Review of Pineal Anlage Tumor With Divergent Histology

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- Pineal anlage tumor is an extremely rare tumor that is not listed in the 2000 World Health Organization Classification of nervous system tumors. It has been defined as a primary pineal tumor with both neuroepithelial and ectomesenchymal differentiation and without endodermal differentiation. We review the literature on this tumor, including the clinical presentation, gross pathology, histopathology, immunohistochemistry, differential diagnosis, and prognosis.

(Arch Pathol Lab Med. 2006;130:1233–1235)

The term pineal anlage tumor was chosen by Schmidbauer et al1 to describe histologically divergent primary pineal tumors. Pineal anlage tumor is an extremely rare tumor that is not listed in the 2000 World Health Organization (WHO) Classification of nervous system tumors.2 It has been defined as a primary pineal tumor with both neuroepithelial and ectomesenchymal differentiation and without endodermal differentiation.

The pineal gland is an encapsulated structure near the center of the brain. It is in an extra-axial location, which makes it more amenable to surgical resection. A pineal mass usually presents with headache and hydrocephalus. Hydrocephalus can worsen and produce nausea, vomiting, obnubilation, cognitive impairment, papilledema, and ataxia. Rarely, these symptoms will present abruptly due to hemorrhage into a pineal tumor (pineal apoplexy). The clinical differential diagnosis of a pineal mass includes a pineal cyst, germ cell tumors, pilocytic astrocytoma, and pineal parenchymal tumor.

The mature pineal gland is composed of well-differentiated pinealocytes that are surrounded by astrocytes. These cells are divided into lobules that are separated by connective tissue. Endothelial cells provide blood flow, and sympathetic nerves innervate the pinealocytes.3 The human fetal pineal gland contains epithelial cells that have abundant melanin, which decreases after birth. The function and reason for the transient appearance of melanin is unknown. A pineal tumor that contains melanin is consistent with a pineal origin and indicates the potential for neuroectodermal differentiation.4 A primary tumor can show a wide variety of differentiation, just as an embryonic pineal cell can differentiate into striated muscle, pigmented epithelium, and neuronal cells.5 The pineal gland functions as a neurosensory photoreceptor organ in fish and amphibians. Transient photoreceptor differentiation occurs in the fetus and neonates of lower animals. Divergent differentiation in a pineal parenchymal tumor may represent the recapitulated development of lower species.6

The 2000 WHO classification of pineal parenchymal tumors lists 3 categories: pineoblastoma, pineocytoma, and pineal parenchymal tumor of intermediate differentiation. Pineoblastomas have highly cellular, patternless sheets of small blue cells. They may have Homer Wright and/or Flexner-Wintersteiner rosettes. They are highly aggressive WHO grade IV tumors with a poor prognosis. Pineocytomas are well-differentiated tumors with small, homogenous, well-differentiated cells. These grow in sheets and can also form large pineocytomatous rosettes. These are WHO grade II tumors with a better prognosis. Pineal parenchymal tumors of intermediate differentiation are highly cellular and have mild nuclear atypia with occasional mitotic figures. Pineocytomatous rosettes are absent, and metastasis is uncommon in a pineal parenchymal tumor of intermediate differentiation. A WHO grade has not yet been assigned to pineal parenchymal tumor of intermediate differentiation.

A pineal anlage tumor is a primary pineal parenchymal tumor with both neuroepithelial and ectomesenchymal (heterologous) differentiation. Only a few cases of similar tumors have been reported.1,5,7,8 The neuroepithelial differentiation can include neuronal, glial, and retinal elements. Pigment, as well as Homer Wright and Flexner-Wintersteiner rosettes, may be present. Ectomesenchymal differentiation typically includes striated muscle, rhabdomyoblasts, and cartilage formation.1 Immuno-staining patterns in other cases are reported to be typical of different well-differentiated tissue components. Cytokeratin stains are negative.1,5,7,8 Retinal S-antigen positivity has been interpreted as evidence of retinal differentiation.8 Cytogenetic and electron microscopic reports were not found in the literature. We saw a case of a 9-month-old boy who presented with pineal anlage tumor without cerebrospinal fluid or spinal metastases. The resection specimen was an aggregate of brownish tan soft tissue fragments, with black cut surfaces and focal white nodules. Histologic sections had an extremely variable appearance. Prominent areas of primitive cells with hyperchromatic nuclei and scant...
cytoplasm were present (Figure 1). In addition, some of the cells contained melanin and were embedded in a chondroid matrix (Figure 2). Both Homer Wright and Flexner-Wintersteiner rosettes were present. Differentiation into more mature ganglionic tissue was also seen (Figures 3 and 4). No rhabdomyoblasts, striated muscle cells, or pineocytomatous rosettes were present. The MIB-1 index of the primitive cell area was 8%, whereas the remaining tissue had a MIB-1 index of less than 1%. Another reported case also had cartilage formation without muscle differentiation.7

Pineal anlage tumors are histologically similar to retinal anlage tumors of the jaw.8 Although a retinal anlage tumor is a locally aggressive tumor,4 some pineal anlage tumors have been reported to be highly malignant, with a fatal outcome occurring in less than 9 months.1,7 This is similar to the prognosis of pineoblastomas.2 Due to the difference in prognosis between retinal anlage tumors and some aggressive pineal anlage tumors, the term pineal anlage tumor has generated some controversy.5

The histologic differential diagnosis for this heterogeneous tumor includes pineal anlage tumor, teratoma, ectomesenchymoma, melanotic neuroectodermal tumor of infancy, and medulomyoblastoma. The typical pineal anlage tumor contains pigmented epithelium, ganglion cells, neuroblasts, glia, cartilage, striated muscle, and rhabdomyoblasts. A teratoma includes all of these elements as well as Schwann cells and endodermal differentiation. An ectomesenchymoma is considered to be a rhabdomyosarcoma with neural differentiation. It has rhabdomyoblasts, Schwann cells, ganglion cells, neuroblasts, and pigmented epithelium. A melanotic neuroectodermal tumor of infancy consists of pigmented epithelium, neuroblasts, and glia. A medulomyoblastoma is a variant of medulloblastoma that exhibits muscle differentiation. It contains neuroblasts, rhabdomyoblasts, and striated muscle.5
In the past, when immunohistochemistry was more limited, only histologic features were available to assess pineal parenchymal tumor prognosis. Of these, neuronal differentiation was reported to be favorable, as noted in a recent study. Further, necrosis and greater than 6 mitoses per 10 high-power fields were associated with a poorer outcome. In another study, MIB-1 (Ki-67) was used to assess the proliferative potential of these tumors and its correlation with histologic features. Eleven pineal parenchymal tumors with divergent differentiation were assessed. A good correlation was found between neuronal differentiation (synaptophysin and neurofilament protein staining) and low MIB-1 indices. MIB-1 reactivity was noted to be lower in cases with pineocytomatous rosettes, but this was not statistically significant. High MIB-1 indices (8.67 ± 1.95) were associated with leptomeningeal seeding and a poor prognosis. Lower MIB-1 indices (1.52 ± 0.86) were associated with no metastatic tumor. Surgical resection has a significant impact on the prognosis of all types of pineal tumors, with the exception of germinomas, which are highly responsive to radiation.

References