Primary Malignant Lymphoma of the Trigeminal Nerve: Case Report and Literature Review

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Key words
- Malignant lymphoma
- Open biopsy
- Surgical approach
- Trigeminal nerve

Abbreviations and Acronyms
CNS: Central nervous system
MPVR: Methotrexate, procarbazine, vincristine, and ranimustine
MRI: Magnetic resonance imaging
PCR: Polymerase chain reaction

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BACKGROUND: **Primary lymphomas of the cranial nerves are extremely rare except for optic nerve lymphoma, and it is difficult to make a correct diagnosis in the initial stage. Here, we report a case of primary malignant lymphoma of the left trigeminal nerve that presented as trigeminal nerve disorder.**

CASE DESCRIPTION: **A 47-year-old man presented with aggravating left facial pain and hypesthesia within all three divisions of the trigeminal nerve. Magnetic resonance imaging (MRI) revealed a swollen left trigeminal nerve with gadolinium homogenous enhancement. An open biopsy had to be taken from two different locations of the tumor via the lateral suboccipital approach followed by subtemporal approach because adequate specimen volume was not obtained for definitive diagnosis at the first surgery. Histopathological examinations with flow cytometric analysis revealed diffuse large B cell lymphoma. Chemotherapy followed by whole-brain radiation therapy was effective. No recurrence was observed during a 15-month follow-up period.**

CONCLUSIONS: **This is a rare clinical presentation of malignant lymphoma of the trigeminal nerve. It is difficult to establish a correct diagnosis of trigeminal nerve lesions during the initial stages without biopsy. Therefore it is important that a sufficient specimen should be taken for biopsy without hesitation in order to diagnose and treat rapidly. The most suitable operative approach must be selected in trigeminal nerve lesions considering functional preservation, operative difficulty, preference of each surgeon, and quantity of specimen to be removed.**

Primary lymphoma of the central nervous system (CNS) usually arises from the brain parenchyma, particularly the white matter (1, 2, 11). Primary lymphomas of the cranial nerves are extremely rare except for optic nerve lymphoma (14). Only nine cases of lymphoma arising from the trigeminal nerve have been reported to date (1, 3, 4, 6-9, 11, 12). In most of these cases, it was difficult to distinguish from other diseases by neuroimaging and the treatment was apprehensive because its aggravation is rapid. Here, we report a rare clinical presentation of malignant lymphoma arising from the trigeminal nerve in which it took a long time to confirm the diagnosis and two open biopsies were obtained via the lateral suboccipital and subtemporal approaches.

CASE REPORT

The patient was a 47-year-old man, suffering from Crohn disease for 2 years, with a 2-month history of progressive left facial pain and numbness. These symptoms initially developed from V3 territory and spread to all three divisions of the trigeminal nerve. Physical examination revealed left facial hypesthesia, left facial spasmodic prickly pain mimicking trigeminal neuralgia, diminished corneal reflex, disturbance of jaw movement, and wasting of the masseter muscle. Tumor markers including soluble interleukin-2 receptor and other laboratory studies were within the normal limits. The cell count from cerebrospinal fluid (CSF) was 3/μL (mono: 3), and twice the cytology of CSF confirmed no malignant cells. There was no evidence of immune deficiency. Magnetic resonance imaging (MRI) indicated that the left trigeminal nerve at its cisternal portion, as well as at the Meckel cave, was swollen and homogeneously enhanced (Figure 1). Dural tail sign was not present. There was neither invasion of brainstem nor mass effect. Computed tomography (CT) scan revealed no evidence of bony erosion or hyperostosis. The patient underwent an operation via the lateral suboccipital approach for histopathological confirmation. Intraoperatively, the trigeminal nerve was swollen and a grayish, soft, hemorrhagic granulomatous lesion surrounding the trigeminal nerve was observed (Figure 2A). A biopsy was taken from this lesion without injuring the trigeminal nerve. The patient was woken up immediately after surgery without new neurological deficits. Histopathological examination revealed numerous small cells with large nuclei-like lymphocytes; however, histopathological examination was eventually not able to establish a definitive diagnosis because polymerase chain reaction (PCR) did not confirm monoclonality as the specimen was not sufficiently large to

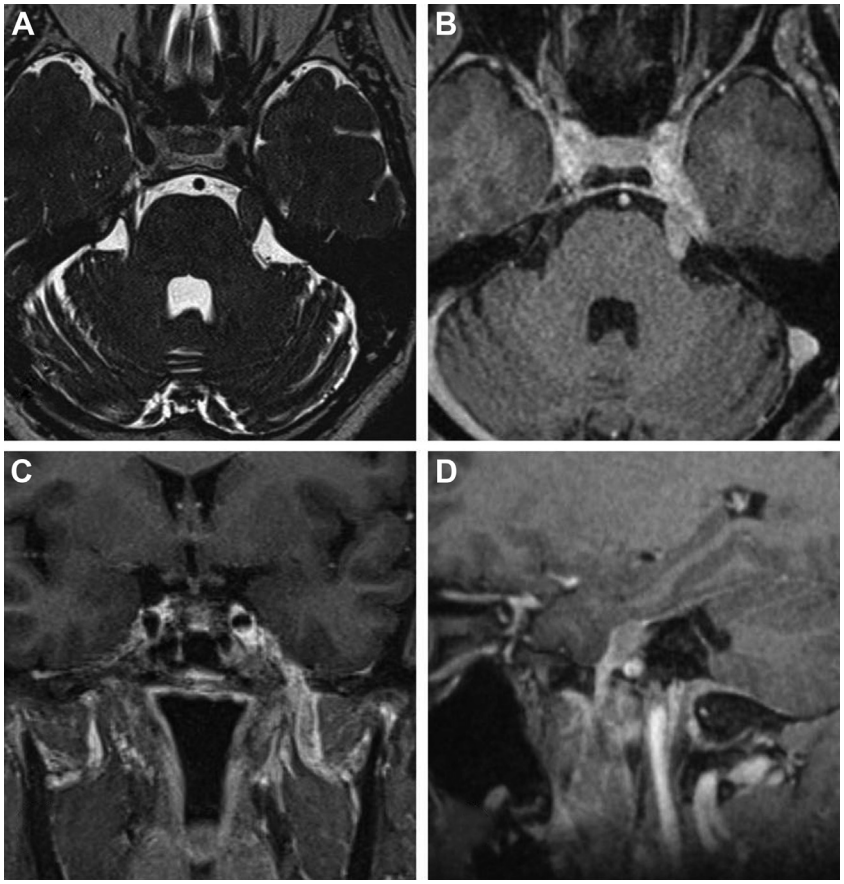

Figure 1. **A**–**D**: Preoperative magnetic resonance imaging (MRI) showing swelling of the left trigeminal nerve (**A**) and heterogeneously enhancing tumor with gadolinium extending along the left cavernous sinus and infratemporal fossa extending into the foramen ovale (**B**–**D**).

make a diagnosis considering preservation of trigeminal nerve function. An inflammatory disease was suspected and close observation was undertaken. One month after surgery, the patient presented to the outpatient service with diplopia caused by left abducens nerve palsy and aggravation of left facial numbness and pain. MRI revealed enlargement of the lesion with extension to the cavernous sinus and infratemporal fossa through the foramen ovale. He underwent resection of the trigeminal lesion via the subtemporal approach based on the previous operative findings. The lesion infiltrating into the subdural space of the middle fossa was removed. The tumor had the same features as in the previous surgery and was partially removed in the Meckel cave (Figure 2). He tolerated the procedure well. The specimen was studied using H & E staining and was examined by light microscopy. The tumor was highly cellular with mitotic figures and diffusely infiltrative. Immunoperoxidase studies revealed neoplastic cells to be positive for CD20 and MUM1 and negative for CD10 and bcl-6. The Ki-67 staining index was 73%. Flow cytometric analysis of CD20 expression in the resected specimen of the patient confirmed that tumor cells were CD20 positive (Figure 3C). Finally, histopathological examinations revealed diffuse large B cell lymphomas, nongerminal center B type (Figure 3A, B). Whole-brain radiation therapy (45 Gy) after administration of methotrexate, procarbazine, vincristine, and ranimustine (MPVR) therapy appeared to have remarkable effects. Although left facial hypesthesia and pain remained slightly, the patient's clinical course was uneventful and he did not experience recurrence over a 1-year follow-up period (Figure 4).

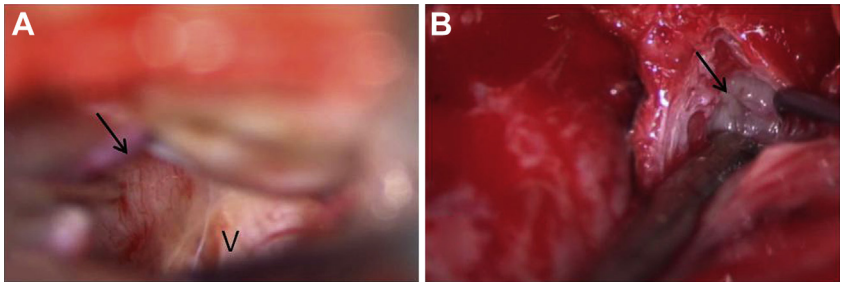

Figure 2. **A**, **B**: Intraoperative photograph showing the lateral suboccipital approach. The tumor (*arrows*) was soft, grayish, and hemorrhagic, and included the left trigeminal nerve (**A**). Second operative photograph showing the view of subtemporal approach. The tumor (*arrows*) in the Meckel's cave had almost same properties as in the first operation (**B**). V: trigeminal nerve.

DISCUSSION/LITERATURE REVIEW

Primary CNS lymphoma accounts for 0.5%–2.7% of all primary brain tumors. Its frequency is increasing due to the more common observation of immunocompromised patients; however, cranial nerve lymphomas are extremely rare except in the optic nerve (1, 2, 11). Only nine cases of malignant lymphoma arising from the trigeminal nerve have been described in the literature (1, 3, 4, 6-9, 11, 12) (Table 1). The patients were aged from 40 to 77 years old (mean 54.5 years), and 7 of the 10 patients (including our patient) were male. According to previous reports, primary CNS lymphoma patients showed a male-to-female ratio of approximately 3:2 with a mean age of 52 years (15). The initial symptom was facial pain in 8 of 10 patients. Preoperative MRI demonstrated homogeneous enhancement of the lesion after gadolinium administration in all patients. Although each case was unique, these lesions extended from the prepontine cistern to the infratemporal