Spindle Cell Ameloblastic Carcinoma in a Labrador Retriever Dog

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ABSTRACT. A 13-year-old castrated male Labrador retriever dog presented with a mass caudal to the first molar of his left mandible. Although the tumor was excised, a recurrent tumor was detected one month later and resected. Both tumors displayed invasive growth and were composed of neoplastic proliferation arranged in irregular lobules, nests and cords continuous with mucosal epithelium. The most prominent feature of the tumors was the presence of many proliferating spindle cells admixed with palisading basal-like cells, acanthocytes and stellate cells. In immunohistochemical examinations, the spindle cells were found to be positive for vimentin; cytokeratin AE1/AE3, 5/6, 14 and 19; and p63. The other neoplastic cells were positive for all of these markers shown above except vimentin. Based on these findings, the tumors were diagnosed as spindle cell ameloblastic carcinoma.

NOTE. Pathology

KEY WORDS: ameloblastic carcinoma, canine, spindle cell.


Except for canine acanthomatous ameloblastoma, odontogenic neoplasms are uncommon in domestic animals [3]. Ameloblastoma originates from the odontogenic epithelium with no known metastasis [6]. In human, ameloblastic carcinoma represents ameloblastoma-like features, cellular atypia and morphological malignancy without metastasis [2]. Only two cases of ameloblastic carcinomas have been reported in domestic animals [4, 9]. In addition, the spindle cell variant of ameloblastic carcinoma is rare in humans [8, 11]. The present report describes a canine case of spindle cell ameloblastic carcinoma.

A 13-year-old castrated male Labrador retriever dog with a mass caudal to the first molar of his left mandible was presented to an animal hospital (Fig. 1). This dog had suffered from mitral insufficiency and had been medicated with an angiotensin-converting enzyme inhibitor for about 10 years. A radiographic examination did not detect any pulmonary metastasis. Although the tumor was excised, a recurrent mass was found without metastasis one month later and resected. He deceased about two months later after the second operation. The cause of death was unknown, because necropsy was not performed. The shape of the bone around the mass was obscure on radiographic examination. Both of the first (5 × 1.7 × 1 cm) and second masses (4.2 × 1.5 × 2.5 cm) displayed a friable surface and a white mildly firm interior. These tissues, fixed in 10% buffered formalin, were routinely processed and embedded in paraffin wax. The tissue sections (3 μm) were stained with hematoxylin and eosin (HE). Immunohistochemical (IHC) examinations were performed using the streptavidin-biotin peroxidase method with commercial kits (Nichirei Corp., Tokyo, Japan). The primary antibodies employed in these examinations are as follows: cytokeratin (CK) AE1/AE3 (Nichirei, Tokyo, Japan; prediluted), CK 5/6 (Clone D5/16 B4; Chemicon, Temecula, CA, U.S.A.; prediluted), CK 14 (Clone LL002; Thermo Scientific, Runcorn, U.K.; diluted 1 in 20), CK 19 (Clone BA17; Thermo Scientific; diluted 1 in 150), p63 (Clone 4A4; Thermo Scientific; diluted 1 in 200) and vimentin (Clone V9; Nichirei; prediluted).

Microscopically, the first and second masses exhibited the same histological features; i.e., they consisted of neoplastic cells arranged in irregular shaped lobules, nests and anastomosing bundles/cords and displayed invasive growth. The neoplastic cords were occasionally continuous with the normal mucosa (Fig. 2). Cysts had formed in the center of some lobules. The major neoplastic cells were spindle-shaped (Fig. 3) and occasionally showed keratinization. Some tumor cell nests were constructed of acanthocytes with occasional peripheral palisading by basal-like cells (Fig. 3), and others were composed of stellate cells arranged in a plexiform pattern (Fig. 4). In each high power field, 0–8 mitotic figures were detected (> 400). The spindle cells exhibited high mitotic index, whereas mitoses were not observed in the acanthocytes. Osteoid and small amounts of bone were scattered in the stroma. In the IHC examinations, the spindle cells and the peripheral cells of the neoplastic nests were found to be positive for CK 5/6, 14 and 19; p63 and vimentin (Figs. 5–7), and sparsely positive for CK AE1/AE3. The other neoplastic cells were positive for all of these molecules except vimentin.

The tumors were diagnosed as spindle cell ameloblastic carcinoma on the basis of the following features: odontogenic-like structures, such as peripheral palisading and stellate reticulum, with atypical spindle cells, a high mitotic rate, invasive growth and no evidence of metastasis. Stromal os-
Fig. 1. A gingival mass is found caudal to the first molar of the left mandible.
Fig. 2. The neoplastic cells are occasionally continuous with mucosal epithelium, and cysts in variable size are formed. HE. Bar=330 μm.
Fig. 3. The major neoplastic cells are spindle-shaped and arranged in irregular bundles. Acanthocytes or basal-like cells are observed together with occasional peripheral palisading. HE. Bar=55 μm.
Fig. 4. Stellate reticulum in the neoplastic cell nest. HE. Bar=30 μm.
Figs. 5–7. Positive immunohistochemical labeling of the spindle cells for CK 14 (5), vimentin (6) and p63 (7). IHC. Bars=30 μm.
teoid and bone tissue are sometimes detected in ameloblas-
toma and are thought to be produced by secondary epithelial
inductive effects [3].

The immunohistochemical characteristics of the spindle
cells suggested that they originated from odontogenic
peripheral cells. CK 5/6 and 14 are expressed in the odon-
togenic epithelia, normal gingiva and several odontogenic
tumors in dogs [1], and the epithelial components of the
human enamel organ and ameloblastoma are positive for CK
14 and 19 [5, 12]. p63, an immunohistochemical marker for
epithelial basal cells, has been detected in the tooth germ
and peripheral ameloblastoma cells in humans [13]. Vimentin
and cytokeratins are coexpressed in parts of the enamel
organ during the early stages of tooth development, human
ameloblastoma and equine ameloblastic carcinoma [4, 7,
10]. Spindle cell sarcomas and malignant melanomas are
generally negative for epithelial markers. Thus, spindle cells
in the present case are regarded as epithelial neoplasm.

Ameloblastoma is the tumor that exhibits odontogenic
epithelial features such as peripheral palisading of basilar
cells, having apical crowding of the nucleus and basilar cyto-
plasmic clearing, and formation of long intercellular bridges
typical of stellate reticulum [6]. Our case differs from amelo-
blastoma in atypia of peripheral cells, namely spindle shaped
cells, and obvious peripheral infiltration. The World Health
Organization classification of human tumors defines amelo-
blastic carcinoma as a tumor that represents the histological
features of ameloblastic differentiation and cytologic atypia
without metastasis [2]. In addition, it demonstrates invasive
growth and can destroy alveolar bone. Peripheral amelo-
blastic carcinoma develops in the gingiva and displays an
ameloblastoma-type histology together with keratinization
[2]. Human spindle cell ameloblastoma exhibits an admixture of proliferating sarcomatoid spindle cells and amelo-
blastomatous epithelial cells [8, 11]. These features agree
with those of the present case, except for the minimum or
absence of bone destruction. The present tumor had continu-
ity with the oral epithelial layer, suggesting that it had a pe-
ripheral origin. In humans, peripheral type ameloblastoma is
thought to arise from odontogenic epithelial remnants or the
basal cell layer of the gingival epithelium, and some of these
tumors fuse with or originate from the mucosal epithelium
[2]. We speculate that this case presented with the minimal or
no bone lysis, because the tumor arose from mucosal cells
rather than from odontogenic epithelial remnants in the jaw.

In conclusion, this report describes a rare canine odon-
togenic neoplasm that was characterized by the presence of
spindle neoplastic cells, which were positive for epithelial
and mesenchymal immunohistochemical markers.

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