Pituicytoma: Primary Astrocytic Tumor of the Pars Nervosa in Aging Fischer 344 Rats

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ABSTRACT

We describe 2 cases of a relatively rare tumor diagnosed as pituicytoma in the pars nervosa of rat pituitary. This tumor was spontaneously noted in one 110-week-old female and one 109-week-old male Fischer 344 (F344)/DuCrj rats during 2-year carcinogenicity studies. Although no gross abnormality of the pituitary was detected in the female rat, whitish discoloration and enlargement of the pituitary were observed in the male. Histopathologically, neoplastic cells in both animals possessed pale eosinophilic, often abundant irregular cytoplasm with nuclei of variable size. The tumor cells were arranged in the spindle or sheet cell pattern with indistinct cell boundaries and showed compression or invading proliferation of surrounding tissues. Prominent pleomorphism of the cells was noted in the tumor in the female rat, and mitotic figures were detected in several portions of the tumor in the male rat. Small-sized cells having scanty cytoplasm with deeply staining nuclei seen in the mass were suspected to be microglia. Moreover, isolated single native pars distalis cells were distributed throughout the tumor masses. Immunohistochemically, cytoplasmic foot process of the tumor cells showed a positive immunoreactivity for glial fibrillary acidic protein. On the basis of morphologic characteristics and glial fibrillary acidic protein staining, this tumor is consistent with astrocytoma.

Keywords. Pituitary; pars nervosa; astrocytoma; neurohypophysis; glial fibrillary acidic protein (GFAP)

INTRODUCTION

Intrinsic tumors of the neurohypophysis in rats include pituicytoma (astrocytoma arising from the neurohypophysis), ganglioneuroma, and craniopharyngiomas. All of these neoplasms are extremely rare within the pituitary. Pituicytoma are believed to originate from native glial cells known as pituicytes in the pars nervosa (6, 11). The term “pituicytoma” has been used as a generic term of a variety of intrinsic neurohypophyseal tumors (6, 7). Recently, the term pituicytoma has been used to indicate only astrocytomas in the pituitary pars nervosa (2, 4, 6). In humans, pituicytoma has been reported to show the histological appearance of a pilocytic astrocytoma that is a distinctive glioma variant (4, 8, 9, 11). In rats, because much less information is available on pituicytoma (2), detailed description of its morphological features are lacking. The present communication illustrates 2 cases diagnosed as pituicytoma in aging Fischer 344 (F344) rats.

At necropsy, the pituitary was carefully removed from the sphenoid bone, fixed in 10% neutral buffered formalin, embedded in paraffin wax, cut at 4 μm in thickness, and stained with hematoxylin and eosin (H&E). Additionally, the pituitary from the second animal, the male, was immunohistochemically stained with glial fibrillary acidic protein antibody (GFAP; DAKO Japan Co Ltd, Kyoto, Japan), a marker of astroglia. The pituitary tumors observed in this report were considered to be spontaneous neoplasms unrelated to treatment with chemicals.

REPORT OF THE CASES

Case 1

A pituitary tumor of the pars nervosa in a 110-week-old female F344 rat (F344/DuCrj; Charles River Japan Inc, Yokohama, Japan) was noted among approximately 1,700 rats used as control and treated animals in 2-year carcinogenicity studies conducted by the Daiichi Pharmaceutical Co Ltd (Tokyo). The animal showed no clinical signs and external abnormalities until scheduled necropsy. Although no gross change of the pituitary was detected, an unencapsulated tumor mass was microscopically observed in the pars distalis (Figure 1). The tumor mass consisted of chromophobic to slightly eosinophilic, elongated sheet cells with blood-filled spaces. The mass elicited minimal compression and invasion of the adjacent pars distalis, and its margin was irregular. The junction between the neoplastic lesions and the pars nervosa or pars intermedia was unclear. Closely packed, irregularly shaped large spindle cells with indistinct cell borders were arranged in sheets. Some tumor cells had fibrillary cytoplasm with foot processes and elongated or oval to round nuclei (Figure 2). Pleomorphism of the cells was noted. Small-sized cells having scant cytoplasm with deeply staining nuclei seen in the mass were suspected to be microglia. Additionally, isolated single native pars distalis cells without any change were distributed throughout the tumor mass. Tumor cell invasion into the adjacent pars distalis was evident.
FIGURE 1.—Pituicytoma of a female F344 rat. Tumor is slightly compressing and invading native parenchyma of the pars distalis. Angiectasis (vascular lake) and sinusoidal pattern are prominent. H&E. ×75.

FIGURE 2.—Pituicytoma of a female F344 rat. A cystic or pseudo-gland is surrounded by sheets of pituicytes with abundant cytoplasm and irregular to oval vesicular nuclei. Native pars distalis cell (arrows) and microglial cells (arrowheads) are seen. H&E. ×300.

FIGURE 3.—Pituicytoma of a male F344 rat. Pseudopalisading of tumor cells around the vein (perivascular arrangement) is noted (arrow). H&E. ×120.

FIGURE 4.—Pituicytoma of a male F344 rat. Sheet of pituicytes with abundant eosinophilic cytoplasm and round to ovoid nuclei are observed. Native pars distalis cells (arrows) and microglial cells (arrowheads) are seen. H&E. ×150.

FIGURE 5.—Immunostaining with glial fibrillary acidic protein (GFAP) in pituicytoma of a male F344 rat. The cytoplasm of tumor cells positively reacts with GFAP antibody. Mitotic figure is noted (arrow). Immunostaining for GFAP ×300.
Case 2

A pituitary tumor of the pars nervosa in a 109-week-old male F344 rat (F344/DuCrj; Charles River Japan Inc) was seen among the 7,800 rats used as control and treated animals in 2-year carcinogenicity studies conducted at the An-Pyo Center (Shizuoka). The animal became moribund and was euthanized by exsanguination at week 104. Clinical signs were attributed to severe chronic progressive nephropathy. Macroscopically, the pituitary displayed whitish discoloration and enlargement (8 × 7 mm). Histopathologically, large tumor cells exhibited pale eosinophilic, irregular cytoplasm with variable-sized nuclei. They were arranged in sheets with indistinct cell boundaries and capillary formation. Pseudopalisading of the tumor cells around the vein (perivascular arrangement) was seen (Figure 3), and nucleoli were conspicuous. Mitotic figures were sporadically detected in the tumor mass. The cell population was uniform, with scant pleomorphism. Small cells with deeply staining nuclei had the appearance of microglia and were considered to have originated from the central nervous system. In addition, a few native pars distalis cells were sparsely distributed in tumor mass (Figure 4). These cells had almost the same shape as normal eosinophilic cells in the pars distalis. The immunohistochemical staining with GFAP antibody showed a positive immunoreactivity of cytoplasm of the tumor cells, whereas the microglial and native pars distalis cells had a negative immunoreactivity (Figure 5). This finding implied that the tumor cells had an astroglial origin.

The aforementioned findings in the 2 cases differed from tumors usually seen in the pars distalis or pars intermedia and closely resembled astrocytomas in other regions of the central nervous system, such as the brain. The absence of neoplastic cells in the ventral hypothalamus adjacent to the pituitary stalk suggested that the tumors had arisen from the pituitary, and the glial cell appearance of the tumors led to the diagnosis of pituicytoma in the pars nervosa.

**DISCUSSION**

Pituicytomas have been reported in various species, including the mouse (13), rat (2), cat (14), dog (10), monkey (3), and human (4, 6–9, 11), and are thought to be primary glial neoplasms in the neurohypophysis. Histopathologically, pituicytomas may be indistinguishable from astrocytomas seen at other sites such as the brain. Bucy (1) first demonstrated that pituicytes resemble astrocytes in the central nervous system and possess foot processes applied to capillary walls. Detailed microscopic findings revealed cytoplasmic glial filaments in pituicytes similar to those seen in astrocytes. According to the report of Liss (5), the pituicytes were classified into 4 groups: bipolar, astrocyte-like, triangular, and glomerular. The bipolar pituicytes represented elongated or oval cells with homogenous or granular cytoplasm. In humans, tumors are formed by one or more different types of pituicytes (6, 10). The pituicytoma described in the present study consisted predominantly of bipolar cells and astrocyte-like cells.

Native pars distalis cells were mixed in the tumor masses, suggesting that pituicytoma showed an invasive growth. On the other hand, microglial cells were observed in the tumor masses, although their source is still unclear. They are distributed ubiquitously throughout the brain and spinal cord, and their main functions are to monitor and sustain neuronal health (12). However, they do not appear usually in the pars distalis (1, 5).

In a previous description of rat pituicytoma, a circumscribed, nonencapsulated mass causing compression of the pars distalis has been reported (2). The tumor consisted of closely packed, small spindle cells arranged in indistinct cords and interlacing bundles. Multiple foci of mineralization were detected (2). Moreover, mitotic figures were not detected in pituicytomas or not mentioned in cases reported for several species (2–4, 6–11, 13, 14). Pituicytomas observed in the present investigation contained native pars distalis cells and microglial cells in the mass and by appearance of mitotic figures, depending on tumor proliferation. Although no distant metastasis was observed in either of these 2 cases, the invasive growth pattern and mitotic activity suggest that these pituicytomas were malignant.

**ACKNOWLEDGMENTS**

The authors thank colleagues at the Pathology Laboratory of An-Pyo Center and Drug Safety Research Laboratory of Daiichi Pharmaceutical Co Ltd, for their valuable suggestions and technical cooperation. We also thank Ms H Fujita, the Technology Research Center of Daiichi Pharmaceutical Co Ltd, for her technical assistance.

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