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Short Original Communication

Pineoblastoma with Ganglionic and Glial Differentiation

Report of Two Cases

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Summary. Two cases of pineoblastoma in infants are reported. Both cases exhibited ganglionic and astrocytic differentiation, and one case also showed retinoblastomatous features. Divergent differentiation has been frequently reported in pineocytomas, but ganglionic and glial features in the highly malignant primitive pineoblastoma are unusual. These cases extend the concept of pineoblastoma and further confirm the differentiating potential of primary pineal parenchymal neoplasms.

Key words: Pineal – Pinealoma

Introduction

Recent reviews of pineal parenchymal neoplasms have discussed their separation into the categories of pineocytoma and pineoblastoma and their cytological differentiating potential [1, 3, 6, 8, 11]. Pineoblastomas are tumors predominantly of young people, similar to the medulloblastoma-neuroblastoma group of neoplasms, characterized by rapid growth and cerebrospinal fluid dissemination. These tumors have shown melanin production, retinoblastomatous foci, and a mosaic pattern, reminiscent of the fetal pineal gland [1, 6, 12]. Pineocytomas have been observed primarily in older age groups, show less tendency toward dissemination, and frequently show divergent glial and neuronal differentiation [3, 6, 9, 11].

We wish to report the following cases which combine typical features of pineoblastoma with differentiation into neuronal and glial lines, thereby expanding the clinicopathological entity of pineoblastoma.

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Case Reports

Case 1

An 18-month-old male infant was admitted to the University of California Davis Medical Center for evaluation of persistent vomiting, ataxia, and difficulty walking of several weeks duration. Examination revealed a large head circumference (49.8 cm), splitting of the sagittal and coronal sutures, and blurring of the right optic disc. A computerized tomography (CT) scan showed hydrocephalus, and a mass in the posterior third ventricle. An Ommaya reservoir and ventricular shunt were placed, and a transventricular biopsy was performed. He received 5,000 rad craniospinal radiation and two courses of vincristine and lomustine (CCNU). He developed lethargy, anorexia, and was unable to walk. Terminally, he developed meningismus and dehydration, and died 6 months after diagnosis.

The surgical biopsy specimen consisted of sheets of tightly packed primitive cells with round to spindle-shaped, densely basophilic nuclei and many mitotic figures (Fig. 1a). No definite rosettes or evidence of maturation was present, and electron microscopy on the biopsy material revealed only immature cells, having few cytoplasmic organelles, scattered intermediate cell to cell junctions, and showing no differentiating features, as have been reported [5, 7, 9, 10].

The general autopsy findings included cachexia and bronchopneumonia. A large, shaggy, hemorrhagic mass was present in the pineal region and cerebellar vermis. It extended into the right lateral ventricle and into the right cerebellar hemisphere (Fig. 2). The tumor was mostly yellow-tan and soft, but there were foci of increased firmness and gray coloration. The lateral and third ventricles were dilated, the fourth ventricle was obscured, and there was a large cavum septi pellucidi. A metastatic deposit was present on the dura of the posterior fossa, and multiple deposits were present in the spinal cord leptomeninges.

Histologically, the tumor showed abundant hemorrhage and necrosis with focal calcification. The predominant tumor cells were arranged in lobules with a thin connective tissue framework and the nuclei were more vesicular than in the surgical specimen (Fig. 1b). Positive staining of tumor cell cytoplasm using the Achúcarro-Hortega impregnation technique for paraffin-embedded tissue [2, 6] confirmed the pineal parenchymal nature of the tumor cells (Fig. 3a, b).

There were multiple less cellular foci which corresponded to the areas of gray firm tissue observed grossly, both in the central portion of the tumor and in the leptomeningeal deposits. These contained bizarre astrocytic and ganglionic cells and a delicate fibrillary background. Astrocytic differentiation was confirmed using the peroxidase-antiperoxidase immunohistochemical method for glial fibrillary acidic protein [4] (Fig. 3c). Neuronal differentiation was

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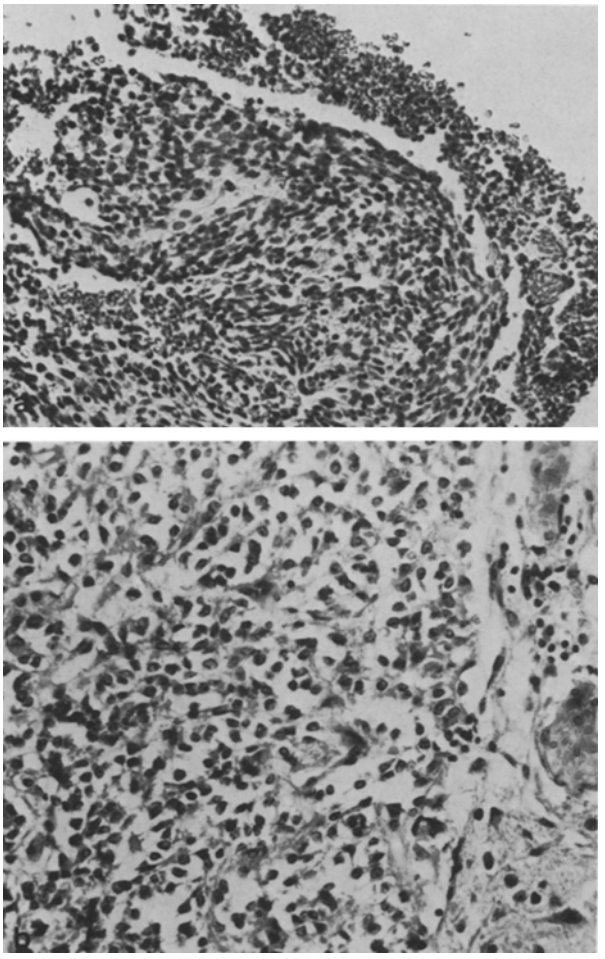

Fig. 1a, b. Case 1. **a** Surgical specimen with undifferentiated tumor cells. HE ×192. **b** Autopsy specimen with "pineocytomatous" appearance. HE ×192

confirmed using cresyl violet Nissl and Bielschowsky silver impregnation (Fig. 4) on paraffin-embedded sections. These foci were clearly separable on the basis of unusual morphology and leptomeningeal location from entrapped normal neurons and glia.

Case 2

A 21-month-old Portuguese male infant presented with acute ataxia and an enlarged head size. Physical examination revealed an occipital frontal circumference of greater than the 95th percentile, bilateral papilledema, and truncal and limb ataxia. CT scan showed hydrocephalus and a central enhancing lesion involving the midbrain and third ventricle. He was treated with a ventriculoperitoneal shunt and 4,000 rad of irradiation to the cranium. He was readmitted 4 months later in status epilepticus and was treated, but became comatose and died. A CT scan on return showed diminution in tumor size, but prominent involvement of the leptomeninges.

At autopsy (examination limited to the head), there were thickened leptomeninges and a grayish-brown tumor in the pineal region which was well demarcated, focally softened, and contained visible and palpable flecks of calcium. The floor of the third ventricle bulged outward and the pineal gland could not be identified. The cerebellum was free of tumor.

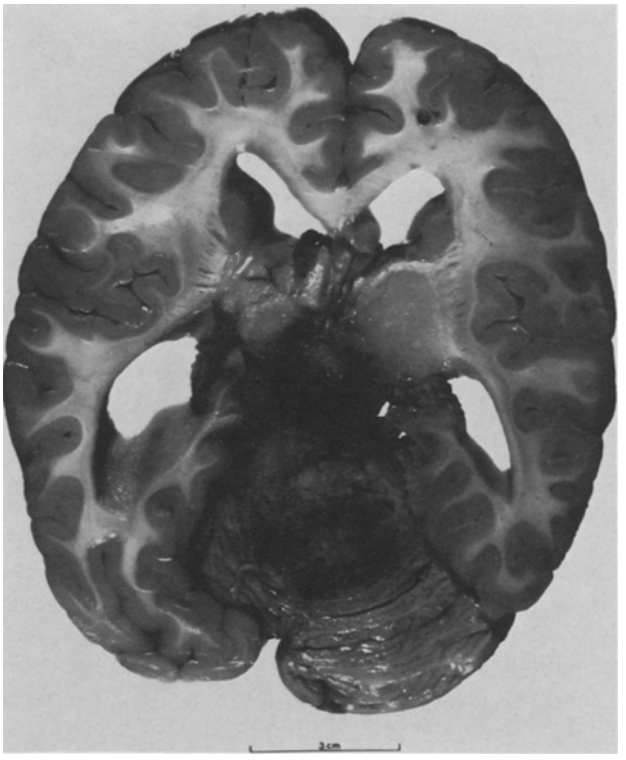

Fig. 2. Case 1. CT scan plane section of pineal and cerebellar tumor

Microscopically, there were sheets of primitive cells, interspersed by foci of calcification, and disseminated throughout the subarachnoid space. Some cells had club-shaped cytoplasmic processes, and there were occasional mitotic figures. There were many Flexner-Wintersteiner rosettes and "fleurettes" (Fig. 5a). In the peripheral portions of the tumor, there were foci of mature ganglion cells (Fig. 5b), some of which were multinucleated and had large amounts of cytoplasm. Astrocytic differentiation was also present.

Discussion

The diagnosis of primary pineal neoplasm in these infants was based upon the anatomic location of the bulk of tumor, and, in case 1, the modified silver carbonate method for pineal parenchymal cells. These neoplasms behaved similarly, showing extensive invasion and dissemination through the cerebrospinal fluid pathways. The predominant histological pattern in both was of undifferentiated small cells. On clinical and pathologic grounds, these tumors represent pineoblastomas.

The multipotential differentiation of pineal parenchymal tumors is well known [3, 6, 9, 11], but most of these examples have occurred in older patients with pineocytomas. Differentiation in pineoblastomas along retinobastomatous lines, as demonstrated in case 2, is uncommon, but has also been reported [6, 12].

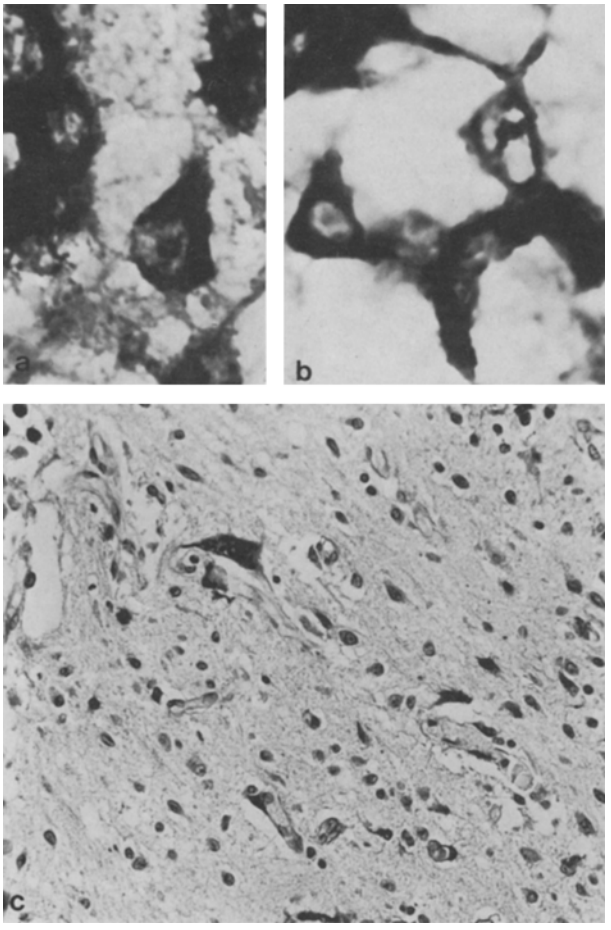

Fig. 3a—c. Case 1. **a, b** Argyrophilic rim of cytoplasm in tumor cells. Silver carbonate impregnation for pineal parenchymal cells, × 1,130. **c** Pericapillary astrocytic cells, having positive reaction of immunoperoxidase stain for glial fibrillary acidic protein. Immunoperoxidase stain with hematoxylin, × 180

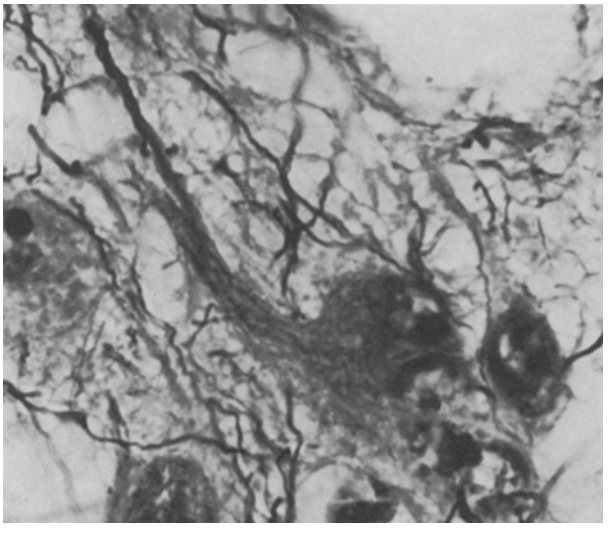

Fig. 4. Case 1. Neuronal differentiation with argyrophilic fibrils extending from neuronal cell. Bielschowsky silver impregnation, × 1,180

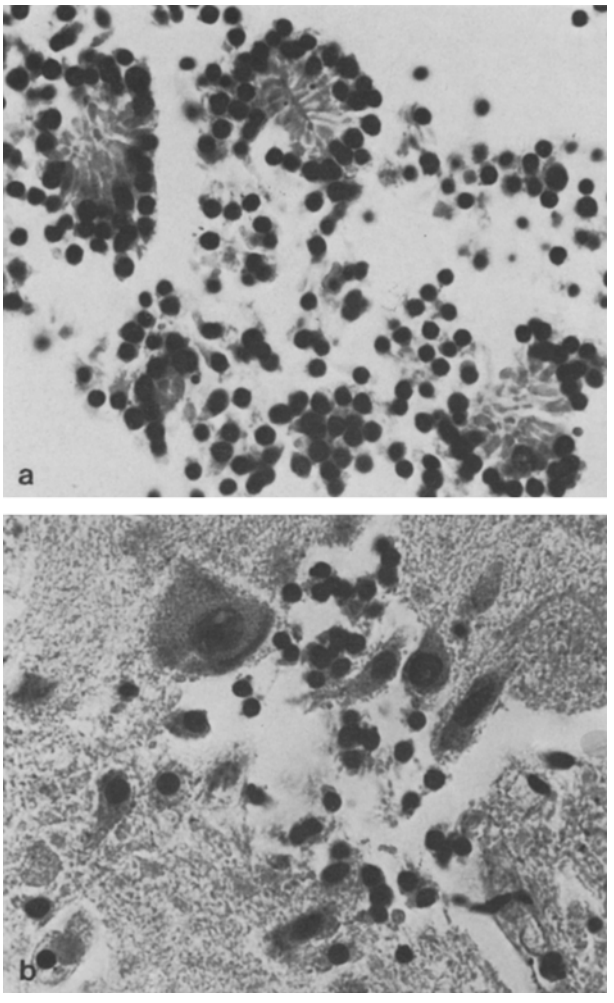

Fig. 5a, b. Case 2. **a** Retinoblastomatous differentiation (fleurettes) and undifferentiated tumor cells. HE × 480. **b** Neuronal differentiation. HE × 480

The possible role of therapy in indirectly facilitating differentiation is suggested by these cases. The tumor cell population in the biopsy in case 1 was undifferentiated, precluding a definitive diagnosis on the basis of light and electron microscopy. At autopsy, following radiation and chemotherapy, the small cell population was inconspicuous, and most of the tumor cells had a pineocytomatous appearance, as well as distinct ganglionic and glial foci. Perhaps, the small cell population was more sensitive to therapy and cells with more differentiating potential proliferated.

In summary, these cases which are clinically and pathologically characteristic of pineoblastomas illustrate the multipotential differentiating capacity of primary pineal neoplasms, heretofore considered to be characteristic of pineocytomas.

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