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POSTERIOR FOSSA NEUROBLASTOMA OCCURRING IN AN ELDERLY MAN

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A case of a neuroblastoma occurring in the cerebellum of a 73-year-old man is reported. The patient presented with progressive truncal ataxia and was found to have an enhancing tumor mass in the cerebellar vermis. By light microscopy, the tumor was a small cell neoplasm and was similar to medulloblastoma, with areas showing structures suggestive of Homer-Wright pseudorosettes. By electron microscopy and immunoperoxidase techniques, however, the tumor showed convincing evidence of neuronal differentiation. The absence of previous reports of this tumor in the posterior fossa of adults suggests that immunoperoxidase techniques and/or electron microscopy of such small cell tumors may be required for accurate diagnosis. HUM PATHOL 19:365–367, 1988.

We report a case of neuroblastoma occurring in the posterior fossa of a 73-year-old man, the first such tumor described in this location in an elderly patient. The light microscopic, immunohistochemical, and electron microscopic features of cerebral and cerebellar neuroblastomas are discussed.

REPORT OF A CASE

A 73-year-old white man was admitted to The Johns Hopkins Hospital on 20 July 1985 for evaluation and treatment of a cerebellar mass. He had a 5-year history of positional vertigo, unresponsive to medical therapy. Five months before admission, the patient noted mild ataxia and difficulty in rising from a seated position. His condition gradually progressed to marked instability in walking, which resulted in several falls. Vestibular function tests were normal, but computed tomography and magnetic resonance imaging scans of the head showed an enhancing mass in the vermis of the cerebellum which effaced the quadrigeminal plate cistern and compressed the fourth ventricle. The results of general physical examination and laboratory work-up were remarkable only for truncal ataxia with a positive Romberg sign and for mild dysdiadochokinesis.

The patient was given dexamethasone, without change in symptoms. On the 6th hospital day, he underwent suboccipital craniectomy with subtotal resection of a soft, gray tumor in the cerebellar vermis. The postoperative course was uneventful, and the patient was discharged on 2 August. Following discharge, he received 4500 rad of whole-brain external-beam irradiation, with a 900-rad cone down to the posterior fossa and 3040 rad to the spinal column, over a 43-day period. The patient's gait gradually improved. The patient remained well until 20 months postoperatively, when he developed recurrence of tumor with multiple tumor nodules present in the region of the fourth ventricle. The patient was referred for additional radiation therapy.

PATHOLOGIC FINDINGS

Small amounts of soft tan-gray tumor tissue were submitted for examination. A portion of the tissue was fixed in 3% glutaraldehyde for electron microscopy. The remainder was submitted in 10% buffered formalin for routine processing. By light microscopy, the tumor was composed of small cells with scanty cytoplasm that infiltrated into the adjacent cerebellar tissue and in some areas were arranged in parallel rows. Only a scant amount of reticulin, immediately surrounding vessels, was present within the tumor. Scattered structures suggestive of Homer-Wright pseudorosettes were present (fig. 1A). Occasional mitotic figures and foci of necrosis were identified. There were no maturing ganglionic-type cells identified within the tumor.

Avidin-biotin complex immunoperoxidase stains demonstrated strong positivity for neuron-specific enolase and neurofilament within tumor cells. Stains for glial fibrillary acidic protein were uniformly negative.

Electron microscopic studies revealed cells with convincing evidence of neuronal differentiation, including cytoplasmic processes containing numerous microtubules and occasional neurosecretory granules (fig. 1B). Primitive intercellular junctions and rare bundles of intermediate filaments were identified. Nuclei were irregularly shaped and had clefts and pockets. No synaptic structures were identified.

DISCUSSION

Neuroblastomas have been reported arising supratentorially and, less frequently, in an infratentorial location. The three histologic subtypes of cerebral neuroblastoma described by Horten and Rubinstein[1] are distinguished primarily by the amount and distribution of connective tissue present within the tumor and are analogous to the subclassification scheme proposed for medulloblastoma.[2] The "classic" variant of neuroblastoma is usually well demarcated from the surrounding brain and is characterized by the presence of scant connective tissue stroma limited to areas surrounding blood vessels. Homer-Wright pseudorosettes are a common feature of this tumor. The desmoplastic variant exhibits abundant connective tissue stroma, which may surround small groups of tumor cells or individual tumor cells. The malignant cells of the desmoplastic neuroblastoma are somewhat larger than those of the classic variant, and they may display vesicular nuclei with prominent nucleoli. The transitional variant shows stromal proliferation intermediate between the classic and desmoplastic forms, and it usually exhibits the cytologic features of the desmoplastic variant. It must be recognized that cerebral neuroblastomas have a spectrum of histologic appearance, and more than one variant may be present within individual tumors. The classification scheme is also

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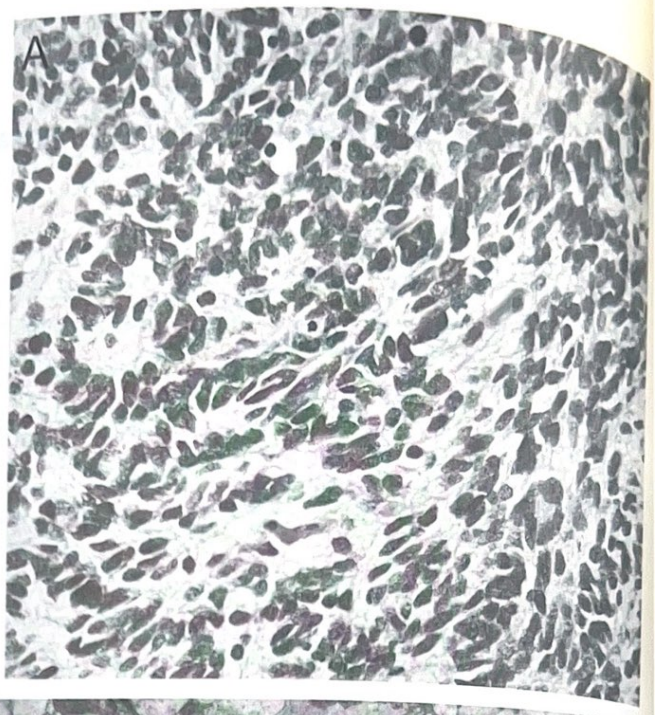

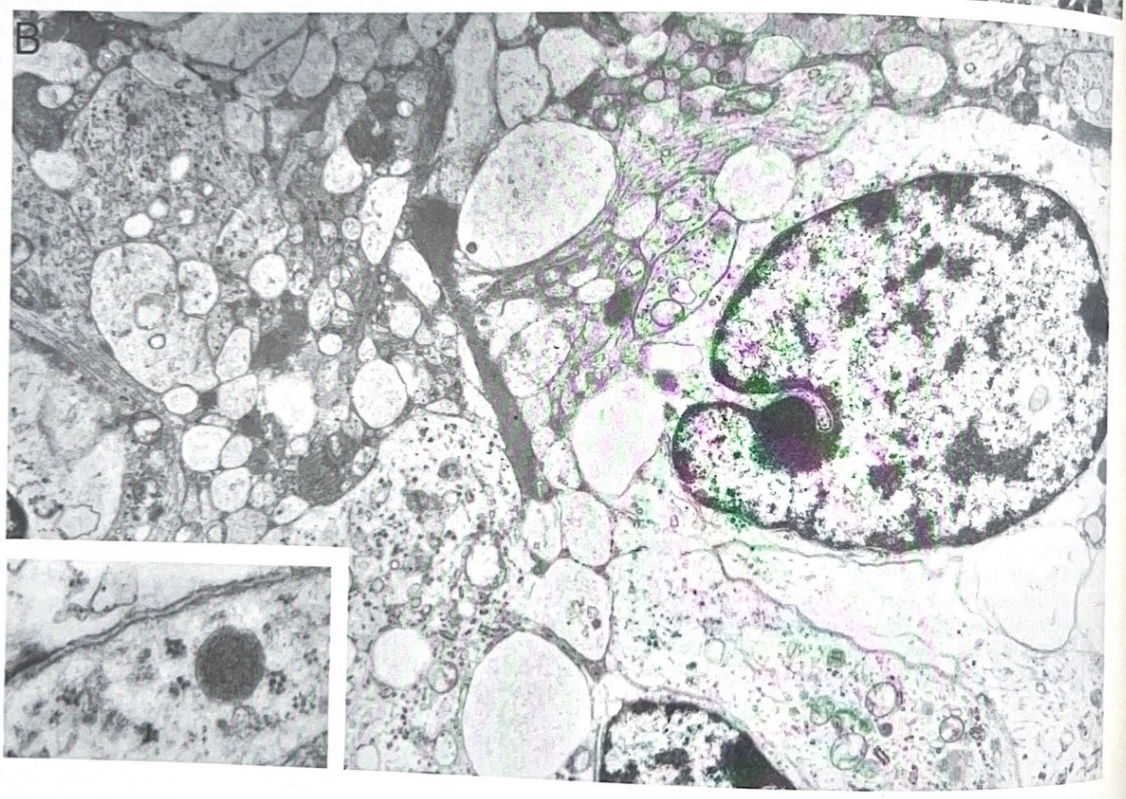

FIGURE 1. A, Cerebellar tumor composed of small cells with scattered structures suggestive of Homer-Wright pseudorosettes. (Hematoxylin-eosin stain. ×575.) **B,** Electron micrograph showing tumor cells with nuclear clefting and numerous cytoplasmic processes. (×6000.) **Inset,** Neurosecretory granule within a cytoplasmic process. (×38,000.)

applicable to the gross appearance of the neuroblastoma, as the amount of connective tissue contributes to the degree of firmness and lobulation of the tumor.

By electron microscopy, cerebral neuroblastomas have slightly to very irregular nuclear contours, with scanty cytoplasm and numerous fine cytoplasmic processes often arranged in fascicles.[3,4] These processes contain dense-core vesicles, microtubules, and intermediate filaments.[5] Ribosomal rosettes are present within the cytoplasm, as are bundles of microtubules. In the more differentiated tumors, the cytoplasmic processes display synapse-like structures with aggregates of small clear vesicles and the typical asymmetric synaptic junction.[3]

Cerebral neuroblastomas are primarily neoplasms of children, with 81% occurring within the first decade of life.[1,6,7] Clinically, they usually present with nonlateralizing

signs of elevated intracranial pressure (44%) and a propensity for local recurrence and dissemination throughout the subarachnoid space.[6]

Only nine cases of neuroblastomas arising in the cerebellum have been reported.[8–15] The oldest patient, prior to our report, was 10 years of age (mean age, 2.7 years). The most common symptoms at presentation were those secondary to increased intracranial pressure or gait abnormalities. Most patients have been treated with surgery and cranioaxial radiation. Of the four prior cases with follow-up, one died 3 weeks following diagnosis; two had recurrent tumor 5.5 and 4 years following treatment, respectively, with the latter case showing maturation to ganglioneuroma; and one had no evidence of disease 1.5 years after therapy.

Typically, cerebellar neuroblastoma is an intraparenchymal vermian tumor. It is lobulated in appearance, with reticulin-containing septae that resemble leptomeningeal infoldings that contain variable numbers of tumor cells.[11,15] The tumor cells have nuclear features similar to those of desmoplastic neuroblastomas and are larger than those of medulloblastoma.[15] They are commonly arranged in parallel rows with interdigitating reticulin. Homer-Wright pseudorosettes provide evidence for neuronal differentiation at the light microscopic level.

By electron microscopy, cerebellar neuroblastomas show findings similar to those previously described for cerebral neuroblastomas.[11,12,15] Although the light microscopic appearance described here is typical, tumors of the cerebellum that show characteristic ultrastructural features have been classified as neuroblastoma despite the lack of prominent neuronal differentiation by light microscopy.[8,15]

The pathologic separation of cerebellar neuroblastoma from medulloblastoma does not have clinical application at present. Of interest, however, are case reports of neuroblastoma in which the malignant cells matured with therapy to ganglion cells.[8,13] Despite the current lack of evidence for clinical significance, the paucity of reported cases and the unusual age of presentation in our case indicate the need to separate these tumors from medulloblastoma so that they may be better studied.

In a child, the clinical significance of classifying lesion as a medulloblastoma when the lesion might show prominent differentiation by electron microscopy is minimal, as treatment would not be affected. However, the potential for misdiagnosis in the adult is more important. In the current case, although light microscopic features suggested neuronal differentiation, the correct diagnosis may not have been made without the aid of electron microscopy. The diagnosis of small cell glioma or small cell variant of glioblastoma multiforme[16,17] would have been strongly considered even though the tumor did not stain for glial fibrillary acidic protein, given the recognized lack of such staining in some high-grade gliomas.[18] The diagnosis of metastatic small cell carcinoma, possibly from lung, would also have been entertained, as this carcinoma may show histologic and immunohistochemical features that are similar to those of neuroblastoma. If so, our patient would have been given a more dismal prognosis and would not have received cranioaxial irradiation.

This report describes the first case of a cerebellar neuroblastoma in an elderly patient. Because ultrastructural study of the tumor was required to confirm the diagnosis and because this entity is not considered in the differential diagnosis of cerebellar tumors occurring in adults, it is likely that similar cases previously have gone unrecognized. The reserving of tissue for electron microscopy on all brain tumors allows ultrastructural examination to be performed on those tumors with an unusual histologic appearance. By more accurate subclassification of these central nervous system tumors, potential differences in prognosis and response to therapy may be elucidated.

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