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NEOPLASTIC DISEASE

Amyloid-producing Odontoameloblastoma in a Black-tailed Prairie Dog (*Cynomys ludovicianus*)

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Summary

A 6-year-old female black-tailed prairie dog (*Cynomys ludovicianus*) was presented with a space-occupying lesion in the left submandibular region. On computed tomography, a low attenuating, poorly circumscribed mass infiltrated the left mandibular bone, with osteolytic change. Microscopically, the lesion was composed of odontogenic epithelium proliferating in nests and embedded in abundant dental papilla-like ectomesenchyme, including dentine and enamel. Multifocal amyloid deposition was observed. Immunohistochemically, the neoplastic epithelial cells were positive for cytokeratin (CK) AE1/AE3, CK14 and p63. Some epithelial cells were positive for amelogenin and some adjacent to the amyloid deposits co-expressed S100. The ectomesenchymal cells expressed vimentin and strong S100 immunoreactivity was observed in odontoblast-like cells. The amyloid was immunolabelled with amelogenin. The tumour was diagnosed as amyloid-producing odontoameloblastoma.

Keywords: amyloid; odontogenic tumour; prairie dog

Amyloid-producing odontogenic tumour (APOT) is a rare oral neoplasm of odontogenic epithelial origin associated with the extracellular deposition of amyloid (Gardner *et al.*, 1994; Head *et al.*, 2003). APOT occurs mainly in dogs and cats (Abbott *et al.*, 1986; Breuer *et al.*, 1994; Ohmachi *et al.*, 1996; Delaney *et al.*, 2013; Hirayama *et al.*, 2017), with few reported incidences in other animal species (Kang *et al.*, 2006; Löhr, 2013). Animal APOT differs histologically from human calcifying epithelial odontogenic tumour (CEOT), since palisading basal-like epithelial cells and stellate reticulum occur commonly in APOT, but not in CEOT (Gardner *et al.*, 1994). Despite being benign in nature, APOT tends to grow in an expansive pattern, with the sequential destruction of adjacent bone and dental structures (Tsai *et al.*, 2007; Delaney *et al.*, 2013). APOT is classified as a non-inductive epithelial odontogenic tumour based on the predominant epithelial components and absence of inductive ectomesenchyme in the reported tumour lesion of dogs and cats (Gardner *et al.*, 1994; Tsai *et al.*, 2007; Delaney *et al.*, 2013; Munday *et al.*, 2017). The present study describes the histopathological and immunohistochemical features of a locally invasive APOT with inductive mesenchymal components in a black-tailed prairie dog (*Cynomys ludovicianus*).

A 6-year-old female black-tailed prairie dog was presented to an exotic animal hospital with a history of anorexia and difficulty in chewing solid foods. Oral examination revealed a round, solid mass approximately 1.5 cm in diameter in the left submandibular region. On computed tomography (CT), a low attenuating, non-encapsulated and poorly circumscribed mass (2.5 × 2.2 × 1.7 cm) infiltrated

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the left mandibular bone with osteolysis (Supplementary Fig. 1). The mass was resected surgically, fixed in 10% neutral buffered formalin, processed routinely and embedded in paraffin wax. Sections (4 μm) were stained with haematoxylin and eosin (HE). Additional sections were also stained with Congo red with and without prior 5% potassium permanganate treatment.

Immunohistochemistry (IHC) was performed using the primary antibodies listed in Supplementary Table 1 and the EnVision + SystemTM horseradish peroxidase (HRP)-labelled polymer (Dako, Tokyo, Japan). Subsequent chromogen treatment with 3, 3′-diaminobenzidine (DAB) and counterstaining with Mayer's haematoxylin was carried out. For double immunofluorescence, the sections were incubated with antibodies specific for cytokeratin (CK) 14 and S100 and then with Alexa 488-labelled anti-mouse IgG (Thermo Fisher Scientific, Waltham, Massachusetts, USA) and biotinylated anti-rabbit IgG conjugated with Cy®5-streptavidin (Invitrogen, Camarillo, California, USA), respectively. The sections were stained also with Congo red and then mounted under VECTASHIELD® Hard Set™ mounting medium with 4′, 6-diamidino-2-phenylindole (DAPI) (Vector Laboratories, Burlingame, California, USA). The sections were examined under a confocal laser scanning microscope.

Microscopically, the lesion was unencapsulated, poorly demarcated and composed of odontogenic epithelium proliferating in cords or nests with irregular, large aggregates of eosinophilic enamel-like material (Fig. 1). Peripheral condensation of ectomesenchyme, resembling the dental papilla, was observed around the neoplastic nests (Fig. 1, inset). In some tumour nests, the peripheral columnar-shaped odontogenic epithelial cells arranged in a palisading pattern and stellate-shaped cells at the centre were interconnected via intercellular bridges. The columnar-shaped cells showed a continuation to nests of eosinophilic, polygonal-shaped cells. Mitotic figures were observed rarely. The multifocal deposition of amorphous, eosinophilic deposits, which were sometimes concentrically mineralized and showed a laminated structure termed 'Liesegang rings', was observed within the interstitial space between the epithelial cell nests. The formation of dental hard tissues (dentine and enamel) was detected within the tumour lesion. The dentine and enamel were bordered by eosinophilic spindle-shaped mesenchymal cells (odontoblast-like cells) and palisading columnar-shaped epithelial cells, respectively (Fig. 2). The amorphous, eosinophilic material stained positively with Congo red (with and without 5% potassium permanganate treatment) and produced apple green birefringence under polarized light, indicating the presence of amyloid (Fig. 3). Tumour cells infiltrated adjacent bone.

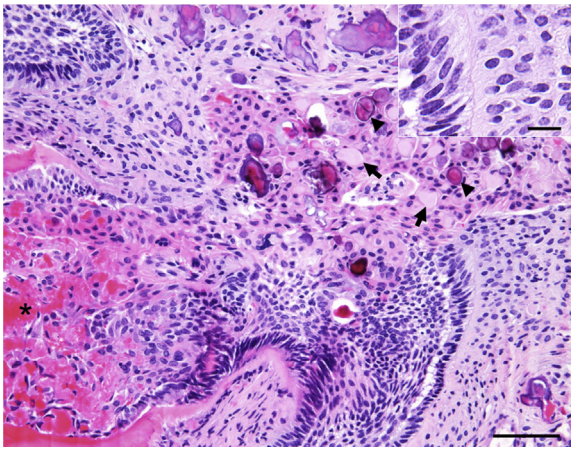

Fig. 1. Neoplastic tissue composed of odontogenic epithelium proliferating in nests with deposits of amorphous eosinophilic material (arrows) and irregular enamel protein (asterisk). Some of the amorphous eosinophilic material is concentrically mineralized into laminated globules ('Liesegang rings') (arrowheads). HE. Bar, 100 μm. Inset: aggregation of dental papilla-like ectomesenchymal cells (right) adjacent to the epithelial nest. HE. Bar, 25 μm.

Immunohistochemically, the epithelial cells were diffusely positive for CKAE1/AE3, CK14 (Fig. 4) and p63. Reactivity to S100 was detected in polygonal-shaped epithelial cells adjacent to the amyloid deposits, as well as in odontoblast-like cells. The ectomesenchymal components displayed diffuse reactivity to vimentin. Some of the epithelial cells and the adjacent enamel-like materials were positive

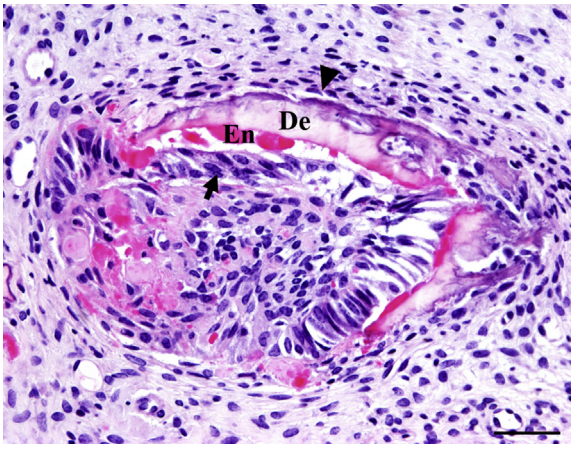

Fig. 2. Dental hard tissues (dentine and enamel) are bordered by palisading columnar-shaped epithelial cells (arrow) and eosinophilic odontoblast-like cells (arrowhead). HE. De, dentine; En, enamel. Bar, 50 μm.