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Ganglioneuroma Originating From the Trigeminal Nerve in the Middle Cranial Fossa

—Case Report—

Hiroshi NAKAGUCHI,¹ Mineko MURAKAMI,¹ Akira MATSUNO,¹
Kazuto YAMAZAKI,² and Yasuo ISHIDA²

Departments of ¹Neurosurger and ²Pathology,
Teikyo University Chiba Medical Center, Ichihara, Chiba

Abstract

A 55-year-old man present with a case of ganglioneuroma manifesting as sudden onset of severe headache. T₁-weighted magnetic resonance imaging demonstrated a heterogeneously enhanced mass (3 × 3 × 2.5 cm) in the left middle cranial fossa compressing the left cavernous sinus. The tumor was totally removed through a frontozygomatic approach. The histological diagnosis was ganglioneuroma originating from the second division of the trigeminal nerve in the middle cranial fossa. Ganglioneuroma can occur wherever ganglion cells exist, but ganglioneuroma originating from the trigeminal nerve is rare, with only two cases reported.

Key words: ganglioneuroma, trigeminal nerve, middle cranial fossa

Introduction

Ganglioneuroma tends to arise in the mediastinum and adrenal gland, although intracranial gangliogenic tumor

occurs occasionally.^{1,3-5,8,9,11,12)} Only one case of ganglioneuroma has arisen from the trigeminal nerve,¹⁾ and one case of cranial “true” ganglioneuroma.⁵⁾ We recently treated a patient with ganglioneuroma arising from the maxillary nerve and extending to the middle cranial fossa, and describe the perioperative course, neuroimaging find-

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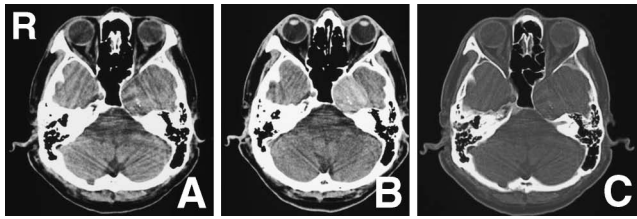


Fig. 1 A, B: Computed tomography scans revealing an isodense mass with high density spots and maximum diameter of 3 cm in the left middle cranial fossa (A), with heterogeneous enhancement by contrast medium (B). C: Bone image.

ings, and pathological features of this extremely rare neoplasm.

Case Presentation

A 55-year-old man experienced sudden onset of severe headache on May 11, 2006, and thereafter complained of continuous head heaviness. Neurological examination revealed clear consciousness, mild drooping of the left angle of the mouth without facial weakness, muscle weakness of the bilateral lower extremities, and gait titubation due to Charcot-Marie-Tooth disease. Over the course of the following 10 years, the patient suffered gradually progressive muscle atrophy of the bilateral lower extremities, motor weakness, and gait disturbance, and biopsy of the gastrocnemius muscle revealed onion bulb formation of the muscle cells, confirming the diagnosis of Charcot-Marie-Tooth disease. A partial deletion was found in chromosome 17. His elder sister also had Charcot-Marie-Tooth disease and had suffered progressive gait disturbance.

Computed tomography (CT) revealed an isodense mass with high density spots in the left middle cranial fossa, with a maximum diameter of 3 cm, and heterogeneous enhancement with contrast medium (Fig. 1A, B). The tumor extended to the cavernous sinus, and had deformed the greater wing of the sphenoid bone and destroyed the apex of the left pyramidal bone. Bone CT images revealed inward transformation of the wall of the sphenoid and ethmoid sinuses without destruction (Fig. 1C). CT without contrast medium demonstrated high density spots in the tumor, regarded as localized intratumoral hemorrhages. T₁-weighted magnetic resonance (MR) imaging revealed a heterogeneously enhanced extraaxial mass lesion in the left middle cranial fossa with a maximum diameter of 3 cm (Fig. 2). Digital subtraction angiography showed elevation of the paraclinoid portion of the left internal carotid artery together with widening of the carotid siphon. Left internal carotid arteriography showed mild tumor stain in the arterial phase. Thallium brain scintigraphy detected no abnormal uptake, suggesting absence of malignant potential in the tumor. Based on the location and neuroimaging studies of the tumor, the preoperative presumptive diagnoses were cavernous angioma of the cavernous sinus,¹⁵⁾ and neurinoma of the trigeminal neurinoma, with possible differential diagnoses of meningioma or metastatic tumor.

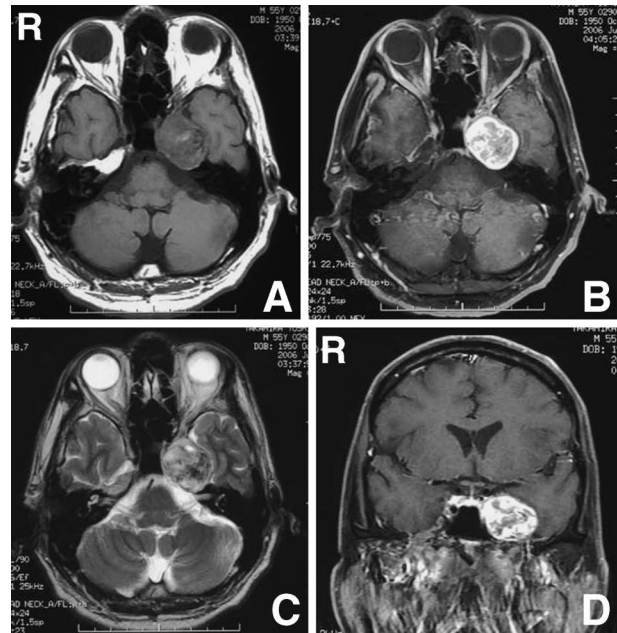


Fig. 2 A, B: Axial T₁-weighted magnetic resonance (MR) images without (A) and with contrast medium (B) showing a heterogeneously enhanced mass lesion in the left middle cranial fossa with a maximum diameter of 3 cm. C: Axial T₂-weighted MR image. D: Coronal T₁-weighted MR image with contrast medium showing a border between the mass lesion and the cavernous sinus, suggesting that the tumor may not have invaded into the sinus.

The tumor was removed piecemeal through a frontozygomatic approach, and no tumor invasion into the cavernous sinus was observed. Histological examination showed the essential components of the tumor included ganglion cells and processes, and ensheathing Schwann-like cells (Fig. 3). The predominant component was intersecting Schwann-like cell bundles, in arrangements varied from compact to dispersed with scattered ganglion cells. Several ganglion cells had atypical ovoid nuclei and brown pigment in the cytoplasm. No neuroblastoma-like cells were observed in the tumor. Immunohistochemistry staining showed the tumor cells were positive for S-100 protein staining and Nissl staining and negative for glial fibrillary acidic protein staining, indicating the tumor cells originated from the ganglion cells.

Pathological review confirmed the diagnosis of ganglioneuroma, maturing subtype. Cyst formation, hemorrhage, hemosiderin deposits, and fibrin precipitation were also observed. The tumor seemed to show a predisposition toward long-standing and gradual outward proliferation, leading to secondary intratumoral degeneration and hemorrhagic transformation. Based on the intraoperative findings, and neuroimaging and pathological studies, the tumor most likely originated from the maxillary nerve.

Postoperatively, the patient reported persistent left facial hypesthesia (V2 and V3 areas) and transient double vision, particularly on downward gaze. T₁-weighted MR imaging with contrast medium disclosed no residual tumor

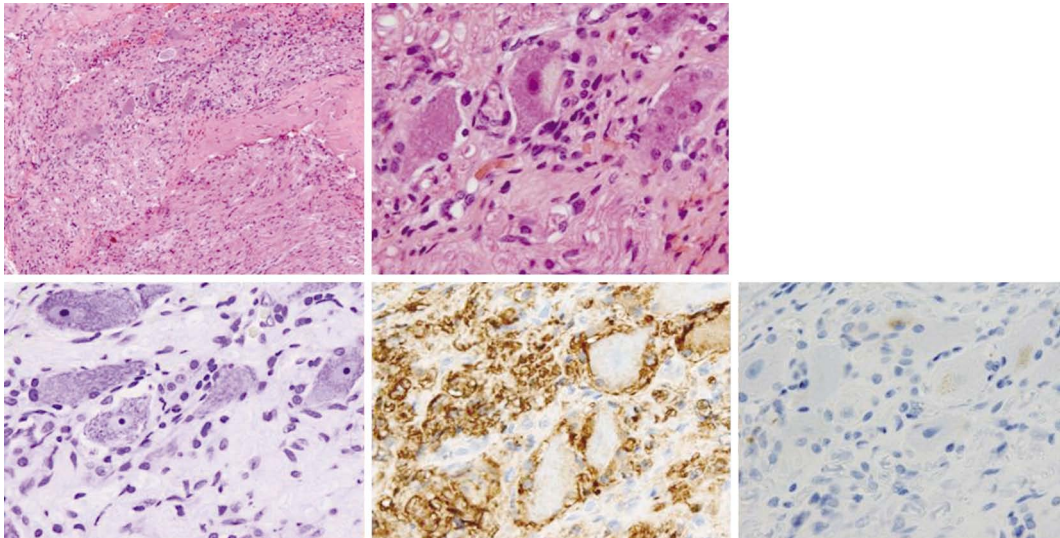


Fig. 3 Upper row: Photomicrographs showing ganglioneuroma consisting of intersecting bundles of Schwann-like cells and scattered ganglion cells recognizable by abundant eosinophilic cytoplasm and ovoid nuclei, and Schwann-like cells with spindle nuclei in the collagenous background. Hematoxylin and eosin stain, original magnifications, left: $\times 100$, right: $\times 400$. Lower left: Immunostaining for S-100 protein antibody is positive in the cytoplasm, supporting the ganglion origin of this tumor. Original magnification $\times 400$. Lower center: Nissl staining revealing rich Nissl bodies in the cytoplasm of the tumor cells, indicating the tumor cells originate from ganglion cells. Original magnification $\times 400$. Lower right: Glial fibrillary acidic protein staining is negative in the tumor cells. Original magnification $\times 400$.

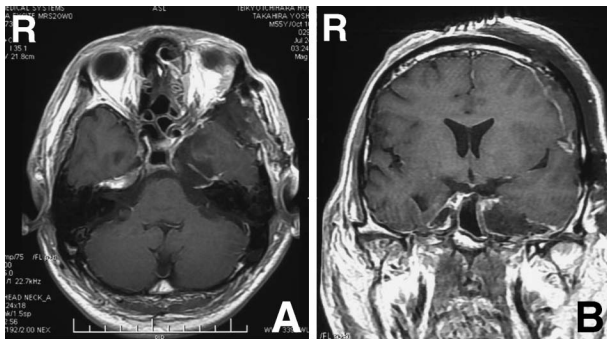


Fig. 4 Postoperative axial (A) and coronal (B) T₁-weighted magnetic resonance images with contrast medium revealing that the tumor has been completely removed.

(Fig. 4). At 1 year after surgery, MR imaging detected no tumor recurrence.

Discussion

Gangliocytoma consists of mature, neoplastic ganglion cells supported by non-neoplastic glial elements, and originates from ganglion cells in the brain parenchyma,¹⁶⁾ including the temporal lobe, floor of the third ventricle, frontal lobe, hypothalamus, intraventricular cavities, basal ganglia, brainstem, cerebellum, pineal gland, and spinal cord.^{2,6–8,10)} Ganglioneuroma is another tumor entity derived from ganglion cells of the peripheral nerve. The term “ganglioneuroma” has been used incorrectly as a synonym for gangliocytoma.^{1,16)} In the most recent World

Health Organization classification of neuroblastic tumors of the adrenal gland and sympathetic nervous system, ganglioneuroma (schwannian stroma dominant) is classified into two subtypes: the maturing subtype and the matured subtype. True ganglioneuroma, with peripheral nerve origin, is a quite rare intracranial tumor with only two previous cases.^{1,5)} Ganglioneuroma is most often located in the mediastinum, followed by the retroperitoneum, including parasympathetic ganglion cells of the adrenal gland as a preferred location.¹³⁾ An 8-year-old girl presented with ganglioneuroma originating from the trigeminal nerve in the left cerebellopontine angle.¹⁾ The tumor was derived from the proximal part of the trigeminal nerve extending from the gasserian ganglion, whereas the tumor in the present case was derived from the distal part of the trigeminal ganglion, probably the maxillary division of the nerve. These are the only two descriptions of ganglioneuroma originating from the trigeminal nerve.

Ganglion cell tumors in the central nervous system (CNS) most frequently affect children and young adults, with about 80% of cases in most series occurring in patients <30 years old. The frequency in children has been estimated to be around 4–4.5% of all CNS tumors.¹⁴⁾ In contrast, ganglioneuroma represents the final stage of maturation for neuroblastic tumors, and is usually observed in patients >10 years old.¹³⁾ Malignant change in ganglioneuromas is rare,¹⁴⁾ and no previous reports of ganglioneuromas have indicated a possible relationship to Charcot-Marie-Tooth disease. Our patient was 51 years old when he sought medical advice. Until that time, he had not experienced any serious symptoms, as the tumor had been growing slowly in the middle cranial fossa over a

long period and had not invaded vital structures of the brain. The nature and origin of ganglioneuroma are obscure. Three hypotheses have been suggested.¹⁾ First, the tumor may originate from a hamartomatous malformation as ectopic sympathetic nervous tissue in the CNS. Second, the tumor may arise from multipotential precursor cells during embryological development. Third, morphological changes leading to ganglioneuroma may result from differentiation of neuroblastoma.

The present tumor originated in the distal trigeminal nerve, extending chiefly from Meckel's cave to the middle cranial fossa, and was removed through a frontozygomatic and anterior petrosal approach. Ganglioneuroma shows little propensity for growth, and small amounts of residual tumor do not lead to recurrence. Preservation of neural and vascular structures during tumor removal is the treatment of choice, and postoperative irradiation should be withheld. Ganglioneuromas cannot be distinguished from other tumors on the basis of imaging characteristics. Histological diagnosis is thus important, and the surgical procedure should be carefully considered.

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Address reprint requests to: Hiroshi Nakaguchi, MD, Department of Neurosurgery, Teikyo University Chiba Medical Center, 3426-3 Anesaki town, Ichihara, Chiba 299-0111, Japan.
e-mail: hnakaguti@gmail.com