Gangliocytoma with Immature Neuronal Cell Elements in the Pituitary of a Rat

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ABSTRACT. A spontaneous pituitary gangliocytoma with abundant, immature neuronal cell elements was found incidentally in a 109-week-old female Fischer 344 rat. The pituitary parenchyma was largely occupied by a tumor nodule with necrotic and hemorrhagic foci and cyst. The tumor was composed of mature ganglion-like (M) cells, small immature ganglion (I) cells and transitional (T) cells, with a fibrillar matrix. The I and T cells were intermingled with the M cells or were arranged in compact clusters, in which the I cells formed perivascular rosette-like structures, sometimes with mitotic figures. Immunohistochemically, all types of tumor cells were positive for neuron-specific enolase, and only the M cells was positive for chromogranin A. This result may be correlated with the degree of cytodifferentiation. — KEY WORDS: gangliocytoma, immature neuronal cell, rat pituitary.

Fig. 1. Pituitary with gangliocytoma and cyst (asterisk). The anterior lobe is compressed at the periphery (arrows). HE stain. ×15.
distribution and with a loosely arranged fibrillar matrix (Fig. 2a). The ganglion-like cells were pyramidal in shape, which contain eccentrically located large, round, pale nuclei with one or two prominent nucleoli (Fig. 2a). Binucleated cells were also observed (Fig. 2b). The cytoplasm was abundant and eosinophilic to weakly basophilic. In some of the large ganglion-like cells, a pale staining area was seen adjacent to the nucleus (Fig. 2a), and Nissl substance was demonstrated at the margin in the cytoplasm (arrowheads). Binucleated cells are occasionally observed (double-arrow). Nissl stain. × 500.

Short fusiform or wedge-shaped small cells were also present in the nodule. They had small, round, relatively pale nuclei and scant basophilic cytoplasm. Nissl substance was inconspicuous. These small cells were intermingled with ganglion-like cells or were arranged in compact clusters (Fig. 3). Mitotic figures were sometimes observed in the small cells. Transitional cells between the large ganglion-like cells and the small cells were abundantly present throughout the nodule. The quantity of Nissl substance was various among the transitional cells. Although no distinctive rosette formation was observed, perivascular rosette-like structures were occasionally found (Fig. 3).

All types of tumor cells were positive for NSE (Fig. 4), but the staining intensity varied among the same types of cells. The apparent ganglion-like cells showed positive reactivity for chromogranin A (Fig. 5). The immunoreactivity for small and transitional types of cells...
was negative or very weak for chromogranin A. The other antibodies showed negative immunoreactivity in the tumor cells.

The tumor did not invade the extra-pituitary region, and there were no neuronal tumors present in other organs or tissues, including cranial ganglia.

In laboratory animals, neuronal tumors are classified into four categories, namely, gangliocytomas, gangliogliomas, ganglioneuroblastomas, and neuroblastomas [13]. Each tumor is defined as follows: neuroblastomas are composed of small undifferentiated cells with characteristic rosettes; gangliocytomas contain more differentiated neuronal elements, and ganglioneuromas are the peripheral counterpart of the gangliocytomas; gangliogliomas involve the neoplastic glial elements in addition to neoplastic neuronal cells [9], and ganglioneuroblastomas have all intermediate levels of differentiation between pure neuroblastomas and ganglioneuromas [3].

In rats, except for the adrenals, only a few cases of mature ganglioneuromas have been reported in the pituitary [8] or the cranial ganglion [5]. However, to our knowledge, there is no report of pituitary gangliocytoma containing a large number of immature neuronal cell elements.

In gangliocytomas (ganglioneuromas), some unique findings such as a pale staining area adjacent to the nucleus [12], marginal demonstration of Nissl substance [2, 12], and binucleated appearance [2, 7] are frequently observed. These are not found in normal neuronal cells. Also, Nissl substance is often meager and satellite cells are usually absent in ganglioneuroma [7]. In the human cases, mitotically active neoplastic cells are not seen, although smaller neurons are sometimes admixed [2]. All of the findings described above were observed in the present case. In addition, necrotic and hemorrhagic foci were seen in the nodule. Therefore, the present case may differ from typical gangliocytomas.

NSE is considered as one of the most useful markers for the diagnosis of neuroblastomas and other neuronal tumors [16]. In the present case, all types of tumor cells, such as ganglion-like cells, small immature cells and their intermediate cells, were positive for NSE. This result may suggest that our case is neuronal in origin, although the staining specificity of NSE in rodents is not established.

Chromogranin A is one of the acidic glycoproteins and is contained in the neurosecretory granules of the adrenal medullary parenchymal cells [15]. The identical glycoprotein is present in other endocrine tissues, including sympathetic ganglia and specific neurons [15]. Positive immunoreactivity to anti-chromogranin A antibody was observed in ganglion-like cells, while small and transitional cells showed negative or very weak reactivity. Therefore, the detection of this glycoprotein in our case might be correlated with the degree of cytodifferentiation.

Although NF is highly specific for neurons and neuronal tumors in humans [1], it was not demonstrated in any tumor cells of the present case. Negative results have been
reported in some human cases of gangliogliomas [4] and a canine case of gangliocytoma [10]. The development of filament protein might be insufficient to detect with the antibody used in the present study, or the negative reactivity might be due to tissue processing limitations [14]. In our case, synaptophysin was also negative. The localization of synaptophysin in tumor cells is apparently more indicative of endocrine cell origin than that of chromogranin [15], but the cause of our negative result remains unknown.

The negative results for S-100 protein and GFAP suggest that this tumor was composed of a single cell type without glial or other mesenchymal elements.

According to several findings described above, we diagnosed this tumor as gangliocytoma of the pituitary, although the exact site of origin was unclear. The most interesting finding is the admixture of abundant, immature neuronal cell elements with mitotic activity. This feature is reminiscent of ganglioneuroblastomas.

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REFERENCES