Malignant Intracranial Teratoma in a Juvenile Wistar Rat

J. Reindel, W. Bobrowski, A. Gough, and J. Anderson

Abstract. An intracranial malignant teratoma was identified in a 91-day-old male Wistar rat manifesting central nervous system-related clinical signs. This tumor occupied the right midbrain and portions of the right caudal cerebrum and cranioventral cerebellum. Microscopically, the tumor contained intermingled cartilage, bone (with medullary hematopoietic tissue), fibrous connective tissue, skeletal muscle, fat, pseudostratified ciliated epithelium, stratified squamous epithelium, serous and mucinous glands, and neural tissue with ependymal and choroid plexus epithelia. Poorly differentiated cells with primitive cartilaginous matrix were present throughout the lining of lateral ventricles, in the aqueduct of Sylvius, and in meninges overlying normal cerebellar tissue indicating tumor metastasis occurred via cerebrospinal fluid. This neoplasm was not identified in extracranial sites and hence was considered a primary intracranial malignant teratoma with metastases via cerebrospinal fluid.

Key words: Brain; central nervous system; malignant teratoma; neoplasm; rat.

Teratomas are uncommon neoplasms comprised of a variety of tissue types derived from at least two of three embryonic germ layers. At least some tissues formed by the totipotential tumor cells are foreign to the site of tumor development. Teratomas most commonly originate in gonads of young animals, but occasionally arise in extragonadal sites. Primary intracranial occurrences of this tumor in animals are rare, reports in the veterinary literature are limited to accounts of one or two individual cases. Intracranial metastases of this tumor via the cerebral spinal fluid have not been previously documented in animals. This report describes a spontaneous malignant teratoma in a juvenile Wistar rat in which the primary mass as well as metastases were located within the cranium.

A 91-day (13-week)-old F1 generation, male Wistar rat from a reproductive teratology study was sacrificed due to deteriorating clinical condition associated with central nervous system-related clinical signs of head tilt, circling, and reduced activity of 1-week duration. A full postmortem examination was performed. Necropsy findings indicated this animal was thin and had an unusual dome-shaped cranium. The cranial vault was distorted and asymmetric. The dorsal surface of the brain was diffusely swollen and the dura was firmly affixed to a mass and adjacent brain. The large friable, white-to-gray colored mass measuring approximately 12 × 12 × 12 mm was located anterior and ventral to the cerebellum largely to the right of midline in the region of the cerebellar pontine angle (Fig. 1). This mass, composed of cystic and solid areas, encompassed at least the right half of the midbrain and infiltrated extensive portions of the cerebellum and right caudal cerebral hemisphere. Lateral ventricles were markedly dilated and cerebral cortices were thin, consistent with internal hydrocephalus. Extracranial evidence of tumor was not apparent. The brain was fixed in 10% neutral-buffered formalin, paraffin embedded, sectioned at 3 μm and stained with hematoxylin and eosin (HE), periodic acid Schiff, Masson’s trichrome, and phosphotungsten acid hematoxylin stains.

Microscopically, this tumor had characteristic features of a malignant teratoma. Large areas of the tumor were composed of haphazardly arranged, intermingled tissue types. Mesoderm-derived tumor components consisted of fat, skeletal muscle, cartilage, fibrous connective tissue, and bone with medullary cavities containing hematopoietic elements (Fig. 2). Ectodermal components consisted of stratified squamous epithelial-lined cysts and neural tissue including ependymal and choroid plexus epithelium. Components of endodermal or ectodermal origin consisted of ciliated psu-
dostratified respiratory epithelium, serous and mucouserous glands resembling salivary tissue, and simple columnar epithelium containing numerous goblet cells reminiscent of gut epithelium.

In large regions of tumor, the haphazardly arranged tissue types were composed of fully differentiated cells. Rudimentary organoid formation was evident. Bronchus-like structures with lumens lined by ciliated pseudostratified columnar epithelium surrounded by irregularly shaped cartilaginous plates were present. In addition, primitive long bones with cartilaginous caps, medullary spaces containing hematopoietic elements, and periosteal attachment to well-differentiated skeletal muscle were observed. Individual and clusters of differentiated striated skeletal muscle fibers were present within the neuropil of the midbrain and granular cell layer of the cerebellum (Fig. 3). No apparent demarkation was evident between these intermingled cell types, and detrimental changes were not apparent in the nervous tissue.

Other portions of the tumor contained less differentiated elements including poorly differentiated tubuloacinar glands, fluid-containing cysts lined with simple cuboidal to columnar epithelium, poorly differentiated chondrocytes within a primitive cartilaginous matrix, branching fronds of choroid plexus and ependymal epithelial cells, and sheets or clusters

---

**Fig. 1.** Brain, dorsal surface; rat. A mass is present in the cerebellar-pontine angle distorting the right cerebellum and cerebrum (solid arrows). Ventricular dilatation and thinning of the cerebral cortex are apparent at the incision of the right lateral ventricle (open arrow). Bar = 5 mm.

**Fig. 2.** Intracranial teratoma; rat. Intermingled within the mass are bone with medullary cavity containing hematopoietic elements (A), adipose tissue, skeletal muscle, and mature cartilage. Note the bronchus-like structure lined by ciliated, pseudostratified columnar epithelia and surrounded by irregular cartilaginous plates and mucouserous glands (B). HE. Bar = 250 μm.
of undifferentiated cells. Poorly differentiated cells with primitive cartilaginous matrix had infiltrated and disrupted cerebellar folia (Fig. 4). Small clusters of poorly differentiated cells with or without cartilagenous matrix were present in meninges overlying the cerebellum distant from the main tumor mass (Fig. 5), throughout the ependymal lining of dilated lateral ventricles (Fig. 6), and within the aqueduct of Sylvius lining. The latter findings were consistent with tumor dissemination via the cerebrospinal fluid. Areas of interface between less differentiated tumor elements and neuropil commonly had evidence of neuropil destruction.

Intracranial teratomas, though rare, have been identified in a number of veterinary species including the horse, ox, guinea pig, rabbit, chicken, duck, and dog.\textsuperscript{1,2,4,6} To our knowledge, only a single case of an intracranial teratoma in a rat has been reported in the literature.\textsuperscript{A} A teratoma originating from the pituitary gland was identified in a 5-week-old male Donryu rat.\textsuperscript{5} Evidence of intracranial metastases or implantation was not indicated in that rat or in other animal species. The rarity of intracranial teratomas in animals precludes meaningful assessment of tumor incidence and species, breed, sex, and age predilection for this tumor type.

In spite of the large number of rats subjected to thorough gross and microscopic evaluation in experimental studies, reports of spontaneous extragonadal teratomas at sites other than an intracranial location are also rare. We found only four additional reports of spontaneous extragonadal teratomas in rats; one in the adrenal of a 35-day-old male Wistar rat,\textsuperscript{7} one in the kidney of a 67-day-old male Wistar rat,\textsuperscript{10} one in the kidney of a 127-day-old male Fischer rat,\textsuperscript{8} and one in the retroperitoneal region of a 6-week-old male Sprague-Dawley rat.\textsuperscript{9} These data and findings in the current report suggest that extragonadal teratomas in rats have a certain predilection for young males.

Information pertaining to intracranial teratomas in human beings is more extensive than for veterinary species.\textsuperscript{9,11} As in animals, intracranial teratomas of human beings are rare. They represent approximately 0.5% of all intracranial tumors, 1.5 to 2% of all central nervous system neoplasms in children, and 3% of teratomas identified at various tissues sites. These tumors tend to be more common in males. Some intracranial teratomas can clearly be classified as congenital, because they can become symptomatic during fetal or neonatal life resulting in dystocia or congenital hydrocephalus.
of poorly differentiated tumor cells clearly defines this tumor as malignant.

References


Request reprints from Dr. J. Reindel, Parke-Davis Pharmaceutical Research, 2800 Plymouth Road, Ann Arbor, MI 48105 (USA).