Ganglioneuroma-paraganglioma of the intradural filum terminale

Case report

ROBERT I. LERMAN, M.D., EDWARD S. KAPLAN, M.D., AND LAUREN DAMAN, B.S.
Departments of Pathology and Neurosurgery, Baptist Memorial Hospital, Memphis, Tennessee

✓ A rare ganglioneuroma-paraganglioma of the filum terminale is reported, and the histological, histochemical, and ultrastructural characteristics of the lesion described. Classification was resolved by the ultrastructure.

Key Words: ganglioneuroma · paraganglioma · filum terminale · pathology · spinal cord tumor

This paper reports a unique tumor of the intradural filum terminale. The neoplasm demonstrated components of a ganglioneuroma and a paraganglioma. Classification of the tumor was clarified by its ultrastructure.

Case Report

This 29-year-old Negro man had a 13-month history of intermittent, severe, spastic low-back pain associated with pain in the left leg aggravated by bending, prolonged standing, or weight-bearing; all of these symptoms started following an automobile accident in July, 1968. Previously, in 1967, the patient had been evaluated by a neurosurgeon because of episodes of recurrent syncope and confusion, with numbness in the arms. A diagnosis of hyperventilation syndrome was made after neurological examination, echoencephalogram, skull films, electroencephalogram (EEG), brain scan, and CSF studies were found to be normal.

Examination. There was limitation of lumbar flexion and extension associated with lumbar spasm and left sacroiliac pain. Straight leg raising to 90° produced discomfort in the back and left buttock. Flexion of the neck to the chest caused low back pain. The patient exhibited cautious movements of the lumbar spine when arising from a chair. There was questionable weakness of the dorsiflexors of the left toes; the deep tendon reflexes were all depressed. There were no pathological reflexes or sensory deficits. Routine blood cell counts (CBC) and chemistries, rheumatoid factor test, and erythrocyte sedimentation rate (ESR) were normal. Lumbar x-ray films revealed mild narrowing of the fifth lumbar disc space. Lumbar puncture revealed a cerebrospinal fluid (CSF) protein content of 218 mg% with normal cell count and cytology. A lumbar myelogram in August, 1969, revealed a 2 × 1.2 cm oval intradural mass superior to the second lumbar disc space. A postoperative urinary VMA determination was negative.

Operation. Laminectomy of L-2, -3, and
Paraganglioma of the filum terminale

-4 allowed palpation of a mass through the dura at the level of L-2; the epidural fat seemed to be decreased at this point. When the dura was opened and the cauda equina retracted, a tumor was exposed attached to the filum terminale 2 cm from its junction with the conus medullaris. The tumor was gently removed after clipping and cutting its attachments.

Postoperative Course. The patient was discharged 12 days following surgery with good function of the legs, bowel, and urinary bladder. He returned to building tires after a satisfactory convalescence of 4 months. Examination on January 17, 1971, revealed that he was doing well, with only an occasional “catch” in his back when lifting objects.

Materials and Methods

Tissue from the tumor was fixed in buffered 10% formalin. Representative samples were then embedded in paraffin, sectioned to a thickness of 5 μ, and prepared for light microscopy with hematoxylin and eosin, cresyl violet, oil red O, mucicarmine, periodic acid-Schiff (PAS), methenamine silver, ferric ferrocyanide, silver nitrate, Masson trichrome, and Gomori’s reticulum stains.

Representative samples were also prepared for electron microscopy by postfixing in 3% cacodylate-buffered glutaraldehyde and 2% osmium tetroxide, and then embedding in DER 334. Semithin sections were prepared on a Porter-Blum MT-2, and then stained with methylene blue. Ultrathin sections were mounted on unsupported 200-mesh copper grids, and then stained in uranyl acetate and lead citrate. The tissue was then examined with a Phillips 300 electron microscope.

Ten ilia terminales from consecutive autopsies served as controls. They were fixed in 10% formalin and embedded in paraffin, both transversely and longitudinally. Sections were stained with hematoxylin and eosin for light microscopy.

Pathological Findings

Light Microscopy

The focally hemorrhagic nodule removed from within the filum terminale was a soft, pinkish, smoothly encapsulated tumor measuring 2.0 × 1.2 cm. There were two distinct morphological patterns identifiable in the tumor by light microscopy, with areas of pure, monophasic growth and areas of admixture.
Fig. 2. *Left:* Paraganglia component showing marked vascularity. H & E, ×200. *Right:* Higher power photomicrograph showing polyhedral, cuboidal, and columnar paraganglia cells arranged in "zellballen." H & E, ×400.

Fig. 3. Electron micrograph of ganglion cell. Numerous intracytoplasmic membrane-bounded granules are apparent. n = nucleus; nu = nucleolus; g = granules; and m = mitochondrium. ×18,000.
Paraganglioma of the filum terminale

FIG. 4. Electron micrograph of ganglion cells. The membrane-bounded granules which average 300 μm are intracytoplasmic, extracellular, and in cell processes. Intracytoplasmic fibrillar material is apparent. m = mitochondrium; er = endoplasmic reticulum; g = granules; and pm = plasma membrane. × 21,600.

These two distinct patterns were individually consistent with a ganglioneuroma and a paraganglioma.

Within the ganglioneuromatous component, numerous ganglion cells were identified by their characteristically prominent, round, vesicular nuclei, conspicuous nucleoli, and abundant cytoplasm containing variable amounts of Nissl substance (Fig. 1). No pigment or argentophilic granules were identifiable within the ganglion cells. Extracellular glial tissue, demonstrated by the Holtzer stain, was quite abundant in some areas.

The paragangliomatous component was characterized by a richly vascular stroma containing numerous dilated, congested capillaries. These branching fibrovascular cores were surrounded by small alveoli and nests of polyhedral, cuboidal, and columnar cells having the classic “zellballen” and peritheliomatous patterns (Fig. 2), consisting of islands of cells surrounded by sinusoidal vascular channels. The nuclei of these cells were uniform, round to oval, and generally vesicular. The nuclear chromatin was finely granular and evenly distributed; no mitotic figures were identified. The cytoplasm was abundant and finely granular. Neither myxomatous nor mucinous areas were demonstrable histochromically. Fresh tissue was not available for chromaffin reactions or for catecholamine analysis.

Electron Microscopy

The ganglion cells of the ganglioneuromatous component were easily distinguished by their size, large nuclei and nucleoli, and abundant cytoplasm (Fig. 3). A moderate number of mitochondria were apparent in these cells; they appeared swollen, and the cristae were disrupted, which was no doubt secondary to inadequate fixation. Fibrillar material lacking periodicity was also noted to be prominent in processes originating from the ganglion cells. Abundant endoplasmic reticulum, often with associated ri-
Robert Lerman, Edward Kaplan and Lauren Daman

FIG. 5. Electron micrograph of paraganglion cells. Ganglion cell process (p) in right upper corner. The paraganglion cells are tightly clustered. × 4300.

bosomes, was arranged in long, narrow, parallel cisternae. Numerous electron-dense granules were demonstrated within the cytoplasm, although some were noted to be partially extracellular, and in the neural processes. The granules in the cytoplasm were randomly distributed, although some appeared to be concentrated in membrane-bounded vesicles along with fragments of degenerated mitochondria (Fig. 4). These granules were bounded by a single limiting membrane; they averaged 300 millimicrons (μm) in diameter, with a range from 204 to 406 μm; they varied from extreme electron density to empty, membrane-bounded vesicles. Synaptic vesicles were noted.

The paragangliomatous component of the tumor was characterized by clusters of tightly adherent cells interconnected by “desmosomes” (macula adherens) (Fig. 5). The nuclei were smaller, the nucleoli were less conspicuous, and the mitochondria were smaller and more elongated than those of the ganglion cells. Smooth and rough endoplasmic reticulum, and sparse intracytoplasmic fibrillar material, were present. Electron-dense granules were apparent, although in a lesser concentration than in the ganglion cells (Fig. 6). Microvillar and blepharoplast structures described previously as typical of ependymomas were not identified. Extracellular collagen and capillaries were present in the stroma.

Controls

The 10 control fila terminales contained elements of ependyma, scattered ganglion cells, and large nerve cells particularly near the conus medullaris, glial tissue, arachnoid and mesenchymal elements; this description is essentially in agreement with that of Tarlov.

Discussion

The classification of this tumor was resolved by its ultrastructural characteristics.
Identification of abundant membrane-bounded granules averaging 300 \( \mu \)m in diameter in both components of the tumor related the two components histogenetically. These granules were morphologically identical to the neurosecretory granules described in a central ganglioneuroma, peripheral ganglioneuroma, neuroblastoma, pheochromocytoma, and the human adrenal medulla. Similar granules have been described in the abdominal and periesophageal ganglia of gastropods, the adrenal medulla of rabbits and rats, carcinoid tumors, carotid body tumors, and in the carotid bodies of cats and rabbits. All of these granules share the basic configuration of a central electron-dense mass separated from an outer membrane by a narrow light zone, and a size generally varying from 200 to 400 \( \mu \)m. De Robertis and De Iraldi have suggested that such structures may represent secretory granules of catecholamines, since they have the capacity to reduce osmium tetroxide and thus appear electron-dense in osmic-fixed tissue. Special staining techniques on paraffin-embedded tissue of our tumor failed to demonstrate neurosecretory granules.

Fresh tissue from the tumor was not available for catecholamine analysis or histochemical techniques. There had been no preoperative determinations, catecholamines, or their metabolites in blood, cerebrospinal fluid, or urine.

Intramedullary CNS ganglioneuromas are rare, but ganglioneuromas of the spinal cord and of the cerebral hemispheres have been reported. However, to our knowledge, a tumor of the paraganglionic system has not been previously reported in the filum terminale. Chromaffin paraganglioma of adrenal (pheochromocytoma) and extra-adrenal origin are known to occasionally show a ganglioneuromatous component which closely resembles that described in our case.

The paraganglionic system consists of groups and bodies of chromaffin-positive and chromaffin-negative cells which are found in greatest numbers in the adrenal medullae.
and the organs of Zuckerkandl. They are also found along the paravertebral sympathetic ganglia and certain cranial nerves, especially the glossopharyngeal and vagus nerves, and are scattered in an irregular pattern throughout the retroperitoneum.4 Paraganglion cells have been described in the kidney, testis, ovary, liver, heart, and urinary bladder, in addition to various other locations.2,21

The neoplasms of paraganglia have classically been separated into two groups, the chromaffin-positive paragangliomas or pheochromocytomas and the chromaffin-negative paragangliomas, including chromalectoma and glomus tumors. A more appropriate classification of paraganglioma is based on clinical, biochemical, histochemical, and morphologic characteristics. The terms “functional” and “nonfunctional” refer to the ability or inability, respectively, to make and secrete sufficient catecholamines to cause clinical signs or symptoms. These may occur spontaneously or only when the neoplasm is manipulated.3

References

Address reprint requests to: Robert I. Lerman, M.D., Department of Pathology, Baptist Memorial Hospital, 899 Madison Avenue, Memphis, Tennessee 38103.