Isolated hypertrophic interstitial neuropathy of the trigeminal nerve associated with trigeminal neuralgia

Case report of an entity not previously described

DAVID S. BASKIN, M.D., JEANNETTE J. TOWNSEND, M.D., AND CHARLES B. WILSON, M.D.

Departments of Neurological Surgery and Pathology, University of California School of Medicine, San Francisco, San Francisco, California

Hypertrophic interstitial neuropathy (HIN) is a specific pathological entity characterized by a collection of Schwann cell processes arranged concentrically around one or more nerve fibers. Although this condition is associated with a number of different hereditary sensorimotor neuropathies, it occurs in a variety of other circumstances as well. Patients with HIN of the peripheral nerves and symptoms of cranial nerve involvement have been reported, but involvement of the cranial nerves by HIN was confirmed by microscopic documentation in only one case. We report the first case in which isolated HIN of the trigeminal nerve was histologically documented in a patient with trigeminal neuralgia who had no symptoms or signs of involvement of the nervous system elsewhere.

Case Report

This 41-year-old right-handed American Indian man was admitted to the Neurosurgery Service at the University of California, San Francisco, on May 7, 1980, with a 3-year history of left facial pain in the distribution of the first and second division of the trigeminal nerve. He described the pain as sharp and knife-like, and reported that it was brought on by activities such as brushing his teeth, shaving, breathing cold air, and talking for a long period of time. The pain was paroxysmal, and could be elicited from a number of trigger points on the left side of the face. Before his admission to our service, the patient had undergone two antral sinus operations for pain control that had provided no relief. Subsequently, he had received carbamazepine and then phenytoin for pain control, again without success. His past medical history was otherwise unremarkable.

Examination. Physical examination upon admission, including a detailed neurological evaluation, showed no abnormalities except for paroxysmal attacks of severe left facial pain that could be triggered by pressure on the left half of the upper lip. The results of a complete laboratory evaluation were normal, as was a computerized tomography (CT) brain scan performed before and after the administration of intravenous contrast material. On the basis of these findings, the patient was scheduled to undergo microvascular decompression of the trigeminal nerve.

Operation. On May 9, 1980, a left suboccipital craniectomy was performed. The dura was opened, and the trigeminal nerve was well visualized. A dramatic bulbous enlargement of the nerve, beginning 5 mm from the trigeminal root entry zone and extending...
approximately 1 cm distally, was noted immediately. After a careful examination of the nerve rootlets, it was evident that the enlargement represented a process occurring with many individual rootlets, and was not caused by a tissue reaction occurring between them. The most conspicuously involved rootlets were those immediately adjoining the motor root. The enlarged portions of the rootlets had a wrinkled, yellowish appearance and many transverse vessels lying on their surface. The superior cerebellar artery was situated well away from the nerve, and there was no evidence of vascular cross compression by either arteries or veins. Three of these abnormal rootlets were excised and sent for pathological analysis. A subtotal rhizotomy was then performed; both abnormal and normal rootlets were cut in the caudal 40% of the sensory root.

Pathological Examination. Microscopic examination of the surgical specimen revealed peripheral nerve fibers surrounded by whorls of Schwann cells and separated by endoneurial fibrosis (Fig. 1 left).

Electron microscopy demonstrated layers of Schwann cell cytoplasm with basement membranes surrounding small myelinated axons (Fig. 1 right). Some of the central axons were unmyelinated. Increased numbers of fibroblasts, collagen fibrils, and Schwann cells were found in the endoneurium.

The patient has done well postoperatively. His facial pain has totally resolved, although moderate hypesthesia persists in the second and third divisions of the trigeminal nerve on the left side.

Discussion

Hypertrophic interstitial neuropathy (HIN), also known as “onion bulb neuropathy,” is a well defined pathological condition of the peripheral nerve. This condition was at one time associated solely with Déjérine-Sottas disease, although a variety of other sensorimotor neuropathies with the specific pathological elements of HIN were described in early reports. It is seen in many hereditary or acquired diseases, including Refsum’s disease, globoid-cell disease.

Fig. 1. Left: Photomicrograph of a 1-μ section of trigeminal nerve biopsy demonstrating proliferation of Schwann cells in onion-bulb formation around myelinated axons. Toluidine blue, × 540. Right: Electron micrograph showing two small myelinated axons surrounded by collagen fibrils and concentric rings of Schwann cell cytoplasm. × 3400.
Interstitial neuropathy in trigeminal neuralgia

and metachromatic leukodystrophies, 22 acromegaly, 26 diabetic neuropathy, 28 and idiopathic polyneuritis, 22 and it has also been produced under experimental conditions. 3, 10, 19, 29

Macroscopically, HIN is characterized by enlargement of the affected nerves. Microscopically, overlapping Schwann cell processes and connective tissue form concentrically around one or several nerve fibers. 24 As the Schwann cells proliferate, an "onion bulb," a structure composed of Schwann cell processes and collagen fibrils, forms around the nerve. 11 There is a decrease in the total number of myelinated fibers and an abnormal distribution of fiber size. Segmental demyelination and remyelination affects most of the myelinated fibers. 13 The myelin sheath may show degeneration that does not involve the adjacent Schwann cell.

Segmental demyelination has been demonstrated unequivocally in HIN. 13 Several experimental studies have indicated that repeated segmental demyelination and remyelination is the primary event in the development of onion bulbs. 10, 19, 29

Biochemical studies have documented increased myelin turnover rates in patients with HIN, including an increased rate of incorporation of radioactive sulfur into nerves of the HIN patients, 21 less than normal lipid in the peripheral nerves of a patient with HIN, and increased concentrations of hydroxyproline, hexosamines, stearic acid, and choline phosphoglycerides. 18 Plasma glycolipid abnormalities 24 and reduced axonal transport of dopamine beta-hydroxylase have also been associated with this disorder. 5

Although HIN occurs diffusely in most patients, there are reported cases of localized HIN occurring in a variety of solitary sites. 7, 9, 14, 23, 25 Some of the patients with localized HIN had a history of trauma at the site of involvement.

Cranial nerve involvement has been reported previously in cases of HIN, 1, 4, 15, 16, 17, 20 but pathological documentation has been obtained in only one case. 4 Kalyanaraman, et al. 16 reported the case of a 23-year-old man who had developed a peripheral neuropathy at age 5 or 6 years, and who had a 12-year history of trigeminal neuralgia and a history of hemifacial spasm for an unknown period of time. Onion-bulb formations were found in a sural nerve obtained from this patient by surgical biopsy. Brawley and Kelley treated a 24-year-old man who had a diffuse peripheral neuropathy, papillary changes, a sixth-nerve palsy, decreased hearing in the right ear, and an elevated protein level in the cerebrospinal fluid. An exploratory suboccipital craniectomy revealed bulbous enlargement of the vestibulocochlear nerve that was caused by onion-bulb formations.

Our case represents an unusual variation in the presentation of HIN, and it is, to our knowledge, the first reported case of trigeminal neuralgia in which microscopic documentation of focal HIN has been obtained. Whereas the patient was completely normal neurologically and showed no evidence of a hereditary or acquired disease associated with onion-bulb formation, the pathological changes observed are specific for HIN. No vascular loop compressed the nerve, and there was no evidence of previous cross compression having caused trauma to the nerve.

As microvascular decompression of the trigeminal nerve is now commonly performed, it may be possible to determine the actual incidence of focal HIN presenting as trigeminal neuralgia. If, at the time of exploration, no vessel is found cross compressing the trigeminal root, we perform a selective section of portio major fibers and obtain a biopsy specimen. The specimen can be taken in this manner without causing unnecessary sensory impairment. Histological examination of these specimens may disclose other, and perhaps milder, cases of HIN.

Acknowledgments

The authors thank Susan Eastwood for editorial assistance in the development of the manuscript, and Beverly J. Hunter for her assistance in its preparation.

References

11. Dyck PJ: Histologic measurements and fine structure of
biopsied sural nerve; normal, and in peroneal muscular atrophy, hypertrophic neuropathy, and congenital sensory neuropathy. Mayo Clin Proc 41:742–774, 1966


Manuscript received May 20, 1981.
Address reprint requests to: David S. Baskin, M.D., % The Editorial Office, Department of Neurological Surgery, 350 Parnassus Avenue, Suite 807, San Francisco, California 94143.