Spontaneously occurring peripheral nerve tumors of rats are infrequent and especially malignant schwannoma in the intracranial trigeminal nerve is rare\(^1\). Experimentally-induced tumors of cranial, spinal, and peripheral nerves have been reported in rats treated with direct-acting alkylating agents (for example, N-nitrosoethylurea, methylmethane sulfonate),\(^2\) and such tumors sporadically with cysts are found in the central and peripheral nerve in rats. However, spontaneous occurrence of intracranial schwannoma with cysts is extremely rare and uncertain. Recently, we encountered with a case of spontaneously occurring malignant cystic schwannoma on the intracranial trigeminal nerve in rats, and will report here on its gross, histological and immunocytochemical characteristics.

A 32-week-old male Crj:Wistar rat (SPF, Charles River, Japan) found in the extreme state of rapid body weight loss, emaciation, unkempt fur, and dyspnea, was euthanized under deep ether anesthesia to death in line with the standard operational procedures for the institutional animal care management. At necropsy, edema-like infiltrative mass was found at the bottom of the cranial cavity (Fig. 1). The pituitary gland and the trigeminal nerve were involved in this mass. The mass compressed the ventral brain. Other findings included small-in-size spleen and liver, involution of thymus, discoloration of prostate, and dilatation of brain ventricle.

The cranium including the tumor was fixed in 10% buffered formalin. A protrusion (probably pituitary gland) from the brain base was removed and used for tissue specimen without decalcification. The entire rest of the cranium, tumor, and brain base was decalcified with 5% formic acid in formalin, and then the center and portion near to the nasal cavity of the tumor was sectioned in a coronar form and paraffin-embedded. For light-microscopic observation, the protrusion, the cranium, and the nasal cavity were stained with hematoxylin-eosin (HE), Klüver-Barre’s stain. For immuno-histochemical observation, each of these specimens was stained with prediluted, ready-for-use antibody products: Anti-Factor VIII Related Antigen polyclonal antibody (Factor VIII) (Code.422182; NICHIREI

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Fig. 1. Gross appearance of malignant schwannoma. The tumor is found at the bottom of the intracranial cavity (arrowheads).
Co., Ltd., Tokyo) and Anti-Prolactin polyclonal antibody (Code.412601; NICHIREI Co., Ltd., Tokyo), using the Histofine SAB-PO kit (NICHIREI Co., Ltd., Tokyo) based on streptavidin-biotin method. Separately, the specimens were stained with a prediluted ready-for-use product, S-100 rabbit polyclonal anti-cow antibody (S-100) (N1573; DAKO Co., Ltd., Japan), using a Vectastain ABC Elite kit (Vector Laboratories, Inc. USA) based on avidin-biotin-peroxidase complex. As control, an appropriate dilution of normal rabbit serum was substituted for each primary antibody. Sections of a normal blood vessel, normal pituitary gland, and peripheral nerve were used as positive controls for Factor VIII, Prolactin, and S-100, respectively.

Histologically, this tumor expanded without a capsule and the margin was not clear with invasion of tumor cells into surrounding tissues. The tumor contained pituitary gland, eroded the skull bone and reached the submucosa of hard plate. The contralateral nerve showed no invasion of tumor cells. The tumor was intermixtures of the solid and cystic areas. Numerous cysts of various sizes were noted in the center of the tumor.

The solid area was densely cellular and consisted of pleomorphic spindle-shaped cells with elongated bizarre nuclei and abundant cytoplasm (Fig. 2). Mitotic figures were also noted in this area. This area was composed of fascicular arrangement of cells, without typical nuclear palisading.

The cystic area was less cellular with oval nuclei and less cytoplasm (Fig. 3). Cysts of different sizes were present in this area. The cystic spaces contained eosinophilic material, and erythrocytes in some cases, and were lined by flat-shaped cells. Nerve cells were scattered in this area and...
were considered ganglion cells because the normal image of ganglion cells was found in the contralateral side without tumor invasion. These ganglion cells in the cystic area showed intracytoplasmic vacuole or degeneration, but no neoplastic characteristics like pleomorphic or bizarre shape.

In this case, the tumor was morphologically intermixtures of the solid and cystic areas. The solid area was densely cellular, and pleomorphic spindle-shaped cells with elongated bizarre nuclei, and mitoses were present. The cystic area was less cellular, and cells with less cytoplasm were sporadically present in the area. The tumor was first suspected of and finally diagnosed as schwannoma because it was positive to immunohistochemical staining with S-100, a useful marker for schwannoma. Thus, the solid and cystic areas were considered histologically Antoni type A and B, respectively.

Another possible diagnosis was suspected as ganglioneuroma because many ganglion cells were scattered at the focal area of the tumor, a characteristic of ganglioneuroma. However, this was denied because the ganglion cells in the cystic area did not increase in number compared with the normal contralateral ganglion cells, and none of these ganglion cells were in neoplastic form.

In humans, the light-microscopic features of malignant schwannoma are characterized by 1) high cellularity, 2) pleomorphism, 3) increased mitotic cells, 4) presence of necrosis, and 5) presence of histological invasion. In the present case of a rat, some of the major histological features were compatible with 1), 2), 3), and 5), so we finally diagnosed this case as a malignant schwannoma. The possible causes of the cyst formation in human schwannoma suggested so far include: 1) the degenerative changes due to ischemia resulting from hyalinized vessels within the tumor, 2) hemorrhages due to vascular fragility resulting from degenerative vessels, and 3) vacuolar formation from degenerated foamy cells. In our rat case, some cysts contained erythrocytes and eosinophilic material. Immunohistochemical staining showed that most cells lining the cysts were positive for S-100 and negative for Factor VIII, while HE staining showed that degenerative vessels were absent in the tumor. We therefore assume from these findings that the origin of the cysts is the tumor per se, and that erythrocytes and eosinophilic material within some cysts resulted from hemorrhage.

In conclusion, the pathologic and immunohistochemical characteristics of this tumor in a Wistar rat indicate that this would be a rare case of spontaneously occurring, intracranial malignant cystic schwannoma.

References