Case Report: Carcinoma of the Extraorbital Lacrimal Gland in a Female Fischer 344 Rat

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ABSTRACT

A large subcutaneous mass was observed at necropsy in the right neck area of a 95-week-old female Fischer 344 rat that served as an untreated control animal in a 2-year carcinogenicity study. Formalin-fixed, paraffin-embedded sections of the mass were stained with hematoxylin and eosin along with the immunohistochemical biomarkers lactoperoxidase, catalase, and amylase. Based on its histomorphological and immunohistochemical features, the lesion was diagnosed as a carcinoma of the extraorbital lacrimal gland.

Keywords: Neoplasm; rat; lacrimal gland; immunocytochemistry; spontaneous

The rat has 2 pairs of lacrimal glands. The intraorbital lacrimal gland is located within the orbit at the caudolateral aspect of the Harderian gland. The extraorbital lacrimal gland (exorbital, outer orbital, Loewenthal’s gland) is situated anterior to the parotid salivary gland at the base of the ear (3). The weight of the extraorbital lacrimal gland in rats of both sexes is reported to approach maximum size at 100 days of age and, in female rats, to remain relatively constant throughout life (9). In males, there is a gradual decline in the weight of the gland during senescence. In albino rats, there is a pronounced androgen-driven sexual dimorphism of the extraorbital lacrimal gland during aging, with male rats having an increased tendency toward irregularity in acinar cell nuclear size and shape, one that is not observed in females (2, 9).

Lacrimal gland is not routinely included as a tissue for histopathological evaluation during toxicity and carcinogenicity studies. However, the extraorbital gland is occasionally observed incidentally because of its proximity to the parotid salivary gland, which is often a protocol-required tissue for bioassays. Although morphologically similar to the salivary gland, the extraorbital lacrimal gland may be distinguished from the submandibular and sublingual salivary glands by the basophilic to magenta character of the basal portion of the lacrimal gland acinar cells, noted upon staining with hematoxylin and eosin (H&E) (5). The lacrimal gland also differs from the submandibular gland based on the absence (especially in male rats) of conspicuous secretory ducts and based on irregularity of nuclear size and shape. The lacrimal gland is distinguished from the parotid salivary gland by its less intensive eosinophilic staining. Because of the morphologic similarity between the extraorbital lacrimal gland and the salivary glands of rats and because of their anatomic proximity, differentiation of neoplasms from these sites could represent a diagnostic challenge.

Lacrimal gland neoplasms of rats and other laboratory rodents are extremely rare (5). The only reported rat lacrimal gland tumor found in the literature was an adenocarcinoma from a Fischer 344 rat (10), but no signalment or history were provided. The National Toxicology Program database contains 2 extraorbital lacrimal gland tumors, a carcinoma and a squamous cell carcinoma, from B6C3F, mice (1). “Mesenchymoid” tumors were induced in the lacrimal gland as well as in various salivary glands of mice following exposure to polyoma virus (4).

An approximately 95-week-old female Fischer 344 rat (Taconic Farms) that served as an untreated control animal in a National Toxicology Program chronic bioassay study was sacrificed in extremis and necropsied. At necropsy, the cause of death was attributed to a dark-colored mass of approximately 35 × 25 × 20 mm that was located in the subcutaneous tissue of the right neck area. Other gross lesions included an approximately 12-mm-diameter subcutaneous mass that was located in the subcutaneous tissue of the right neck area. Other gross lesions included an approximately 12-mm-diameter subcutaneous mass in the right inguinal area (determined histopathologically to be a mammary gland fibroadenoma), thickened cranium (osteopetrosis), mammary gland cysts, and a 3 × 3-mm dark focus on the left clitoral gland (no corresponding microscopic lesion). Tissues were fixed in 10% neutral-buffered formalin. Paraffin-embedded sections were prepared and stained with H&E. Formalin-fixed, deparaffinized sections of the neck tumor as well as control lacrimal and salivary gland tissue from a young naïve Fischer 344 rat were processed.
for immunocytochemistry. Antibodies against bovine lactoperoxidase (6), human catalase (Athens Research and Technology, Athens, GA), and human amylase (Sigma Chemical Co, St Louis, MO) were used for immunofluorescence staining. After blocking the sections, primary antibodies were applied, and immunostaining was detected using fluorescein isothiocyanate (FITC)-conjugated second antibodies (Dako, Carpinteria, CA). In control experiments, rabbit IgG was used to evaluate the background staining. The antibody designations and dilutions are summarized in Table 1.

With conventional microscopy on H&E–stained sections (Figures 1–3), the mass from the neck area was composed of large plump, magenta-staining cells forming cysts and atypical acinar structures. The cells typically ranged from approximately 30 to 70 microns in diameter, and cell borders were clearly defined. Nuclei were round to ovoid with a single nucleolus and occasionally with coarsely clumped, centrally located chromatin. Mitotic figures were occasionally seen. The cell cytoplasm was usually of a homogeneous or granular magenta staining, but varying degrees of fine to coarse cytoplasmic vacuolization were also observed. Focal or focally extensive areas or necrosis were common, and frequently observed small cystic spaces that apparently resulted from tumor necrosis often contained mineralized concretions. The larger cystic spaces contained a homogeneous, eosinophilic to amphophilic, colloidlike material. In the solid

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<th>Antibody</th>
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<tr>
<td>Lactoperoxidase</td>
<td>Mansson-Rahemtulla et al (6)</td>
<td>Rabbit/anti-bovine</td>
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<td>Catalase</td>
<td>Athens Research 01-05-030000</td>
<td>Rabbit/anti-human</td>
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<td>Amylase</td>
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portions of the mass, the tumor cells often appeared to be arranged in atypical acinar formations, with the nuclei usually occupying the basilar aspect of the cell. In the better-differentiated areas, the cells bore a definite resemblance to those of the adjacent nonneoplastic lacrimal gland (Figure 2). Although the tumor displayed areas of invasion into subjacent skeletal muscle and fascia, no evidence of distant metastasis was observed. The results of immunocytochemical staining are shown in Table 2. Control salivary gland stained positively to antibodies against lactoperoxidase, catalase, and amylase, whereas control lacrimal gland and the tumor stained positively only for lactoperoxidase and catalase.

Lactoperoxidase and catalase are normal components of both lacrimal and salivary glands (7). Although amylase has been reported to occur in tears (8), this enzyme is not typically regarded as a significant tear component, and it was not detected in our immunofluorescent staining of control lacrimal gland. Based on the histomorphologic similarity of the tumor cells to those of normal lacrimal gland and based on the tumor location and on the results of immunocytochemical staining, the tumor was classified as a carcinoma of the extraorbital lacrimal gland. This case points out the need for careful consideration of lacrimal gland neoplasia as a differential diagnosis for masses involving the head and neck of rats.

REFERENCES