole brain radiotherapy (36–45Gy) has continued to be employed to consolidate responses and to provide more durable disease control.²² These data are primarily for treating high grade B cell PCNSLs. But, in this case, our patient had low grade MZBL stage I (stage I extra-nodal without B symptoms). Extrapolation of data in treating early stage MZL in solitary extra-nodal location indicates that local treatment is the preferred treatment and, therefore, we followed surgery with 36Gy of localized irradiation to the tumor bed and, for fear of late toxicity in a young patient with an early stage indolent lymphoma, we used IMRT.

Conclusion

This is a single case report of a known pathological entity found in an unusual location. Lesions in the gasserian ganglion are usually benign tumors such as meningiomas or schwannomas. The message we convey is the importance of clinical correlation. The short duration of symptoms, severe constant pain and involvement of other cranial nerves, for example, the abducens nerve, should raise the suspicion of a different pathology. The administration of SRS in a lymphoma without definite pathological diagnosis would be hazardous, owing to the systemic and malignant nature of lymphomas. Surgery and histopathological examination should be the first option, whenever the primary diagnosis is doubtful.

Conflict of Interests

The authors have no conflict of interests to declare.

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