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 enaméblastoma. 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), 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
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. Post-mortem 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.](image-url)
had multiple small anastomosing nests and cystic sheets of neoplastic epithelium (metastases) within the subcapsular sinuses and invading the medulla of the node. The epithelial cells were multifocally keratinized and anaplastic and expressed cytokeratin (Supplementary Fig. 3). The lesion was diagnosed as a metastatic mandibular ameloblastic carcinoma.

An adult Amargosa vole (Microtus californicus scirpensis) from the captive breeding colony at the University of California, Davis was evaluated by colony staff and Campus Veterinary Services for a left-sided maxillary mass. A neoplastic or inflammatory mass was suspected and based on a poor prognosis, humane destruction was elected. The head was submitted for gross and histopathological evaluation. Grossly, a 1.2 × 1.2 × 0.8 cm cavitated mass expanded the left maxilla, compressed both nasal passages and deviated the rostral and left maxillary incisor tooth to the right (Fig. 4). The apical regions of the mandibular and maxillary cheek teeth protruded from the ventral aspect of the mandible and into the calvarium.

Histologically, the left maxilla was partially obliterated and the nasal passages were compressed by a large, ~0.7 cm diameter, cystic, neoplastic mass. The cyst was lined by variably thick, stratified epithelium and contained rafts of blood cells and acellular, eosinophilic debris. The cyst wall was comprised of neoplastic epithelium forming complex interlinked trabeculae and thin plexiform ribbons, often continuous with and forming complex projections from the cyst lining. The neoplastic epithelium demonstrated multiple rounded botryoid protruberances (Supplementary Fig. 4) with a prominent, single to multilayered border of palisading epithelial cells with rarely evident antibasilar nuclei. The centripetal epithelial cells were squamous-like, spindle-shaped to stellate, forming complicated interlacing streams and whorls with rare stellate reticulum-like intercellular junctions (Supplementary Fig. 5). The associated subepithelial fibrous stroma had multifocal irregular aggregates of amphophilic to basophilic matrix interrupted by irregularly sized lacunae (cementum). The remnant maxillary bone formed a variably thin rim of interlinking bony trabeculae at the lesion periphery. The lesion was diagnosed as cystic ameloblastoma of the maxilla.

A 6-month-old, client-owned, adult Syrian hamster (Mesocricetus auratus) was presented to the CAPE Service with a 3-week history of a rapidly enlarging right mandibular mass. Radiographic imaging demonstrated severe lysis of the right mandible with associated calcification or mineralization of the soft tissues. The clinical diagnosis was mandibular neoplasia. At the client’s request, the hamster was humanely destroyed and submitted for necropsy examination. The right mandibular incisor was displaced caudally and dorsally. The rostral portion of the right mandible was expanded by an irregular, 2 cm diameter, hard, white mass that extended to the rostral portion of the left mandible. The rostral portion of the mass contained a 1.5 × 1 × 0.5 cm cavitation that was surrounded by friable red tissue. The mass extended to the right zygomatic arch and orbital bone.
Histologically, the mandible was expanded and partially obliterated by a mass comprised of multiple islands of neoplastic epithelium separated by interlinking bands of fibrous stroma. The neoplastic epithelium formed round to oval follicles, interlinking plexiform ribbons and botryoid architectural structures (Supplementary Fig. 6). Centrally, many of the epithelial structures were cystic. Peripherally, the epithelial structures were often palisaded with a row of cuboidal to columnar basal-like cells. Nuclei were oval-shaped and rarely antibasilar. Centripetally, the epithelial cells often maintained a basal-like appearance with long intercellular bridges (stellate reticulum, Supplementary Fig. 7). The mandible was replaced by a peripheral rim of parallel, interlinking spicules of woven bone (periosteal hyperplasia). The lesion was diagnosed as ameloblastoma of the mandible.

These rodent epithelial tumours demonstrated histological features consistent with odontogenic histogenesis. Diagnostic features include the well-described cardinal odontogenic features (i.e. palisading basal-like epithelial cells with antibasilar nuclei and centralized stellate reticulum-like cells). Central cystic degeneration is a common feature of odontogenic epithelium (Regezi et al., 2012) and was identified in several of these lesions. In addition, the architectural arrangement of the neoplastic odontogenic epithelium in these rodent tumours was consistent with an odontogenic histogenesis. This odontogenic architecture included plexiform ribbons, broad interlinking trabeculae and, most notably, irregular epithelial structures with bosselated margins (rounded protuberances), a feature referred to by some pathologists as ‘ink drop’ or ‘medusoid’ architecture. For oral lesions, proliferative epithelium exhibiting medusoid features should be suspected of being odontogenic (Meuten, 2017).

Malignant ameloblastomas are rarely identified in man and occur more often in the mandible than the maxilla. A malignant ameloblastoma is a histologically typical ameloblastoma that has metastasized to the local lymph nodes or distant organs (Regezi et al., 2012). Direct extension of an ameloblastoma into an adjacent anatomical site (e.g. the nasal cavity) does not qualify for a malignant designation. In man, ameloblastoma-associated metastatic foci most often affect the lung; regional lymph nodes are the second most common sites. Previous reports of metastasis of odontogenic tumours in animals are limited to a single ameloblastic fibro-odontoma in an 11-year-old collie dog (metastatic foci were identified in the lymph nodes, lung, liver and eye) (Ueki et al., 2004).

Ameloblastic carcinoma is an ameloblastoma with cytological atypia (Barnes et al., 2005). Ameloblastic carcinomas can occur in the absence of metastatic foci. Therefore, a malignant ameloblastic carcinoma is an ameloblastoma with cytological atypia that also has evidence of local or distant metastasis. The lesion identified in the rat was associated with marked destruction and expansion of the left mandible together with metastasis to the submandibular lymph node. To the best of our knowledge, there is no previous documentation of a malignant ameloblastic carcinoma in any animal.

**Acknowledgments**

The authors are grateful for the helpful comments and insights provided by Drs. R. R. Dubielzig (University of Wisconsin, Madison), C. Reilly (UC Davis and Insight Veterinary Specialty Pathology) and J. Foley (UC Davis). We are also grateful for the technical expertise of the University of California, Davis, histotechnology staff, Dr. K. Murphy for manuscript editing, and clinicians Drs. J. Emerson, M. Gleeson and M. Sadar. Funding for vole colony management and disease assessment was provided by the California Department of Fish and Wildlife, Palm Springs Field Office, Bureau of Land Management, and the US Fish and Wildlife Service (grant no. #F14AP01006). This study adhered to the ethical use of animals in research as put forth by the UC Davis School of Veterinary Medicine Institutional Animal Care and Use Committee (IACUC).

**Conflict of Interest Statement**

The authors declare no conflict of interest with respect to the publication of this manuscript.
Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jcpa.2017.07.002.

References


[Received, April 12th, 2017]

[Accepted, July 4th, 2017]