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Toxicol Pathol 2004; 32; 264
DOI: 10.1080/01926230490274326

Toxicologic Pathology, 32:264–268, 2004

ISSN: 0192-6233 print / 1533-1601 online
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A Case Report of a Choroid Plexus Carcinoma Spontaneously Occurring in the Right Lateral Ventricle of a 14-Week-Old, Female Donryu Rat

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ABSTRACT

We encountered a brain tumor arising in the right lateral ventricle of a 14-week-old, female Donryu rat and investigated its histological and immunohistochemical characteristics. Macroscopically, the tumor appeared as a grayish mass with a size of 10 mm in diameter, present in front of the right hemicerebrum and well circumscribed on the cut surface. Histological examination revealed the tumor to be a hypercellular mass occupying the front part of the right lateral ventricle and expanding into the area in front of the hemicerebrum, continuing to the ependymal area at its edge. The tumor was constituted by columnar- or pleomorphic-shaped, highly atypical cells of epithelial origin surrounding fibrovascular cores as single or multiple cell layers. Growth was papillary with high proliferating activity. Immunohistochemically, the tumor cells proved positive for cytokeratin but negative for vimentin, S100 protein or glial fibrillary acidic protein, a profile characteristic for the epithelial cells of the choroid plexus, whereas the ependymal cells were found to be positive for all 4 items. In conclusion, the present tumor was diagnosed as a rat choroid plexus carcinoma, only the third such case to be reported in the world literature, with particular features.

Keywords. Choroid plexus carcinoma; lateral ventricle; Donryu rat; ependymal cell; cytokeratin; vimentin.

INTRODUCTION

Naturally occurring tumors in the central nervous system are rather uncommon in rats (Maekawa et al., 1986; Maekawa and Mitsumori, 1990; Solleveld and Boorman, 1990; Solleveld et al., 1990; Chandra and Frith, 1992; Chandra et al., 1992), and spontaneous choroid plexus tumors are extremely rare (Mohr, 1994). Only 1 benign and 1 malignant choroid plexus tumors in Fischer 344 rats are listed in the database of the National Toxicology Program of the United States (Solleveld and Boorman, 1990). In the other literature, only two choroid plexus papilloma cases (Thompson et al., 1961; Chandra et al., 1992) and one choroid plexus carcinoma case (Pace, 1998) have been reported in Sprague–Dawley or related rats. Furthermore, to our knowledge, there have been no reports of chemical induction of choroid plexus tumors in rats. In our recent research, we encountered a brain tumor suspected to have a choroid plexus origin in a 14-week-old, female Donryu rat. The present paper describes the results of our histological and immunohistochemical assessments of this tumor.

CASE REPORT

Pregnant female Crj:Donryu rats were purchased from Charles River Japan Inc (Kanagawa, Japan). The case was found in 1 of the female offspring delivered from the Donryu rat given nonylphenol, an estrogenic endocrine disrupting chemical, at a daily gavage dose of 100 mg/kg body weight throughout the pregnancy and lactation periods. Rats were housed in plastic cages and kept in an air-conditioned animal room under constant conditions of 24 ± 2°C and 55 ± 10% humidity with a 12-hour light/dark cycle and maintained on basal diet, CRF-1 (Oriental Yeast Inc, Tokyo, Japan) and tap water ad libitum. This animal experiment had been approved by the Animal Experimentation Committee of Sasaki Institute prior to the execution and was conducted under the monitoring by the committee in accordance with the National Institutes of Health Guideline for the Care and Use of Laboratory Animals, Japanese Government Animal Protection and Management Law Number 105 and Japanese Government Notification on Feeding and Safekeeping of Animals Number 6.

The particular animal was euthanized for necropsy at 14 weeks of age because of adoption of a stooping position and apparent hypoactivity. At macroscopic assessment of the whole body, a mass was found in its brain. This was excised, together with the major organs, fixed in 10% neutrally buffered formaldehyde solution and processed routinely for embedding in paraffin. Appropriate numbers of serial sections at a thickness of 4 μm were prepared from each specimen, and one was stained with hematoxylin and eosin for histological examination. The second section of each specimen was stained by the Masson's trichrome method, and the third was used for immunohistochemical assessment for cell proliferating activity using proliferating cell nuclear antigen (PCNA) labeling as a parameter with antibody clone PC10 (Dakocytomation Japan, Kyoto, Japan).

In addition, the cellular nature of the lesion was immunohistochemically assessed and compared with findings for the ependyma and the choroid plexus epithelia

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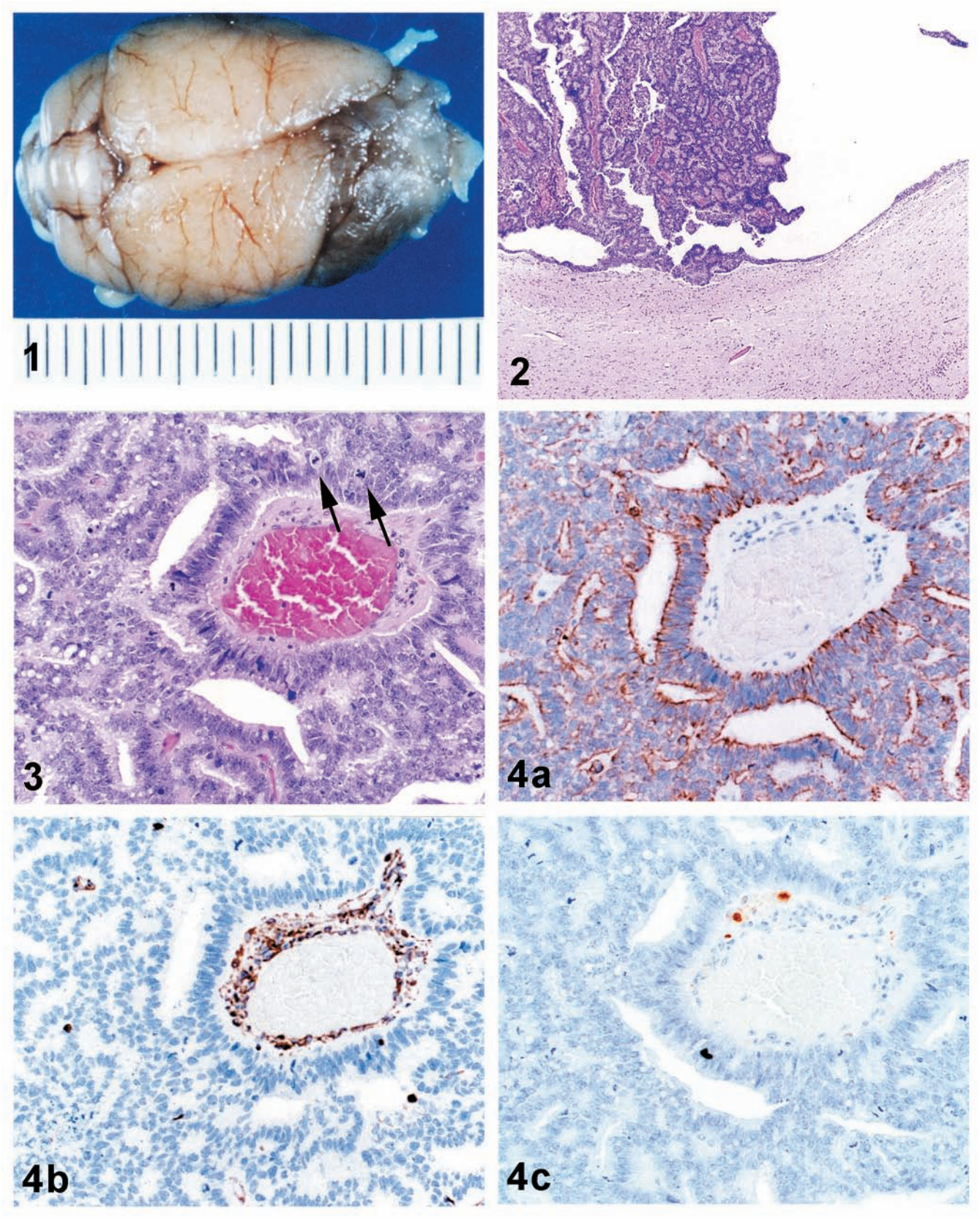


TABLE 1.—Immunohistochemical characteristics of the tumor cells, the epithelial cells of the choroid plexus and the ependymal cells.

Item	Tumor cells	Epithelial cells of the choroid plexus	Ependymal cells
MNF116	+	+	+
Vimentin	−	−	++
S100 protein	−	−	+
GFAP	−	−	±

Symbols used are: −, negative; ±, occasionally positive; +, mostly positive; and ++, generally positive with strong intensity.

in the hind part of the right lateral ventricle using anti-cytokeratin (MNF116; clone MNF116), anti-vimentin (clone V9), anti-S100 protein (rabbit antiserum) and anti-glial fibrillary acidic protein (GFAP; rabbit antiserum) antibodies (all from Dakocytomation). For the immunohistochemical staining, sections were incubated with anti-PCNA antibody (1:100), anti-cytokeratin antibody (1:100), anti-vimentin antibody (1:50), anti-S100 protein antibody (1:400) or anti-GFAP antibody (1:100) at 4°C overnight and then processed according to the manufacturer's instructions for the labeled polymer method (for PCNA, MNF116 and vimentin using an Envision Plus kit of Dakocytomation) or the labeled streptavidin biotin method (for S100 protein and GFAP using a LSAB-2 kit of Dakocytomation). The sections were then counterstained with hematoxylin.

The tumor mass in front of the right hemicerebrum was grayish in color and measured 10 mm in diameter (Figure 1). It was well circumscribed at a cross section, and no other macroscopic abnormalities were detected. Histological examination revealed the tumor to be a hypercellular mass occupying the front part of the right lateral ventricle and expanding into the area in front of the hemicerebrum, continuing to the ependymal area at its edge (Figure 2). The tumor compressed the adjacent brain tissue and invaded the surrounding non-tumoral tissue. The tumor consisted of columnar- or pleomorphic-shaped, highly atypical cells with round to oval nuclei and abundant eosinophilic cytoplasm (Figure 3). Each nucleus possessed one obvious nucleolus and scattered chromatin. The tumor cells grew in papillary formations and exhibited numerous mitotic figures (Figures 2 and 3). High proliferative activity was confirmed by high labeling for PCNA (data not shown). In the hematoxylin and eosin-stained specimens, the tumor cells surrounded fibrovascular cores as single or multiple cell layers (Figures 2 and 3). In the Masson's trichrome-stained specimens, distinct demarcation by collagen fibers was generally observed between the tumoral parenchyma and the vascular component (data not shown). Necrotic foci were scattered in the tumor. No other histological changes worthy of mention were detected in the other assessed organs.

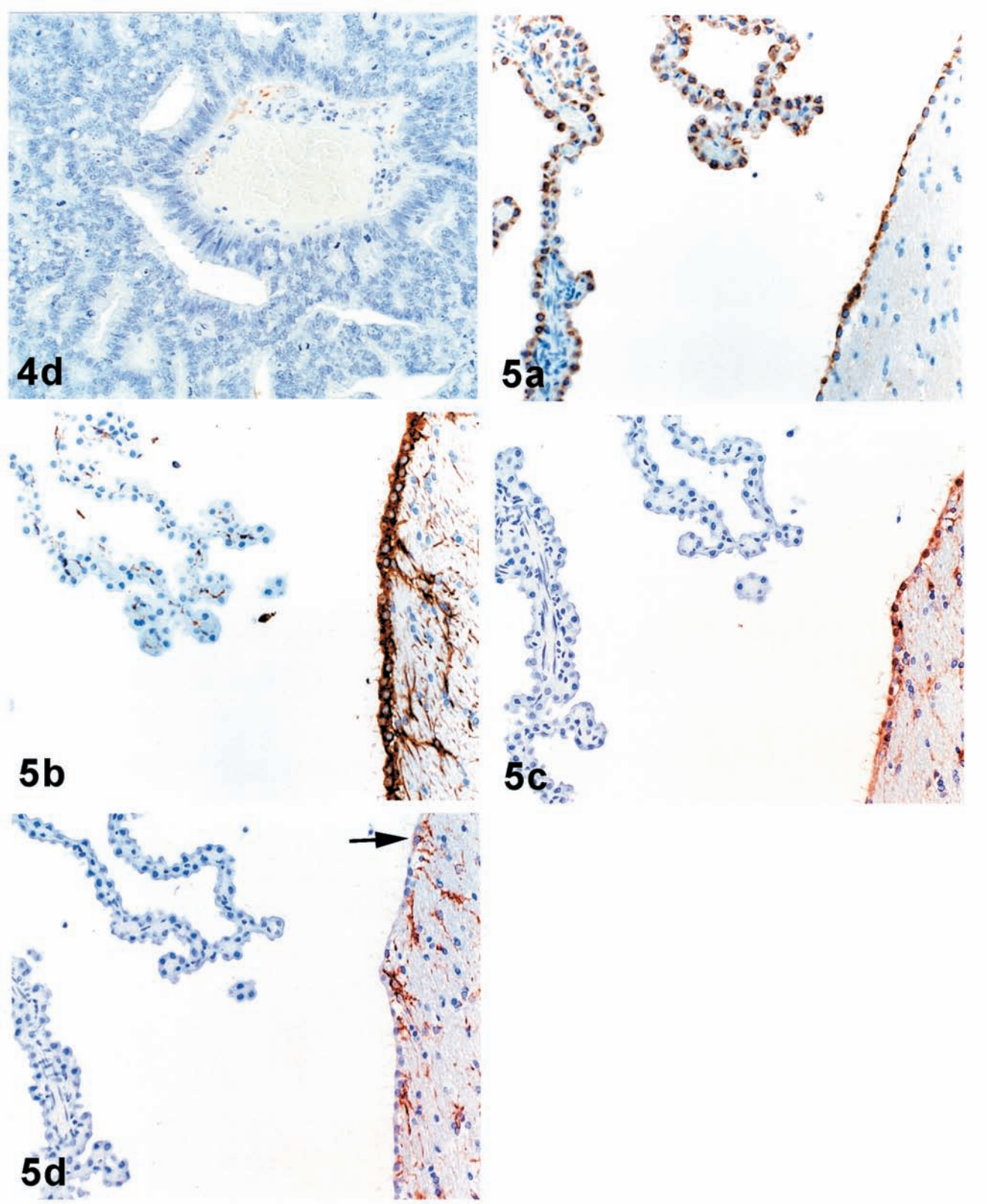
Table 1 summarizes the immunohistochemical characteristics of the tumor cells, the epithelial cells of the choroid plexus and the ependymal cells. The tumor cells (Figure 4a), the epithelial cells of the choroid plexus (Figure 5a) and the ependymal cells (Figure 5a) were all positive for MNF116, an epithelial marker. The tumor cells were negative for vimentin, a mesenchymal marker, (Figure 4b) as well as for S100 protein (Figure 4c) and GFAP (Figure 4d). Similarly the epithelial cells of the choroid plexus were negative for vimentin (Figure 5b), S100 protein (Figure 5c), and GFAP (Figure 5d). In contrast, the ependymal cells were strongly positive for vimentin (Figure 5b), mostly positive for S100 protein (Figure 5c) and occasionally positive for GFAP (Figure 5d).

The above results indicate the epithelial character of the tumor cells in the present case. Considering the location, this tumor could have originated from either the choroid plexus epithelium or the ependyma. The tumor exhibited papillary growth, a histological pattern common in choroid plexus tumors (Mohr, 1994; Solleveld and Zurcher, 1994). The perivascular area contained distinct collagen fibers, and the tumor cells did not appear to make direct connections to the vessels in the present case. With ependymal tumors, in contrast, the presence of a perivascular zone free from tumor cell nuclei with juxtaposition of tumor cells and vessels is one of the characteristic observations (Jänisch, 1990; Jänisch and Schreiber, 1994). Furthermore, the immunohistochemical characteristics of the tumor cells proved identical to those of the choroid plexus epithelial cells, with clear differences from those of the ependymal cells. Most strikingly, neither the tumor cells nor the choroid plexus epithelial cells were positive for vimentin, while the ependymal cells displayed strong staining. It is known that rat ependymoma is characterized by the presence of filaments positively reacting with anti-vimentin antibodies (Solleveld and Boorman, 1990). Also S100 protein- and GFAP-positivity are characteristic for ependymal cells. Atypias of the tumor cells were significant, and proliferative activity was high as evidenced by the mitoses and PCNA immunohistochemistry. Furthermore, the tumor cells invaded the adjacent non-tumoral tissue. A malignant nature was, therefore, apparent. In conclusion, the tumor in the present case was diagnosed as a choroid plexus carcinoma. Many human choroid plexus tumors generally have showed cytokeratin-, vimentin-, and S100 protein-positivity; besides, they have been positive to a lesser extent for GFAP (Kleihues and Cavenee, 2000). The immunohistochemical characteristics with vimentin, S100 protein, and GFAP were different from those of the present case.

Although this tumor was found in a rat exposed to chemical treatment throughout the pregnancy and lactation periods, this was the only case of a brain tumor in 120 animals of the

Figures 1–4c

FIGURE 1.—Macroscopic appearance of the tumor mass in the brain. The mass is present in front of the right hemicerebrum. The scale represents a length of 1 mm. 2.—Histological appearance of the tumor at low magnification. The tumor is present in the space of the cerebrum. The space is located in anatomic site of the right lateral ventricle. Hematoxylin and eosin staining. 3.—Histological appearance of the tumor at high magnification. Single- or multi-layered neoplastic epithelium arranges around fibrovascular core, those components developing papillary formation. The columnar to pleomorphic neoplastic cells possess round to oval nuclei and abundant eosinophilic cytoplasm containing vacuolation frequently. Arrows indicate mitotic figures. Hematoxylin and eosin staining. 4.—Immunohistochemical staining of the tumor for (a) MNF116, (b) vimentin, (c) S100 protein, and (d) GFAP. (a) Almost all of the tumor cells are positive for MNF116. (b) Mesenchymal tissue of the tumor is positive for vimentin, the tumor cells being negative. (c) The tumor cells are negative for S100 protein.



Figures 4d–5

FIGURE 4.—(d) The tumor cells are negative for GFAP. 5.—Immunohistochemical staining of epithelial cells of the choroid plexus and ependymal cells for (a) MNF116, (b) vimentin, (c) S100 protein and (d) GFAP. (a) Normal ependymal cells are positive for MNF116 as well as normal epithelial cells of choroid plexus. (b) Normal ependymal cells are strongly positive for vimentin. Normal epithelial cells of choroid plexus are negative. (c) Cytoplasm and nuclei of ependymal cells are mostly positive for S100 protein. Normal epithelial cells of choroid plexus are negative. (d) A part of normal ependyma is positive for GFAP (Arrow). Normal epithelial cells of choroid plexus are negative.

entire group in the particular study. And furthermore, the maternal treatment with 100 mg/kg nonylphenol by po exerted no influence on female offspring (Yoshida et al., 2003). It is thus suggested that the lesion was spontaneous in nature. The age of the occurrence of the present choroid plexus carcinoma (14 weeks old) was much younger than in the preceding cases (Pace, 1998). The present tumor showed a massive growth pattern with expansion, whereas the preceding cases displayed an infiltrative growth pattern or poor differentiation without infiltrative growth (Solleveld and Boorman, 1990; Pace, 1998). It can thus be stated that this third case of a choroid plexus carcinoma in a rat presented with particular features.

ACKNOWLEDGMENT

The authors would like to express their gratitude to Ms. Hiromi Ichihara-Tokuda for her expert technical assistance.

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