

Intraneural perineurioma of the third cranial nerve: occurrence and identification

Case report

RAMI ALMEFTY, B.A., BRUCE L. WEBBER, M.B.B.CH., AND KENAN I. ARNAUTOVIĆ, M.D.

Semmes–Murphey Clinic and Department of Neurosurgery, University of Tennessee Health Science Center; and Pathology Group of the MidSouth, Memphis, Tennessee

✓ Intraneural perineurioma is a true but rare neoplasm that originates from perineurial cells and mainly affects peripheral nerves. It must be distinguished from other hypertrophic neuropathies that are either inflammatory or demonstrate an onion-bulb formation that originates from Schwann cells. Complying with this strict definition, only three additional cases of cranium-related perineurioma have been identified: two lesions arose extracranially and involved cranial nerves, and one occurred intracranially but did not involve a nerve.

The authors describe a 27-year-old woman who presented with left third cranial nerve palsy and was found to harbor a mass lesion in the superior orbital fissure and cavernous sinus. After subtotal resection had been performed, pathological studies confirmed the presence of perineurial tumor cells in a pseudo-onion bulb formation. The cells stained positively for epithelial membrane antigen but not for S100 protein, clearly distinguishing the disease from one that originates in Schwann cells.

KEY WORDS • brain neoplasm • intraneural perineurioma • hypertrophic neuropathy • third cranial nerve palsy • onion-bulb formation

INTRANEURAL perineurioma is a rare, benign intraneural neoplasm composed exclusively of perineurial cells with unique immunohistochemical characteristics.^{10,13} The lesion was first identified histologically by Da Gama Imaginario, et al., in 1964.^{4,7} In 1978, Lazarus and Trombetta¹¹ were the first to identify the lesion's origin in perineurial cells and to distinguish it from both a schwannoma and neurofibroma. In the literature, IPN previously was referred to as localized hypertrophic neuropathy, hypertrophic neuropathy, localized hypertrophic mononeuropathy, intraneural fibroma, and hypertrophic neurofibrosis because of confusion over whether it is a true neoplasm. Nevertheless, Emory and colleagues⁵ demonstrated that it is a true neoplasm associated with the loss of a gene on chromosome 22 and, therefore, IPN is believed to be the most appropriate term. Clinically, IPN is found extremely rarely and mainly involves peripheral nerves. Because of the lesion's similarity to a schwannoma in its onion-bulb formation of cells, it is difficult to determine how many true cases of cranium-related IPN have been previously reported. After an extensive literature review, we can confirm that there have been only three other cases. Two lesions involved cranial nerves

extracranially: in one the facial nerve in the mastoid segment¹² and in the other the mandible nerve.⁹ The third lesion was intracranially located in the choroid plexus of the third ventricle and was not associated with a nerve.⁶ We believe that the present case is the first in which an intracranial lesion involved a cranial nerve, specifically the third cranial nerve. In this article we wish to report the first occurrence of IPN of the third cranial nerve; heighten the awareness of its occurrence; review its MR imaging, pathological, and clinical manifestations; and provide suggestions for its management.

Case Report

History. This 27-year-old woman presented with long-standing esotropia and transient episodes of diplopia since childhood. A year before presentation her left pupil became dilated and her double vision remarkably increased. This was also associated with long-standing headaches.

Examination. On physical examination the patient exhibited left eye proptosis and partial left third cranial nerve palsy with a fixed pupil. Magnetic resonance imaging of the brain (Fig. 1) revealed a 1.5-cm fusiform soft-tissue mass extending from the apex of the left orbit posteriorly to the cavernous sinus. The mass appeared isointense before addition of contrast agent and displayed moderate diffuse con-

Abbreviations used in this paper: EMA = epithelial membrane antigen; IPN = intraneural perineurioma; MR = magnetic resonance.

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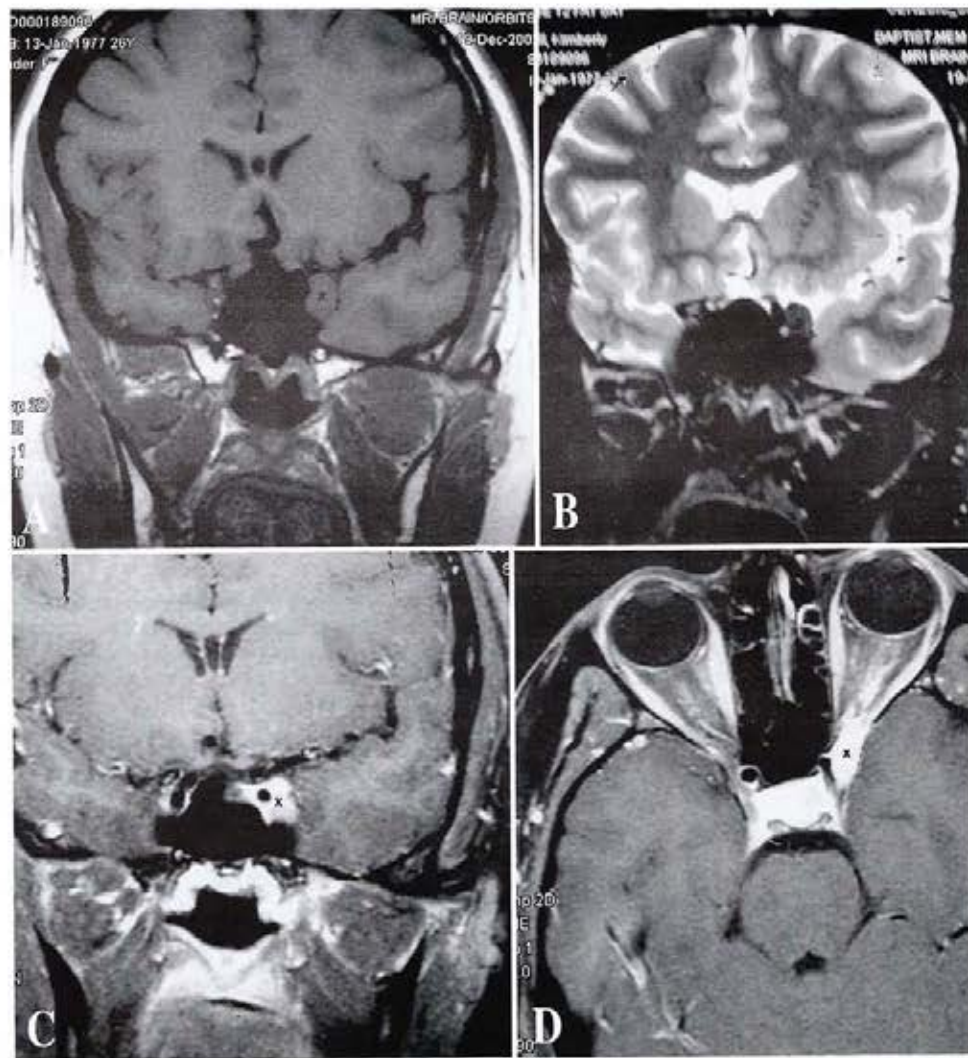


FIG. 1. Preoperative MR images. A: Coronal T₁-weighted image revealing a tumor that is isointense compared with the rest of the brain. B: Coronal T₂-weighted image showing a low-density tumor. C: Contrast-enhanced coronal image demonstrating bright enhancement of the lesion in response to Gd. D: Contrast-enhanced axial image with fat suppression demonstrating a fusiform tumor along the course of the third cranial nerve.

trast enhancement afterward. The appearance of the lesion mimicked a meningioma.

Operation and Postoperative Course. The patient underwent a craniocorbital skull base craniotomy and microsurgical subtotal resection of the tumor, which was assisted by stereotactic neuronavigation. Intraoperatively, the tumor was identified as a thickened and enlarged third nerve in both its intradural and cavernous sinus course. The tumor was firm, fibrous, and avascular. A small portion of tumor within the third cranial nerve fibers was left in situ, so that we could avoid disruption of the remaining nerve fibers and, hopefully, provide some recovery of third cranial nerve function. At the 10-month follow-up examination, we observed slow recovery of function in the third cranial nerve and MR imaging demonstrated a stable minimal residual lesion (Fig. 2).

Pathological Findings. The pathological evaluation demonstrated a neoplasm in which cells collected in a pseudo-

union bulb formation (Fig. 3). Immunohistological studies of the tumor cells showed a weakly positive reaction for EMA and no reaction for S100 protein; these findings confirmed the tumor cells' origin in perineurial cells. In addition to tumor cells, S100-positive Schwann cells were found at the center of the pseudo-union bulb formations within the tumor. Application of the Bielschowsky stain showed axons at the centers of these formations. These features are consistent with a diagnosis of IPN and with the lesion's perineurial cell origin.

Discussion

Intraneural perineurioma is a rare, benign intraneural neoplasm composed exclusively of perineurial cells, which penetrate the endoneurium and form concentric layers around nerve fibers in characteristic pseudo-union bulb formations. It is a rare clinical finding that usually involves pe-

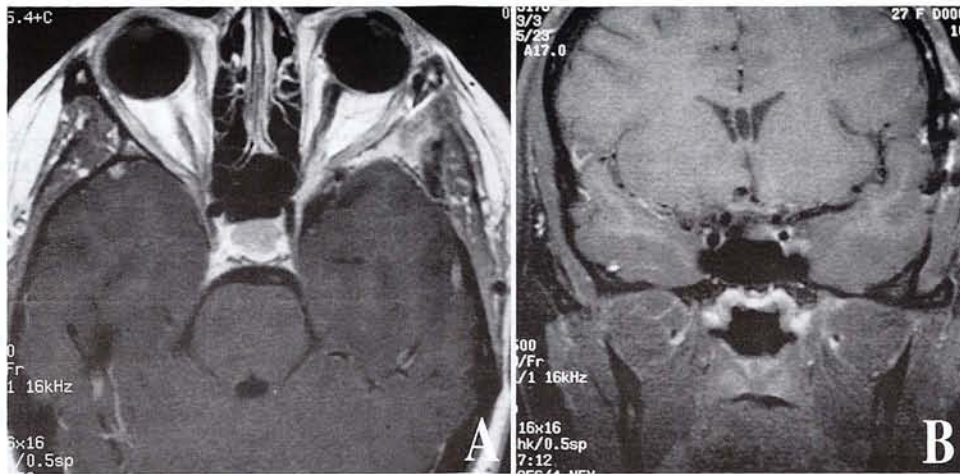


FIG. 2. Postoperative axial (A) and coronal (B) MR images depicting the site of subtotal resection.

ripheral nerves; involvement of cranial nerves has seldom been reported.

Clinically, patients with IPN are typically adolescents or young adults who exhibit progressive muscle weakness over years and less frequently sensory disturbance. Localized muscle atrophy may be apparent; electromyography demonstrates denervation and MR imaging enlargement of nerve segments. Whorls of perineurial cells around nerve fibers (pseudo-onion bulb formations) can be observed on

cross-sections of the affected nerve. Intraneural perineuriomas consist of multiple layers of neoplastic, normal-appearing perineurial cells that surround nonneoplastic myelinated or unmyelinated axons and Schwann cells. A histopathological study of the pseudo-onion bulb cells demonstrates immunoreactivity for EMA but not for S100 protein. This feature distinguishes the perineurioma from a Schwann cell process, which contains a true onion-bulb formation and gives rise to hypertrophic neuropathy, but is EMA negative

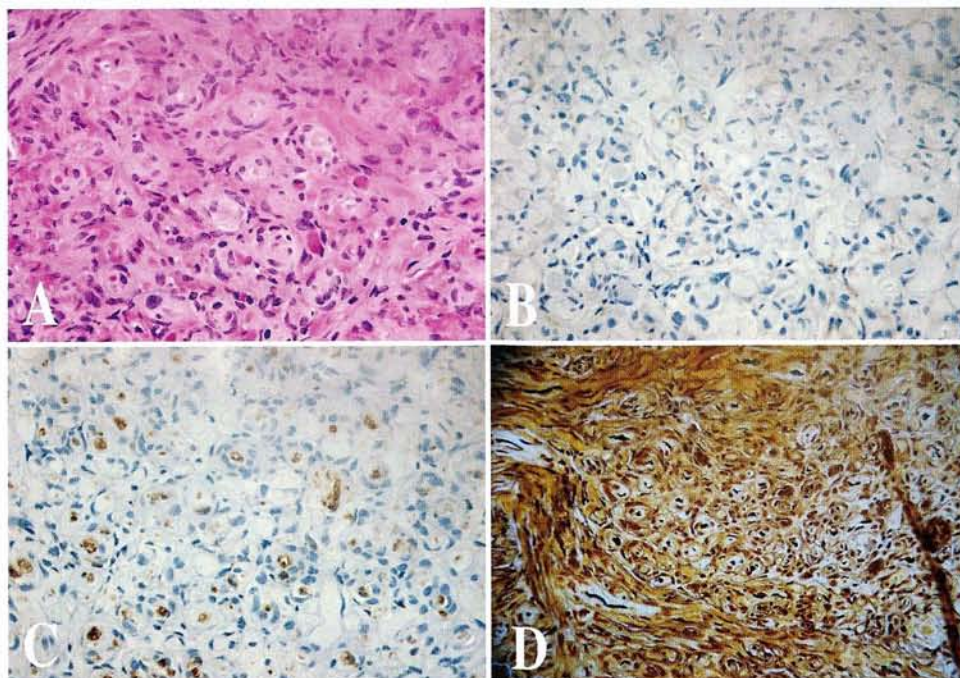


FIG. 3. Photomicrographs showing tumor specimens. A: Concentric whorls of cells with a pseudo-onion bulb appearance. H & E. B: Concentric whorls with positive staining in the centrally located Schwann cell around the nerve fiber. Immunohistochemical staining with an antibody against S100 protein. C: Weakly positive staining in concentric cells around the central nerve fibers. Immunohistochemical staining with an antibody against EMA. D: Concentric whorls with centrally located dark-staining axons. Bielschowsky stain. Original magnification $\times 400$.

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and S100 positive.¹⁵ Normal Schwann cells existing in the center of the bulblike structure stain positively for S100, as occurred in our case.

There are a few other reported cases of cranial nerve neoplasms with onion-bulb formation and hypertrophic neuropathy: three occurred in the trigeminal nerve,^{1,2,10} four in the eighth cranial nerve^{13,14} and one in the facial nerve.⁸ Although the clinical and neuroimaging findings were similar, in these cases the Schwann cell was acknowledged as the origin of the tumor. Tumors of perineurial cell origin can be distinguished from tumors of Schwann cell origin by immunostaining. Perineurial cells are EMA positive and S100 negative, and Schwann cells are S100 positive and EMA negative.

All reported cases of IPNs have been benign tumors that have not displayed recurrence or metastasis. Given that so few cases have been reported, a consensus has yet to be reached involving its management. Some surgeons have suggested more conservative management because resection has frequently damaged sensory nerve function, even when nerve grafts have been used. On the other hand, surgical removal has been suggested if the IPN can be easily separated from the nerve or if the tumor is causing a significant motor deficit.³ In our case, a subtotal resection of the tumor was performed. Approximately 25% of the tumor was left on the third nerve fibers to avoid disruption of the remaining third nerve fibers and to provide some recovery of the third nerve; the postoperative results were promising.

Conclusions

Perineurial cell tumors do occur in cranial nerves. Immunohistopathological studies can be performed to differentiate these lesions from tumors having origins in Schwann cells and from other hypertrophic neuropathies.

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Address reprint requests to: Kenan Arnautović, M.D., Semmes-Murphey Clinic and Department of Neurosurgery, University of Tennessee, 6325 Humphrey Boulevard, Memphis, Tennessee 38120. email: kenanarnaut@yahoo.com.