Spontaneous Malignant Pineocytoma in a Female Wistar Rat

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Spontaneous tumors of the cranial cavity are infrequently seen in rats with the exception of anterior pituitary tumors [9]. Among them, tumors of the pineal gland are extremely rare, and the spontaneous incidence has been reported to be 0.01–0.44% [1, 3, 5, 8, 10]. There have been several reports in which the light microscopic findings of pineal gland tumors in rats were described. However, no detailed description of the electron microscopic feature has been given, except for two reports [2, 12]. We encountered a malignant tumor originating from parenchymal cells in the pineal gland of a rat and could obtain fresh samples for electron microscopy from it. The present report describes the gross, histological, and ultrastructural features.

This pineal gland tumor occurred in a specific pathogen-free Wistar female rat purchased from the CLEA Japan Inc. This rat was an animal from the control group in a 30-month chronic toxicity/carcinogenicity study of a certain pesticide and was fed a commercial powdered diet and tap water ad libitum. The rat was killed in extremis at 89 weeks of age after showing marked loss of body weight and reddish eye-discharge. At autopsy, the pineal tumor was observed as a hemorrhagic gelatinoid mass, 8 mm in diameter, located dorsally between the cerebral hemispheres and the cerebellum (Fig. 1). The mass was demarcated clearly from the adjacent normal brain tissue. Besides this pineal tumor, the animal had a cyst of the anterior pituitary, atrophy of the liver, spleen, and kidney, and absence of the clitoral gland. For light microscopy, the brain with the pineal tumor was fixed in 10% neutral phosphate-buffered formalin, embedded in paraffin, sectioned at 5 μm, and stained with hematoxylin and eosin. Sections of the tumor were also stained with Wilder's reticulin stain, azocarmine G and aniline blue, and periodic-acid-Schiff reaction. For electron microscopy, a part of the tumor mass was fixed in 2% glutaraldehyde and 1% osmium tetroxide, embedded in Epon 812. Ultrathin sections were stained with uranyl acetate and lead citrate and examined with a transmission electron microscope.

Light microscopically, the tumor mass was well-vascularized and was mostly encapsulated with fibrous connective tissues. The brain tissue neighboring to the tumor tissue was compressed and atrophic. Although there was an infiltration of tumor cells into the meninges, no invasive growth to the brain parenchyma was observed. The tumor was characterized by solid growth of tumor cells with numerous dilated vascular spaces (Fig. 2). Tumor cells were apposed to each other and were often arranged along blood vessels or in lobulated patterns which resembled the normal structure of the endocrine gland. In a silver impregnation, these lobulated structures were furthermore divided by a delicate connective tissue stroma into small clusters or nests. The tumor consisted of two types of cells (Fig. 3). The first cell type was the major component of the tumor and was a large, polyhedral, pale-staining cell with abundant, slightly eosinophilic cytoplasm, a large, lucid, round to oval nucleus, and up to three distinct nucleoli. The nuclei were sometimes pleomorphic and gigantic nuclei were occasionally seen. Mitotic figures were frequently observed in this cell type. The second cell type was a small, dark, polygonal cell having intensely eosinophilic cytoplasm and a hyperchromatic, irregular-shaped nucleus. Hemorrhage and necrosis were common in the area where vascular dilatation was marked. Calcification was prominent in the necrotic foci. In addition to this pineal tumor, the following findings were observed in this rat: foci of

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Fig. 1. Pineal gland tumor at the junction of cerebrum and cerebellum.

Fig. 2. Solid growth of tumor cells with numerous dilated vascular spaces. HE. ×92.
hepatocellular alterations, focal hepatocellular necrosis, increased brown pigmentation of the spleen, epithelial hyperplasia of the urinary bladder, focal hyperplasia of the anterior pituitary, and decreased hematopoiesis of the bone marrow.

Electron microscopically, the tumor was composed of large, electron lucent cells interspersed with small, electron dense cells (Fig. 4). The difference between these two cell types was attributable to the density of cellular components and the morphology of these cells were essentially the same. The tumor cells had abundant cytoplasm containing a large number of free ribosomes, polysomes, and mitochondria. Other organelles such as endoplasmic reticulum and Golgi apparatus were poorly developed. The nuclei of tumor cells were usually round to oval and had a narrow rim of heterochromatin, but often showed prominent invaginations, resulting in irregular profiles. The tumor cells were closely apposed to each other and there were occasional cellular junctions between the cell membranes of the adjacent cells (Fig. 5). They sometimes contained a few dense-cored vesicles, 80–140 nm in diameter, in their cytoplasm, which were considered to be neurosecretory granules (Fig. 6). In intercellular spaces, a small number of collagen fibers were seen. No distinct basal lamina or glandular structure was found in the tumor cells.

The pineal gland in rats is an endocrine organ situated beneath the sinus confluence, and dorsal to the inferior and superior colliculi. This gland is considered to have hormonal influences on the testis, ovary, thyroid, pituitary, and adrenal and to regulate general somatic development [4]. It is mainly composed of pinealocytes (parenchymal cells) secreting melatonin that are arranged in trabecular or acinar pattern, besides glial cells, sympathet-
MALIGNANT PINEOCYTOMA IN A RAT

endoplasmic reticulum, variable amounts of free ribosomes, numerous mitochondria and round to pleomorphic nuclei containing infrequent nucleoli [2]. The morphologic features of our case were similar to those of the reported pineal gland tumors [2, 12], though malignant findings such as pleomorphic tumor cells, increased mitotic figures, hemorrhage, and necrosis were observed frequently in our case. In the normal pineal gland in rats, clear-cored vesicles and dense-cored vesicles ranging in size from about 40–100 nm in diameter are observed in sympathetic noradrenergic nerve fiber endings [6]. Similar, but larger, dense-cored vesicles are occasionally present in the cytoplasm of pinealocytes. These vesicles are one of the neurosecretory granules and the dense-cored vesicles in the pinealocytes are considered to contain melatonin [7].

In the literature of ultrastructural features of rat pineal gland tumors, it has been described that the tumor cells have few uniquely diagnostic features [2]. However, the dense-cored vesicles observed in the tumor cells in our case are quite identical to those in the normal pinealocytes and their presence strongly suggests that the present tumor is derived from neuroendocrine cells. Based on these findings, it was considered to be appropriate to diagnose this tumor as malignant pineocytoma originating from the pineal parenchymal cell. There is a lack of data on the biological behavior of pineal gland tumors in rats, because of their infrequent spontaneous occurrence. Further investigation is needed to elucidate their nature.

REFERENCES


