



SHORT PAPER

Adenosquamous Carcinoma with Cilium Formation, Mucin Production and Keratinization in the Nasal Cavity of a Red Fox (*Vulpes vulpes schrencki*)

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Summary

A diagnosis of adenosquamous carcinoma was made in an 11-year-old red fox. The animal showed emaciation and purulent nasal discharge. Necropsy revealed diffuse thickening of the nasal mucosa and tumours on the soft palate, and there was an oronasal fistula contiguous with the tumours. The nasal and oral lesions were composed of adenocarcinomatous cells and squamous cells, the latter predominating in the oral lesions. The marrow of the palatine bone also contained neoplastic tissue, which consisted of cysts and keratin masses surrounded by well-differentiated squamous cells. Although inconspicuous in the oral cavity and marrow, ciliated cells with or without mucin were observed in the adenocarcinomatous and cystic elements. Neoplastic basal cells and less-differentiated adenocarcinoma cells, which were identifiable by immunolabelling for cytokeratin 5 (CK5) and CK18, were considered to be pluripotential. These cells, which lined tubular structures, were distinct from intermediate cells in mucoepidermoid carcinoma, which can differentiate into squamous and mucin-producing cells but have a nondescript appearance.

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Mucoepidermoid carcinoma is the most common type of malignant salivary gland neoplasia in man (Cheuk and Chan, 2000). The seromucinous glands of the nasal cavity and larynx are histologically similar to the minor salivary glands that are dispersed in the submucosa of the oral cavity, and are susceptible to a similar range of neoplasms (Cheuk and Chan, 2000). Salivary gland mucoepidermoid carcinomas may occur in the sinonasal tract and nasopharynx (Wening and Pilch, 2000). Adenosquamous carcinoma in the sinonasal tract is an aggressive neoplasm that originates in the surface epithelium (Alos *et al.*, 2004), and its prognosis is much worse than that of poorly differentiated mucoepidermoid carcinoma (Wening and Pilch, 2000). In dogs, however, adenosquamous carcinoma and mucoepidermoid carcinoma are less distinct, and both are included

in the same category in the classification of sinonasal tumours (Wilson and Dungworth, 2002). Canine epidermoid carcinomas of the upper respiratory tract have been reported (Confer and DePaoli, 1978), but it is not known whether they are associated with the nasal gland.

Reports of neoplasms in red foxes (*Vulpes vulpes*) are few, but a mammary adenocarcinoma (Janovsky and Steineck, 1999) and a thyroid C-cell carcinoma (Hirayama *et al.*, 1999) were investigated histologically. This paper reports a case of adenosquamous carcinoma of nasal epithelial origin in a red fox (*Vulpes vulpes schrencki*), the tumour being distinguishable from mucoepidermoid carcinoma on the basis of the characteristics of pluripotential cells.

An 11-year-old red fox showed emaciation, debilitation, and a purulent nasal discharge. Despite antimicrobial treatment, the animal died 1 month after the

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first examination. At necropsy, the nasal passages were filled with purulent discharge and food, and the mucosa was diffusely congested, haemorrhagic and swollen. On the soft palate, there was a raised nodule ($2 \times 1.5 \times 1$ cm), contiguous with a second nodule (1 cm in diameter). An oronasal fistula 1 cm in diameter was found immediately adjacent to the nodules. No other abnormalities were detected.

Tissue samples were fixed in 10% buffered formalin, embedded in paraffin wax, sectioned at $4\text{ }\mu\text{m}$, and stained with haematoxylin and eosin (HE) and alcian blue (pH 2.5). Selected paraffin wax sections were de-waxed and labelled by the avidin–biotin–peroxidase complex (ABC) method. The primary antibodies, which were prediluted, were rabbit polyclonal antibody to cytokeratins (CKs) (BioGenex Laboratories, San Ramon, CA, USA), and mouse monoclonal antibodies to CK5 (XM26) (Lab Vision, Fremont, CA, USA), CK10 (DE-K10) (Lab Vision), CK18 (Ks18.04) (Progen, Heidelberg, Germany), and vimentin (Dako, Carpinteria, CA, USA). Subsequent procedures were performed by means of an immunoperoxidase labelling system (Nichirei, Tokyo, Japan).

Microscopical examination revealed that the neoplastic tissue in the nasal cavity consisted of two elements: adenocarcinomatous cells and malignant squamous epithelial cells. The former cells, growing in a tubulopapillary form, were columnar, ciliated, and contained mucinous material or eosinophilic inclusions (Figs 1 and 2). In addition, non-ciliated, goblet cell-like cells were observed. Large numbers of plasma cells were present in the stroma. In some parts of the lesion, the tubules were lined by a single row of less-differentiated, cuboidal or flattened cells. The squamous element was composed of sheets or lobules of moderately differentiated squamous cells, within which there were whorls of concentrically arranged, well-differentiated

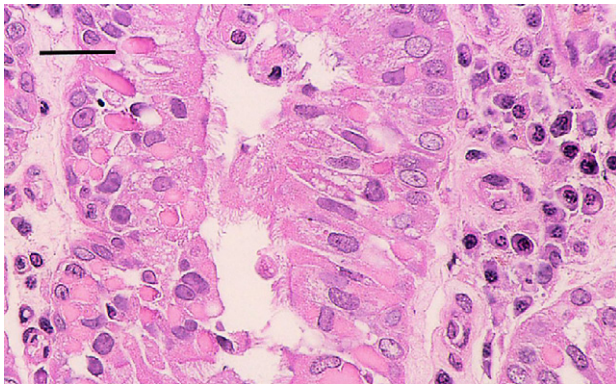


Fig. 1. Nasal cavity. In this adenocarcinomatous region, neoplastic cells with cilia and eosinophilic inclusions are observed. Several plasma cells are present in the stroma (right). HE. Bar, $25\text{ }\mu\text{m}$.

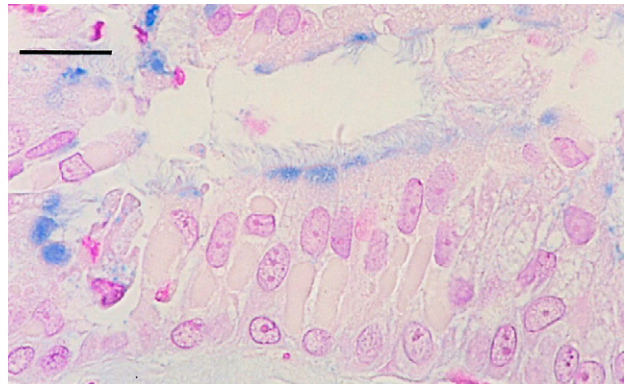


Fig. 2. Nasal cavity. Adjacent section shows the same ciliated cells as those in Fig. 1. Mucin is visible at the apex of the cells. Alcian blue. Bar, $20\text{ }\mu\text{m}$.

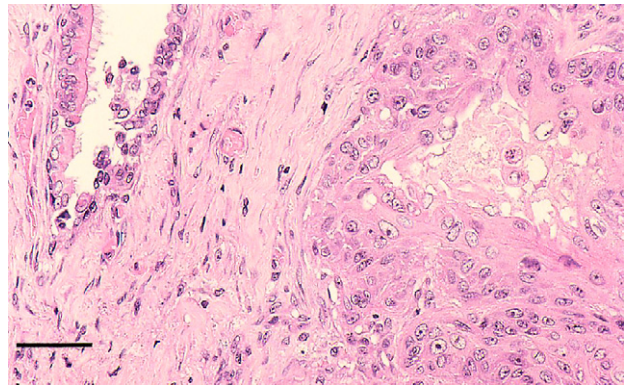


Fig. 3. Oral cavity. Visible in this field are an area of squamous cells (right) and a neoplastic tubule, partly lined by ciliated cells (upper left). HE. Bar, $50\text{ }\mu\text{m}$.

squamous cells and centrally located keratinized cells containing pyknotic nuclei. The two elements were not intermingled, but foci of squamous metaplasia were seen in the glandular areas. Mitotic figures per $\times 400$ field numbered 6–10 in the squamous element and 1–2 in areas of well-differentiated adenocarcinomatous cells.

The oral lesions were predominantly occupied by areas of squamous cells (Fig. 3). These areas contained necrotic centres and the surface of the lesions was necrotic and covered by colonies of bacteria. Neoplastic tubules, frequently filled with mucin, were present near the areas of squamous cells. The tubules were lined by a single layer of cuboidal or flattened cells, and some cuboidal cells showed cilia or eosinophilic inclusions, or both (Fig. 4). In a few tubules, the epithelial cells were partly replaced by squamous cells. In the fistula site, the neoplastic tissue was similar to that in the oral cavity, although the neoplastic tubules were more prominent. The marrow of the palatine bone was replaced by cysts and laminated masses of keratin surrounded

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