Morphologic Alterations in the Cilia of a Cat

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Abstract. Based upon ultrastructural findings and computed tomography, a presumptive diagnosis of feline primary ciliary dyskinesia was made in a 2.5-year-old cat. The cat demonstrated morphologic alterations in the ultrastructure of oviductal cilia. In the oviduct, axonemal abnormalities were detected in 132 (20%) of 660 cross-sectioned cilia. The main ultrastructural ciliary defects were a lack of central microtubules, transposition of peripheral doublets to the center of the axoneme, supernumerary microtubules, and morphologic abnormalities of peripheral doublets. Computed tomography of the chest was consistent with early lesions of bronchiectasis, suggesting chronic stagnation of respiratory secretions, attributed to abnormal function of respiratory cilia. Specifically, the cranial branches of the cat's bronchi were wider and thicker than those of five healthy controls. Foci of pleural thickening and interstitial enlargement were also observed.

Key words: Cats; immotile cilia syndrome; oviductal mucosa; primary ciliary dyskinesia.

In the field of veterinary medicine, there is little information about the incidence and quantitative characterization of primary and acquired ciliary abnormalities, the latter being known to occur both in normal and pathologic tissues. The ability to differentiate between primary and acquired ciliary defects is important in the diagnosis of immotile cilia syndrome (ICS), also known as primary ciliary dyskinesia, a rare hereditary disease characterized by an inability of the cilia to beat normally. The first report in the veterinary literature of the morphologic alteration of ICS was in 1982 in dogs. More recently, ICS has been reported from pigs. In both species, several different subgroups of the disease have been described. Dynein defects are the most frequent; however, rare variants, such as ciliary aplasia and abnormally long cilia, have recently been reported in porcine ICS. Herein, we describe ciliary abnormalities in a cat. The ultrastructural features, incidence, and distribution pattern are consistent with primary defects.

An ovariohysterectomy was performed on a 2.5-year-old cat, and samples from the ampulla of the oviduct were immediately fixed for 3-4 hours in 1% tannic acid containing 2% glutaraldehyde in phosphate buffer (pH 7.2-7.4) at 4 C. The specimens were then block-stained in 1% uranyl acetate in distilled water, dehydrated in graded alcohols, and embedded in Spurr’s resin. Ultrathin sections were stained with uranyl acetate and lead citrate and examined with a Zeiss EM9 2S electron microscope. Blood samples for routine hemogram and serum chemistry were collected. IgG and IgA levels were measured and serum antibodies to feline immunodeficiency virus (FIV) and feline leukemia virus (FeLV) antigens were studied with an enzyme-linked immunosorbent assay (ELISA). Computed tomography (CT) studies of the chest were performed on the affected cat and five healthy control cats. In both the affected cat and the healthy cats, CT was carried out in sternal recumbency under general anesthesia, with 1-mm slice collimation and 3-mm slice gap, from the lung apices through the diaphragm (scan time = 1.3 seconds). Images were reconstructed with a high-resolution filter and evaluated with a lung window setting (center, −500 UH, width 2,500).

No clinical signs were evident. A routine hemogram revealed a mild eosinophilia, and serum IgA and IgG levels were within the normal reference range at our laboratory. ELISA for detecting antibodies to FIV and p27 FeLV antigens were negative.

The microtubular pattern was evaluated in 660 cross-sectioned cilia. Alteration from the normal 9+2 pattern was found in 132 cilia (20%). Twenty-two cilia (3.3%) showed morphologic abnormalities involving peripheral microtubules; 66 cilia (10%) had central microtubular defects and 44 cilia (6.7%) had supernumerary microtubules. Most of the pathologic cilia with central abnormalities were characterized by a lack of microtubules, so that cilia showed a tubular pattern. Isolated cilia with only one missing central microtubule were also seen (Fig. 2). Dynein arms were, however, normal in the cilia. In most cilia with axonemal supernumerary microtubules, two extra microtubular singlets were present, making a 9+4 microtubular pattern. Isolated cilia with only one missing central microtubule were also seen (Fig. 2). Dynein arms were, however, normal in the cilia. In most cilia with axonemal supernumerary microtubules, two extra microtubular singlets were present, making a 9+4 microtubular pattern. Isolated cilia with only one missing central microtubule were also seen (Fig. 2). Dynein arms were, however, normal in the cilia. In most cilia with axonemal supernumerary microtubules, two extra microtubular singlets were present, making a 9+4 microtubular pattern. Isolated cilia with only one missing central microtubule were also seen (Fig. 2). Dynein arms were, however, normal in the cilia. In most cilia with axonemal supernumerary microtubules, two extra microtubular singlets were present, making a 9+4 microtubular pattern. Isolated cilia with only one missing central microtubule were also seen (Fig. 2). Dynein arms were, however, normal in the cilia. In most cilia with axonemal supernumerary microtubules, two extra microtubular singlets were present, making a 9+4 microtubular pattern. Isolated cilia with only one missing central microtubule were also seen (Fig. 2). Dynein arms were, however, normal in the cilia. In most cilia with axonemal supernumerary microtubules, two extra microtubular singlets were present, making a 9+4 microtubular pattern. Isolated cilia with only one missing central microtubule were also seen (Fig. 2). Dynein arms were, however, normal in the cilia. In most cilia with axonemal supernumerary microtubules, two extra microtubular singlets were present, making a 9+4 microtubular pattern. Isolated cilia with only one missing central microtubule were also seen (Fig. 2). Dynein arms were, however, normal in the cilia. In most cilia with axonemal supernumerary microtubules, two extra microtubular singlets were present, making a 9+4 microtubular pattern. Isolated cilia with only one missing central microtubule were also seen (Fig. 2). Dynein arms were, however, normal in the cilia. In most cilia with axonemal supernumerary microtubules, two extra microtubular singlets were present, making a 9+4 microtubular pattern. Isolated cilia with only one missing central microtubule were also seen (Fig. 2). Dynein arms were, however, normal in the cilia. In most cilia with axonemal supernumerary microtubules, two extra microtubular singlets were present, making a 9+4 microtubular pattern. Isolated cilia with only one missing central microtubule were also seen (Fig. 2).
Acute viral infections can impair ciliogenesis, resulting in an altered configuration of the normal 9 + 2 pattern, and these defects usually involve supernumerary central microtubules. Acute viral infections can probably be excluded in the present case. Although we examined cilia from more than one site, we did not observe any dilatation of endoplasmic reticulum cisternae, any increased vacuolization, or any condensation of the mitochondrial matrix, which are characteristic ultrastructural changes associated with acute viral infections. The abnormal cilia in this cat were randomly distributed. In contrast, during the acute phase of viral infection, transient abnormal cilia cluster in focal sites of injury.

CT investigations were strongly suggestive of a functional significance associated with the morphologic alteration of cilia. At 15 mm anterior to the tracheal bifurcation, the bronchial/tracheal width ratio of the affected cat was 0.35, a value well in excess of the 95% confidence interval for the control cats. However, because these estimates are based on a small number of cats, further CT scans of the feline chest are necessary before definite conclusions can be reached. Bronchiectases are caused by prolonged stagnation of secretion in the respiratory tree. The bronchial dilations in this cat might be the expression of an impaired mucociliary clearance. With a microphoto-oscillographic technique, a moderate degree of abnormal ciliary beating was revealed in a patient in which 7% of cilia had supernumerary microtubules. A symmetrical configuration of 8 + 1 doublet microtubular allows some residual microtubule sliding, thus causing reduced ciliary motility. Lack of central microtubules and transposition of one doublet microtubule to the center of the axoneme were the most characteristic ciliary defects in this study. To our knowledge, no similar axonemal abnormalities have previously been reported in animals with ICS. The axonemal alterations in this cat are similar to those in a human patient, whose abnormal cilia were termed type III dyskinetic cilia.

This feline case could emphasize an important aspect of comparative pathology. The spectrum of ciliary defects in ICS is pleomorphic in domestic animals and shows many ultrastructural similarities to the human disease. The morphologic pattern of the subgroups of ICS known in humans may be present in domestic animals, and more studies of ciliary motility in domestic animals are needed to gain insight into the poorly understood pathogenetic mechanisms of primary and acquired ciliary defects. For example, recent studies have shown that pigs with ICS are a good animal model of human ICS. Such animal studies improve our knowledge of the role of cilia in the homeostasis of economically important organ systems.

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Malignant Intracranial Teratoma in a Juvenile Wistar Rat

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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 mucoserous 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.1,3 At least some tissues formed by the totipotential tumor cells are foreign to the site of tumor development.1 Teratomas most commonly originate in gonads of young animals, but occasionally arise in extragonadal sites.1,3,8 Primary intracranial occurrences of this tumor in animals are rare,1 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 pseudocysts and highly differentiated epithelial-like tissue.