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DISEASE IN WILDLIFE OR EXOTIC SPECIES

Ameloblastoma of the Jaw in Three Species of Rodent: a Domestic Brown Rat (*Rattus norvegicus*), Syrian Hamster (*Mesocricetus auratus*) and Amargosa Vole (*Microtus californicus scirpensis*)

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Summary

Ameloblastoma is a locally aggressive tumour derived from the odontogenic epithelium of the developing tooth germ. This uncommon odontogenic tumour is generally considered benign, but rarely, both distant metastasis and cytological atypia occur and this malignant version is referred to as malignant ameloblastic carcinoma. Here we document a spontaneous malignant ameloblastic carcinoma in a rat (*Rattus norvegicus*) with metastasis to the submandibular lymph node. We also describe ameloblastomas in two other muroid rodents, an Amargosa vole (*Microtus californicus scirpensis*) and a Syrian hamster (*Mesocricetus auratus*). To our knowledge, this is the first report of a malignant ameloblastic carcinoma in any animal and the first report of ameloblastoma in a vole and hamster.

Keywords: ameloblastic carcinoma; ameloblastoma; mandible; rodent

Ameloblastoma is a locally aggressive tumour derived from the odontogenic epithelium of the developing tooth germ, specifically the specialized epithelial cells referred to as ameloblasts. Ameloblastomas have been recognized for at least 150 years and have been referred to previously by a variety of now antiquated terms including adamantinoma and enamelblastoma. This tumour has been identified in a wide array of vertebrate species including man and other primates (Regezi *et al.*, 2012), dogs (Tollett *et al.*, 2016), cats (Gardner, 1998), horses (Gardner, 1994), sheep (Glastonbury and Venning, 1998), rabbits (Volker *et al.*, 2014), rats (Lewis *et al.*, 1980; Ernst and Mirea, 1995; Murphy *et al.*, 2017), a transgenic mouse (Cardiff *et al.*, 1993), polyomavirus-infected mice (Gollard *et al.*, 1992), a black rat snake (*Pantherophis alleghaniensis*) (Comolli *et al.*, 2015) and Chinook salmon (*Oncorhynchus tshawytscha*) (Grim *et al.*, 2009). Although ameloblastomas have not been reported previously in hamsters or voles, a complex odontoma has been reported in a vole as an incidental mandibular lesion (Walsh *et al.*, 1987) and an odontoma has been reported in a female hamster (McInnes *et al.*, 2013). Odontogenic tumours other than ameloblastomas that have been identified in rats include a spontaneously arising ameloblastic odontoma (Li *et al.*, 2017), a mutagen-induced odontoameloblastoma (Murphy *et al.*, 2017), a spontaneously arising odontoameloblastoma (Burrough *et al.*, 2010) and a

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spontaneously arising odontoma (Jang *et al.*, 2002). Several transgenic mice have also developed odontomas (Wright *et al.*, 1995; Lu *et al.*, 2009).

Although considered benign tumours, ameloblastomas are progressive, locally destructive lesions that can result in substantial bone loss, facial deformities and the potential for tooth loss and pathological fracture. Since their histogenesis involves the tooth germ epithelium, ameloblastomas are unique to the oral cavity and can arise either centrally within the jaw bones (from the enamel organ, odontogenic rests or reduced enamel epithelium within the periodontal ligament) or peripherally within the gingival mucosa (from the dental lamina). As a result of degeneration/necrosis within the neoplastic epithelium, ameloblastomas are frequently cystic. Keratinization within the neoplastic odontogenic epithelium can also occur and the presence of intralesional keratin is not thought to affect the prognosis. Here we describe naturally occurring ameloblastomas in three different species of rodent.

Details of the clinical history and medical examination of three rodents with ameloblastoma were collated. Humane destruction was performed due either to client request or poor prognosis. Postmortem evaluation was performed at the University of California Veterinary Medical Teaching Hospital (for the rat and hamster) or Comparative Pathology Laboratory (for the vole). Representative tissues were collected and preserved in 10% neutral buffered formalin for approximately 48 h. Jaw and skull bones were decalcified in 15% formic acid as needed for sectioning (72–96 h). Decalcified tissues were processed routinely and embedded in paraffin wax. Sections (5 μm) were stained with haematoxylin and eosin (HE). For the rat tissues, immunohistochemistry (IHC) was performed using murine monoclonal antibodies against pan-cytokeratin or vimentin (pan-cytokeratin Lu-5, BioCare Medical, Concord, California, USA and vimentin clone Vim 3B4, Dako, Glostrup, Denmark). For pan-cytokeratin and vimentin IHC, the positive control tissue was normal canine mucosa and submucosa, respectively. Negative controls lacked the primary antibody. IHC was performed according to protocols provided by the manufacturers.

A 3-year-old neutered female domestic brown rat (*Rattus norvegicus*) was presented to the Companion Exotic Animal Medicine and Surgery (CAPE) Service, University of California, Davis, California, USA, for a firm swelling on the left caudal aspect of the face, as well as substantial weight loss. Examination revealed muscle wasting, elongation and oblique wear of the incisors and the aforementioned mass that was localized to the caudal aspect of the left jaw. The left mandibular molar and premolar teeth were absent. A 2.5 × 2 × 1 cm, variably hard to slightly compressible, pale tan, discrete mass expanded and distorted the left mandible at the level of the molar teeth (Fig. 1).

Microscopically, the ramus of the left mandible was expanded and partially effaced by a neoplastic population of epithelial cells forming islands, plexiform ribbons and arborizing trabeculae demonstrating multiple rounded protuberances (bosselated margins, Figs. 2 and 3) embedded in fibrovascular stroma. These neoplastic epithelial structures were peripherally bordered by palisading cuboidal to columnar epithelial cells with antibasilar nuclei (ameloblastic histogenesis). Centrally, the epithelial structures variably demonstrated long, spider-like intercellular desmosomal junctions with marked contraction of the epithelial cell body (stellate reticulum) and/or cystic degeneration (Fig. 3). Multifocally, epithelial structures demonstrated varying degrees of squamous differentiation with frequent formation of keratin at the centre of epithelial islands ('keratin pearls', Supplementary Fig. 1). Neoplastic epithelium multifocally invaded and effaced both the mandibular bone and skeletal muscle and extended to the mucosal surface (ulceration).

Cytokeratin IHC revealed strong, diffuse, cytoplasmic and membranous immunoreactivity of the neoplastic epithelium; individualized and small clusters of neoplastic epithelial cells breached the basement membrane and invaded the subjacent stroma (Supplementary Fig. 2). Non-specific immunoreactivity to vimentin was noted in the keratinized or necrotic aspects of neoplastic and remnant normal surface epithelium. The submandibular lymph node

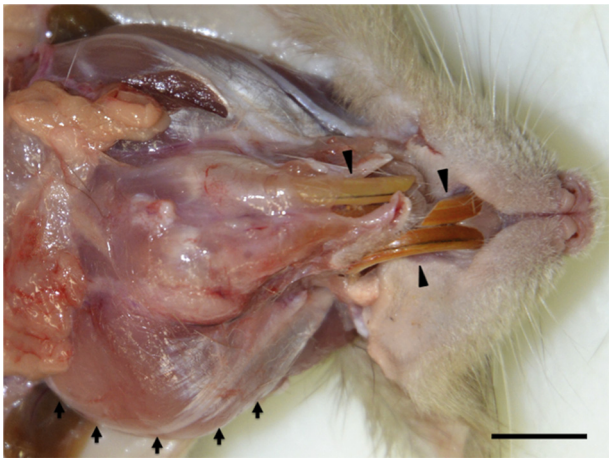

Fig. 1. Mandibular mass and incisor malocclusion, rat. Black arrows delineate the enlargement of the caudal left mandible, while the incisors are indicated by black triangles. Bar, 15 mm.