**Case reports**

**Malignant melanotic neuroectodermal tumor arising from the pineal body**

A. Ogata 1, Y. Fujioka 1, K. Nagashima 1, K. Tashiro 2, T. Aida 3, and H. Abe 3

Departments of 1 Pathology, 2 Neurology and 3 Neurosurgery; Hokkaido University School of Medicine, N-15, W-7, Kita-ku, Sapporo 060, Japan

**Summary.** A case of a melanotic neuroectodermal tumor arising from pineal region of a 4-year-old girl is presented. The tumor had spread diffusely to the meninges, consistent with malignant behavior. Histologically, the tumor consisted primarily of epithelial elements arranged in tubules, cords and nests separated by fibrous vascular tissue in addition to a small neuroblastomatous focus. Melanin pigment was frequently observed in the epithelial tumor cells, and melanin-laden macrophages were also often observed. No teratoid elements were found. Immunohistochemically, tumor cells were positive for neuron-specific enolase but were nonreactive for S-100 protein, epithelial membrane antigen, glial fibrillary acidic protein, vimentin, a-fetoprotein and human chorionic gonadotrophin. Ultrastructurally, the epithelial nature of the tumor cells could be easily demonstrated. In addition, melanosomes in various stages in maturation were observed, indicating melanogenesis of the tumor. On the basis of the tumor location and the histological similarities previously observed for the fetal pineal body, it is very likely that this melanotic epithelial tumor could have originated from the fetal pineal gland.

**Key words:** Melanotic neuroectodermal tumor – Immunohistochemistry – Ultrastructure – Pineal origin

Melanin formation in intracranial tumors other than malignant melanoma is unusual, but has been found in medulloblastoma [21], meningioma [10], ependymoma [12] and schwannoma [13]. In addition to these, another group of tumors, in which the melanin-containing tumor cells have an epithelial structure and a neuroblastic or medulloblastic component, has been described. This has been categorized as a cerebral form of “melanotic neuroectodermal tumor of infancy (MNTI)” which occurs most frequently in the maxilla [2, 3, 4, 9]. The majority of MNTI affects children who are less than 1 year old [3, 9], and takes a benign course, although a few recurrent cases have been reported [16]. Recent studies have suggested that the neoplasm arises from tissue derived from the neural crest [2, 15, 18, 19]. Intracranial occurrence of this tumor is very rare and we are aware of only eight cases having been reported. They were from the pineal region [1], 3rd ventricle [24], 4th ventricle [23], medulla oblongata [22] and cerebellum [6, 7, 21, 24]. The possible origin of the tumor in the brain has recently been postulated as the fetal pineal body by Dooling et al. [5]. However, there have been only two cases suggestive of a pineal origin [1, 24]. In this report we present evidence for a third case of MNTI arising from the pineal region, supporting the concept of a fetal pineal origin.

**Case report**

A 4-year-old girl was admitted to the Hokkaido University Hospital, with a 1-week history of headache, nausea and vomiting on September 10, 1984. On examination she had weakness of her right arm, a right hemiparetic gait and urinary incontinence. The symptoms progressed rapidly, and the neurological examination 1 month later revealed Parinaud's sign, right hemiparesis, a right Babinski's sign, a right hemisensory disturbance, ataxic gait on the right side and tremors of right upper and lower extremities. Brain CT-scan showed a slight high density mass with contrast enhancement occupying the pineal region, with extension into the left basal ganglia. Hydrocephalus was also noted. Urinary vanillmandelic acid (VMA) and homovanillic acid (HVA) were both within normal limits. Serum a-fetoprotein and human chorionic gonadotrophin were not elevated. No ophthalmological abnormalities were detected. Partial removal of the tumor with shunt placement was performed and the patient received adjuvant chemotherapy and irradiation. A reduction of tumor size was observed, but the patient was readmitted because of back pain and paraplegia of the lower extremities 2 months after discharge. Two months later partial resection of the residual tumor was done with chemotherapy and radiation therapy. The patient is now in good condition for 17 months after our last follow-up.
Fig. 1. Coronal section through the pineal body. A black mass, 5 x 6 cm in size, is seen in the pineal region with invasion of the ventricle and left basal ganglia. Note a few metastatic nodules in the left medial part of the temporal lobe and hippocampus later. Myelography disclosed multiple spinal metastases. She was treated with irradiation to the spinal cord and whole brain, but died after repeated convulsion on October 7, 1985.

Pathological findings

General autopsy showed bronchopneumonia and congestion of both lungs, atrophied adrenal glands and generalized muscular atrophy. The skin, maxilla and visceral organs were free of any lesions.

The brain weighed 1,150 g and showed enlargement of the left cerebral hemisphere. Multiple areas of subarachnoid dissemination were observed as black masses. On coronal section of the brain, a relatively well-demarcated hard and black tumor was found in the pineal region. This extended into the left basal ganglia and measured approximately 5 x 6 x 6 cm (Fig. 1). The pineal body could not be identified macroscopically. Multiple black tumors were found in the cerebellum, brain stem and subarachnoid space of the spinal cord.

Histologically, in a small area of the specimen which had been taken during surgery, there was a neuroblastomatous area (Fig. 2A). No Homer-Wright rosettes were found. The remaining large area and the material taken at autopsy were exclusively composed of pigmented epithelial cells arranged in cords and sheets, and morphologically resembled primitive neural tubules (Fig. 2B). The tubules consisted of high columnar cells with an internal limiting membrane and were separated from adjacent tubules by reticulin fibers and vascular stroma. Brown and black pigmented granules were found in the epithelial cells (Fig. 2C), which stained with Fontana-Masson stain. The pineal gland was replaced by a necrotic tumor mass and fibrous connective tissue.

Immunohistochemically, tumor cells were positive for neuron-specific enolase. They were nonreactive for S-100 protein, glial fibrillary acidic protein, vimentin, neurofilament, α-fetoprotein, and human chorionic gonadotrophin [antibodies used were from DAKO, except for monoclonal antibody to the 200- and 160-kDa subunits of anti-neurofilament (Labsystem)].

Ultrastructurally, tumor cells forming tubules had microvilli in the apical portions of adjoining cells (Fig. 3). Between the cells of the apical portion, zonula occludens were found, occupying 0.1 to 0.3 µm of the boundary. In the lateral cell border, there were zonula adherens, about 200 nm in length. In the cytoplasm there were numerous melanosomes, mitochondria, Golgi apparatus, lysosomes and microtubules. Melanosomes in various stages of maturation were observed (Fig. 4). The stage IV melanosomes were round to oval, 800 nm x 300 nm in size, and had an electron-dense appearance without any intrinsic structures. The stage I melanosomes found were round, homogeneously granular, measuring 300–400 nm x 300 nm. A small number of type II melanosomes with intrinsic parallel narrow beaded rods were detected. The stage III melanosomes, 800 nm x 400 nm were ovoid, often with parallel, densely beaded