Melanotic nerve sheath tumors

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A solitary intraspinal, extradural melanotic tumor was subtotally resected in a 59-year-old man who had a 17-year history of radicular pain and later evidence of progressive spinal cord compression. The neoplasm revealed the histological features of a benign nerve sheath tumor with massive but uneven melanin production. In electron micrographs the tumor cells contained masses of melanosomes of the type seen in normal skin melanocytes and in B type melanocarcinomas. In the 16-month postoperative period there has been only minimal radiological indication of local recurrence and no metastases.

Case Report

This 59-year-old man first had intermittent radicular pain in the chest 17 years before admission; it recurred at monthly intervals and was moderately severe. Difficulty in walking, weakness in the legs, and hesitancy in urination began in May, 1971, when the back pain became continuous. Neurological findings then were consistent with compression of the spinal cord at T-7. Spine films showed erosion of the right side of the 7th thoracic vertebra, and myelography demonstrated an incomplete block at the same level. These findings were thought to be most consistent with a metastatic bone lesion.

Operation. Laminectomy (T-6, -7, -8) in February, 1972, exposed a large extradural encapsulated, firm, focally pigmented tumor, located posterior to the spinal cord mostly on the right side; it extended into the right perivertebral region and into the chest through an intravertebral foramen. On the right side one dorsal root emerged from the

Key Words • nerve sheath tumors • melanotic schwannoma • melanin • melanosomes

Within the normal nervous system, melanin pigment can be seen in the pia mater, especially in the posterior fossa, in the pigmented neurons of the brain stem, sympathetic ganglia, and spinal ganglia. In pathological states, melanin may occur in melanomatous meningiomas, in meningeal melanosis, and in malignant melanomas of the meninges. In the peripheral nervous system, melanin has been observed in a rare type of nerve sheath tumor reported as "melanotic schwannoma" or "pigmented neurofibroma." The histogenesis of this tumor and its relationship to cellular blue nevi and ordinary pigmented nevi has been discussed by Bird and Willis. In the cases reported previously, the neoplasms were usually situated in the subcutaneous tissues. In only two cases were pigmented peripheral nerve tumors observed in deep structures. This report concerns a solitary intraspinal pigmented nerve sheath tumor at T-7, extending through the intervertebral foramen.
tumor. No intradural mass was observed. The tumor was resected subtotally.

Second Operation. Postoperatively the patient experienced mild paraparesis and increased radicular pain, and 4 months later, because of the pain, an intradural rhizotomy was performed. A recurrent tumor mass 5 cm in diameter was removed from the perivertebral soft tissues.

When the patient was seen in October, 1973, his general state was good and the weakness in his legs was improving under physical therapy. Recent x-ray studies demonstrate a slight lateral increase of the residual intrathoracic perivertebral (extrapleural) tumor but no metastases.

Pathological Examination. The specimens from both operations appeared similar and consisted of pieces of firm blackish tissue. Some fragments of the first specimen contained a fibrous capsule. Specimens from the first operation consisted of 5 cc of small (up to 1 cm) fragments; the fragments from the second operation weighed a total of 20 gm.

Histology. The specimens from the two operations were almost identical. In low magnification, the neoplasm in many areas revealed structure resembling that of a plexiform neurofibroma (Fig. 1 upper left). The tumor was moderately cellular. The cells were spindle-shaped with oval, slightly elongated, fairly chromatic nuclei that often contained nucleoli. Mitotic figures were not seen. Most of the cells were of uniform shape; however, in the recurrent tumor slight focal pleomorphism was present. The cells were arranged parallel to each other, forming bundle-like patterns with occasional irregular palisades (Fig. 1 upper right). The interwoven bundles gave the tumor a plexiform appearance. The fibrous stroma was moderately rich and resembled that of a

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Fig. 1. Photomicrographs of the neoplasm. Upper Left: The plexiform architecture of the unevenly pigmented neoplasm is seen. H & E, × 30. Upper Right: Pigmented cells form an irregular palisade. H & E, × 160. Lower Left: Scattered groups of plump tumor cells are overloaded with melanin; some melanin is interstitially distributed. H & E, × 160. Lower Right: The predominant architecture of the tumor is consistent with that of Antoni's type A schwannoma. H & E, × 160.
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neurofibroma with focally thick collagenous trabecules. Melanin was unevenly distributed in the tumor (Fig. 1 upper left). Groups of tumor cells contained abundant melanin (black in Fontana stain, iron stain was negative); occasional melanin granules also were observed interstitially (Fig. 1 lower left). In other areas the tumor cells contained no visible pigment, and the architecture resembled the Antoni's type A schwannoma (Fig. 1 lower right). In the recurrent neoplasm more cells contained pigment, and the pigment was also denser and coarser. Scattered in the tumor were clusters of plump cells resembling epithelial cells, with or without pigment. Transitional forms between these and the fusiform cells were observed.

In one section normal-appearing peripheral nerve tissue was seen within the tumor. Preparations of the recurrent neoplasm displayed invasion of the neighboring muscle tissue; however, some original fragments revealed a distinct fibrous capsule. Nerve fibers (axons) were seen only focally in the area of the spinal nerve.

Electron Microscopy. For ultrastructural studies, 1 mm fragments of formalin-fixed tumor were washed with cacodylate buffer, refixed in 2% buffered glutaraldehyde, and postfixed with 1% buffered osmic acid. Following dehydration, the fragments were embedded in Araldite and sections cut on an LKB ultramicrotome using glass knives. Thin sections were examined and photographed in a Siemens 101 electron microscope.

Two cell types were identified. The first type was characterized by a large irregular, elongated nucleus with chromatin granules condensed at the nuclear envelopes (Fig. 2 left); many cells contained one or two distinct

![Fig. 2](image-url)
nucleoli. The cytoplasm contained masses of melanosomes displaying various degrees of electron density (Fig. 2 left). There was a slight variability of shape and size of these organelles which usually were short cigar-shaped (Fig. 2 right). Melanosomes were so abundant in some cells that they virtually filled the cytoplasm (Fig. 2 left). Lysosomes and smooth endoplasmic reticulum were not identified in these cells, probably because of compression by melanosomes. No transient forms between melanosomes and other organelles were observed. Many of these cells displayed peripheral condensation on the plasma membrane, resembling basement membrane with filaments.

The cells of the second type, fusiform in shape, displayed a system of distended cisterns in a pattern characteristic of fibroblasts; some cells contained a few melanosomes (phagocytized?). Abundant short periodicity collagen was seen in close relation to these cells; no basement membrane was present on these cells.

Discussion

A melanotic nerve sheath tumor (MNST) was first described by Bjornboe in an atypical case of von Recklinghausen's disease. Since then, 19 cases have been reported. All but two were subcutaneous; one was intraperitoneal and one intramandibular. The tumors were usually solitary. Occasionally the neoplasm appeared in combination with meningeal melanomatosis, adamantinoma, and melanocarcinoma in the same case. Only one of these cases was associated with von Recklinghausen's disease. The tumors grew very slowly, often being present from birth. Most cases were in young adults; females were slightly more commonly affected. Eighteen cases were in Caucasians and one in a Negro with a scalp lesion. Histologically the reported tumors displayed the architecture of a plexiform neurofibroma. Some had scattered clusters of polyhydral cells. The content of reticulin and collagen was variable. The distribution of melanin varied from focal and abundant to only sparse. With one exception the cytoarchitecture usually seemed benign. The invasive quality did not seem to parallel the degree of pigmentation; our recurrent large tumor had more pigment than the original biopsy specimen.

The particular importance of our case, which belongs to the very rare "deep" variant, was its unique location in the spinal column. Although there was no direct evidence that a nerve was the primary site, this origin was strongly suggested by the location, distribution, history, and histological features. The nerve entering the tumor could have represented the site of origin or merely have been casually embedded in the neoplasm. The tumor was not connected with skin, esophagus, or trachea, the closest organs from which a melanocarcinoma theoretically could extend into the vertebral canal.

Microscopically our tumor fulfilled the criteria of a benign nerve sheath neoplasm. The long history and lack of metastases confirmed its basically benign character, comparable to that of schwannomas or neurofibromas. The electron microscopical finding of abundant variable-sized melanosomes demonstrates that many tumor cells have the organelles necessary for active melanin elaboration. The morphology of these organelles is not yet well understood. Wolff and Honigsmann suggest that melanosomes are derived from lysosomes through fusion. Similar to lysosomes, melanosomes contain acid hydrolases, and ferritin injected into the skin can be traced to the melanosome membranes. Conversely, Ide saw melanosomes developing from the smooth surface of the endoplasmic reticulum rather than lysosomes; according to Ide, tyrosinase is transported to melanosomes by tyrosinase-containing vesicles originating from Golgi apparatus.

Our findings show that melanin encountered in MNST is of the "peripheral" type in contrast to the "central" type seen in pigmented neurons and which possess different ultrastructure related to that of the lipofuscin. The presence of melanosomes in cells of a solitary intraspinal tumor distant to usual melanoblast-melanocyte sources is an unusual phenomenon which may possibly be explained by development of the tumor from aberrant or ectopic melanoblasts or melanocytes. MNST were first linked with the melanocytic system by Masson, who
hypothesized that all melanoblasts are of neuroectodermal origin, and melanocyte precursors are probably transported to the periphery in buds of peripheral nerves. An MNST could then arise from retention of the migrating melanocytic "Anlagen" during fetal development. If one accepts this hypothesis, it is surprising that MNST's are not more common. The frequent congenital occurrence of MNST suggests that these neoplasms appearing in older individuals were derived from some previously inconspicuous nests of melanoblasts segregated in embryonal development. The long 17-year history in our case is consistent with the usual slow growth of the reported MNST, and is in keeping with the "hamartomatous" neurogenic origin.

A second hypothesis to explain the histogenesis of the tumor may be that the neoplastic Schwann cells are capable of undergoing a "melanomatous" transformation. This alternative has been suggested by the studies of Nakai and Rappaport, who produced pigmented skin tumors in Syrian hamsters with dimethyl benzanthracene. Both Schwann cells and endoneurial fibroblasts were identified in these growths by electron microscopical techniques. Melanin was seen in Schwann cells and in the cells of perineurium which could represent modified Schwann cells.

A third hypothesis may be based on the presumption that some mesodermal components of the nerve sheath are capable of melanin formation when neoplastically proliferating. Goldberg has suggested that connective tissue cells can produce melanin. Finally, the tumor may be a mixture of two histogenetically related cell lines: those of a nerve sheath origin and those of a melanoblastic origin. This theory has been postulated for blue nevi and melanocytic neurofibromas. Indeed, the similarity of MNST to cellular blue nevi is striking since the plexiform pattern is histologically typical for both tumors. The only difference that Leopold and Richards could find between pigmented plexiform neuromas and blue nevi was poorly developed reticulin in the latter, a finding later disproved by Bird and Willis. Indeed, some cutaneous tumors reported as MNST probably represent cellular blue nevi. In the present case the definite histogenesis is obscure although the cells in the tumor containing melanosomes often had ultrastructural features most consistent with Schwann cells. Differentiation of MNST from fusiform melanocarcinoma is of great practical importance. The MNST is a basically benign growth although capable of local invasion. It does not usually produce metastases and its growth is slow. Prognosis is excellent if the tumor can be resected entirely. With subtotal excision the prognosis is more favorable than with the usually speedy progression and metastases from any type of melanocarcinoma.

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