

MANDIBULAR ODONTOGENIC SARCOMA (AMELOBLASTIC FIBRODENTINOSARCOMA) IN AN AGED CAT – SHORT COMMUNICATION

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A 13-year-old male cat presented with an ill-defined mass in the rostral mandible causing destruction and loss of alveolar bone. Microscopically, the mass consisted of cords or islands of benign odontogenic epithelium and a malignant, pleomorphic spindle-shaped cell component with dysplastic dentine formation. Immunohistochemically, neoplastic mesenchymal cells proved to be strongly positive for vimentin and negative for cytokeratins, desmin, actin and S100 protein; the Ki67 proliferation index was high. Morphological and immunohistochemical features largely overlap those reported for ameloblastic fibrodentinosa sarcoma, an uncommon histologic subtype of odontogenic sarcoma recognised in humans but not reported previously in animals. Ki-67 expression assessment may help to discriminate between malignant and benign forms of odontogenic tumours but the final diagnosis is mainly morphological.

Key words: Feline, fibrodentinosa sarcoma, odontogenic, sarcoma

Odontogenic tumours are uncommon in domestic animals, with the exception of canine acanthomatous ameloblastoma (Walsh et al., 1987; Poulet et al., 1992; Head et al., 2002, 2003). They represent a heterogeneous group of proliferative lesions that include epithelial and mesenchymal tumours. Epithelial tumours are further divided based on whether neoplastic ameloblasts have the inductive potential for mesenchymal cells into odontogenic components (Walsh et al., 1987; Poulet et al., 1992; Head et al., 2003; Sakai et al., 2008). Therefore, epithelial odontogenic tumours can be divided into non-inductive tumours without odontogenic mesenchymal component, such as ameloblastoma, amyloid-producing odontogenic tumour, and acanthomatous ameloblastoma, and inductive tumours with odontogenic mesenchyme, such as feline inductive odontogenic tumour or inductive fibroameloblastoma, ameloblastic fibroma, dentinoma, ameloblastic odontoma, complex odontoma, and compound odontoma (Walsh et al., 1987; Poulet et al., 1992; Head et al., 2003).

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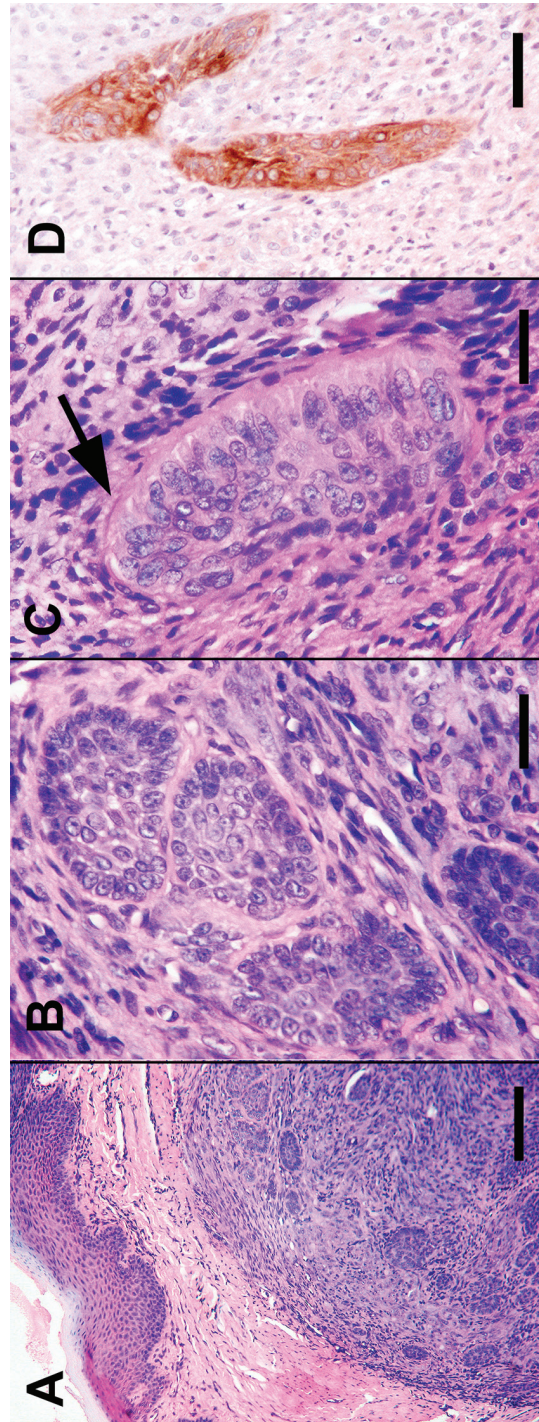


Fig. 1A–D. Ameloblastic fibrodentinosa. A. Low magnification showing the biphasic odontogenic tumour occupying the subepithelial connective tissue. Haematoxylin and eosin (HE) staining; bar = 100 μ m. B. Epithelial component consists of columnar or cuboidal peripheral ameloblastic-like cells with no signs of atypia. HE; bar = 25 μ m. C. Epithelial cells showing focal reverse nuclear polarity and basilar cytoplasmic clearing. Juxta-epithelial early hyalinisation in the connective tissue is also present (arrow). HE; bar = 25 μ m. D. Cytokeratins are diffusely positive in the epithelium and negative in the mesenchymal component. Immunohistochemistry (IHC); bar = 50 μ m

The WHO Histological Classification of Tumours of the Alimentary System of Domestic Animals does not contain sarcomatous forms of odontogenic tumours (Head et al., 2003). As far as we are able to find, only two malignant odontogenic tumours with sarcomatous component have been reported previously in a dog (Galán et al., 2007) and a bull (Sartin et al., 1998). The purpose of this report is to describe the morphological and immunohistochemical features of a neoplasm composed of benign odontogenic epithelium, resembling ameloblastoma, and a malignant mesenchymal population exhibiting features of fibrosarcoma with deposits of dentinoid-like material in an aged cat. To the authors' knowledge, this is the first description of such a lesion in the cat.

A 13-year-old male intact European Shorthair cat was presented with an irregular, painless, firm mass, approximately $2 \times 1 \times 1$ cm, located in the rostral lower jaw. Radiography revealed destruction and loss of alveolar bone. The mass was first noticed by the owner six weeks prior to the veterinary consultation. Three months previously, another similar mass had been surgically removed from the same area by a different veterinarian, but it was not investigated further. The regional lymph nodes were not enlarged at that time. Haematological and biochemical analyses did not show any abnormality. Pulmonary metastasis was not detected in thoracic radiographs. The mass was surgically removed by nodulectomy for diagnosis. On gross examination, it was solid to fibromatous in consistency and of whitish colour on cut section. The tissue was fixed in 10% buffered formalin, processed routinely, embedded in paraffin wax, sectioned at 5 μ m, and stained with haematoxylin and eosin and Congo Red stains. Furthermore, immunohistochemical labelling was performed with mouse monoclonal primary antibodies raised against cytokeratins (clone AE1/AE3, Dako, Glostrup, Denmark), vimentin (clone V9, Dako), desmin (clone D33, Dako), actin (clone HHF-35, Dako), Ki67 (clone MIB-1, Dako), and rabbit polyclonal primary antibody against S100 protein (Dako).

Histopathological examination revealed a non-encapsulated biphasic tumour expanding the subepithelial connective tissue and elevating the overlying hyperplastic mucosa (Fig. 1A), composed of irregularly shaped islands, anastomosing strands, solid bands of benign odontogenic epithelium and abundant, malignant mesenchymal tissue. The epithelial component was composed of islands and cords of cuboidal to columnar peripheral ameloblastic-like cells arranged in a palisading pattern with central loose appearance and occasional reminiscence of stellate reticulum (Fig. 1B). Focal reverse nuclear polarity, crowding of the nuclei, basilar cytoplasmic clearing and juxta-epithelial early hyalinisation in the connective tissue were also noted (Fig. 1C). The mesenchymal component predominated over epithelial elements (Fig. 2A). It consisted of closely arranged plump and spindle cells with nuclear pleomorphism, hyperchromatism or vesicular nuclei with small to indistinct nucleoli, and numerous mitotic figures. Small necrotic foci were recognised. Variable-sized deposits of Congo Red-negative,

extracellular, eosinophilic dense material, compatible with dentinoid material formation, were noted closely related to mesenchymal cells (Fig. 2A). Immunohistochemically, cytokeratin was strongly positive in the odontogenic epithelium and negative in the mesenchymal component (Fig. 1D), while vimentin was strongly positive in the mesenchymal component and negative in the odontogenic epithelium (Fig. 2B). Ki-67 was expressed by up to 50% of the mesenchymal cells (Fig. 2C) and 20% of the epithelial cells. Tumour cells were negative for desmin, actin, and S100 protein. Based on the morphologic and immunohistochemical features, a final diagnosis of ameloblastic fibrodentinosa sarcoma was made.

Malignant odontogenic tumours with sarcomatous features are extremely rare in animals. To the authors' knowledge, only two cases have been previously reported in animals (Sartin et al., 1998; Galán et al., 2007). In humans, odontogenic sarcomas are rare malignancies of the jaws composed of a completely benign epithelium scattered throughout malignant mesenchymal tissue that can arise by malignant transformation from an originally benign odontogenic pre-existent neoplasm having become sarcomatous, or it may also arise *de novo*. They include ameloblastic fibrosarcoma (AFS), ameloblastic fibrodentinosa sarcoma (AFDS), ameloblastic fibrodontosa sarcoma (AFOS), and odontogenic carcinoma (OCS) (Kobayashi et al., 2005; Barnes et al., 2010; Lai et al., 2012; Hemavathy et al., 2013; Loya-Solis et al., 2015). AFDS is a very rare subtype similar to AFS in which parts of the odontogenic epithelium have exerted sufficient inductive influence to result in a limited amount of immature or dysplastic dentine (dentinoid) formation, even though the mesodermal component is sarcomatous (Barnes et al., 2010; Hemavathy et al., 2013).

In the current case, the diagnosis was based on the concomitant occurrence of both soft (odontogenic epithelium and mesenchyme) and hard dental tissue (dentinoid) deposition. The epithelium was composed of benign ameloblast-like cells with scant reminiscence of stellate reticulum. Stellate reticulum is reported for many odontogenic tumours but it is not a consistent feature (Poulet et al., 1992). Cuboidal or columnar peripheral cells arranged in a palisading pattern, reverse nuclear polarity, basilar cytoplasmic clearing, or juxta-epithelial hyalinisation of the connective tissue were all present in our case, and are useful diagnostic criteria when stellate reticulum is not present, especially for malignant and/or undifferentiated forms (Poulet et al., 1992; Loya-Solis et al., 2015). Poorly differentiated tumours tend to show greater stromal cellularity with a decrease in the epithelial component. It has been suggested that anaplasia of mesenchymal tissue is correlated with the degeneration of benign odontogenic epithelium, and the loss of benign odontogenic epithelium in these tumours results from overgrowth of the malignant mesenchymal portion of the lesion (Hemavathy et al., 2013). The malignant character was manifested by the presence of cellular atypia, mitoses and a high (up to 50%) Ki-67 immunohistochemical expression in the mesenchymal component. This index was even higher than in

human ameloblastic fibrosarcomas (estimated to be 13.5%) (Sano et al., 1998). The eosinophilic dentinoid was regarded as a neoplastic component since it was detected within malignant mesenchymal tissue.

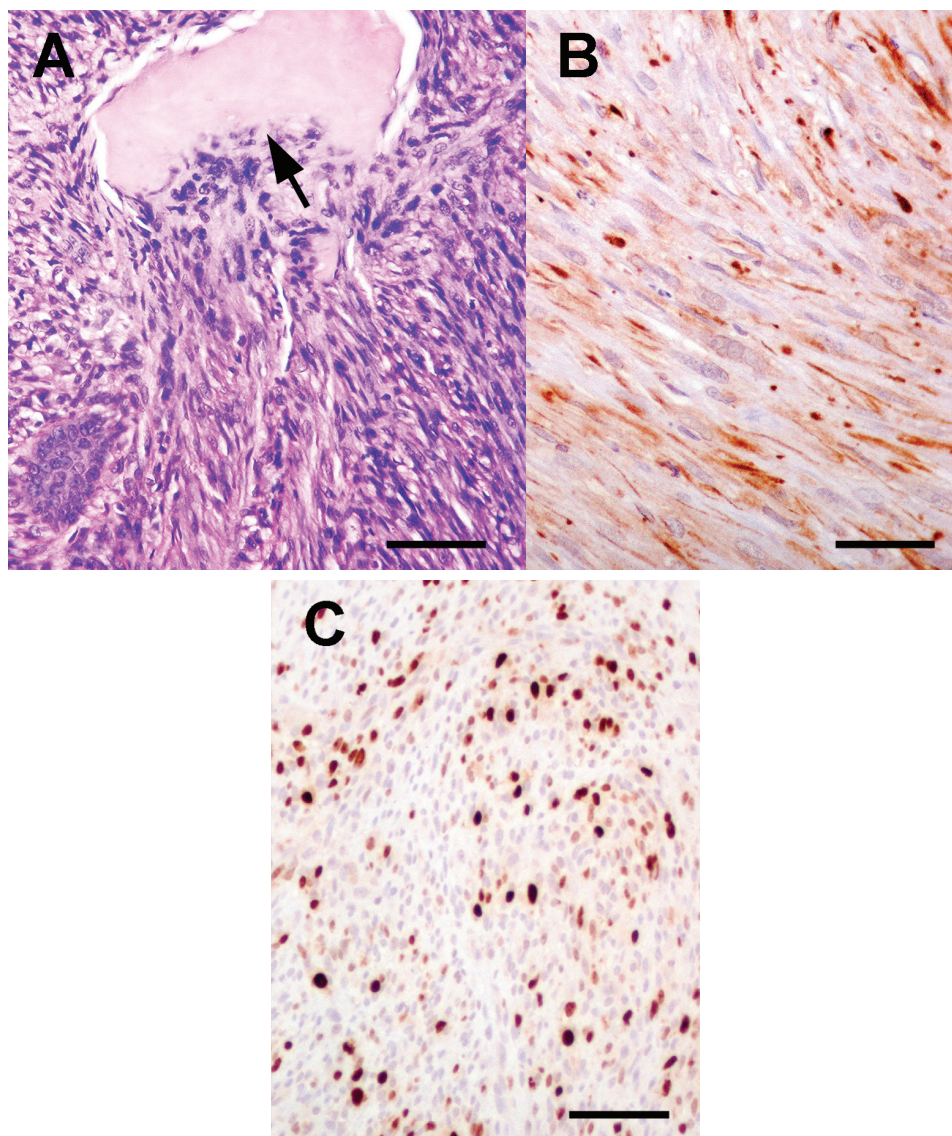


Fig. 2A–C. Ameloblastic fibrosarcoma. A. Sarcomatous component predominates over the epithelial elements and is composed of spindle cells with nuclear pleomorphism. Note extracellular, eosinophilic dense material compatible with dentinoid closely related to mesenchymal cells. HE; bar = 50 μ m. B. Sarcomatous cells show specific, intense, cytoplasmic labelling to vimentin. IHC; bar = 25 μ m. C. Immunolabelling for Ki-67 is present in a high proportion of malignant mesenchymal cells. IHC; bar = 50 μ m

Ameloblastic fibrodentinosa sarcoma should be included in the list of differential diagnoses of odontogenic tumours in small animals. Ameloblastic fibroma (AF) is the main differential diagnosis of AFS. It consists of cords and islands of proliferating odontogenic epithelial cells loosely embedded in irregularly shaped foci of mesenchymal cellular connective tissue resembling dental papilla (Poulet et al., 1992; Sano et al., 1998). AF has no atypia or mitoses and dentin is not formed, as occurs in the present case. Feline inductive odontogenic tumour (FIOT) is a rare odontogenic neoplasm in which benign islands of odontogenic epithelium have inductive potential to form aggregated foci or spherical condensations of dental pulp-like mesenchymal cells (ectomesenchyme) (Gardner, 1998; Sakai et al., 2008). These cells lack malignancy. In the present case, atypia and mitoses were consistently observed. Immunohistochemistry for Ki-67 antigen usually reveals less than 2% of positive cells in both epithelial and mesenchymal cells of FIOTs (Sakai et al., 2008), whereas in our case this percentage is clearly higher. In addition, FIOT occurs in cats up to 3 years of age (Gardner, 1998) while the subject of the present case was aged. Feline amyloid-producing odontogenic tumour (APOT) is a rare neoplasm of aged cats which produces mineralised substance and amyloid immersed in irregularly shaped islands and sheets of odontogenic epithelium within a stroma of inactive fibrous connective tissue (Ohmachi et al., 1996). Amyloid nature of the eosinophilic, dense material noted in our case is unlikely since the Congo Red stain was negative. Moreover, amyloid is produced by ameloblast-like cells in APOT, whereas in the present case the material was observed to be within the mesenchymal component. Finally, microscopic features of the mesenchymal component in odontogenic sarcomas are virtually identical to those shown by oral fibrosarcoma (Head et al., 2002). However, the presence of odontogenic epithelium or other odontogenic components (such as dentin or enamel) allows differentiation.

The present case was clinically aggressive, including destruction of alveolar bone, although no metastasis was reported at the time of diagnosis. Cases of malignant sarcomatous odontogenic tumours reported previously in animals were also locally aggressive lesions, but metastases were not described. In humans, the prognosis associated with AFS is fairly good following surgical resection; about 37% recur and only two cases of metastasis have been reported (Loya-Solis et al., 2015).

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