

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.

KEY WORDS: ameloblastic carcinoma, canine, spindle cell.

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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 6 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 ($5 \times 1.7 \times 1$ cm) and second masses ($4.2 \times 1.5 \times 2.5$ 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 ($3 \mu\text{m}$) were stained with hematoxylin and eosin (HE). Immunohistochemical (IHC) examinations were per-

formed 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 ($\times 400$). 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-

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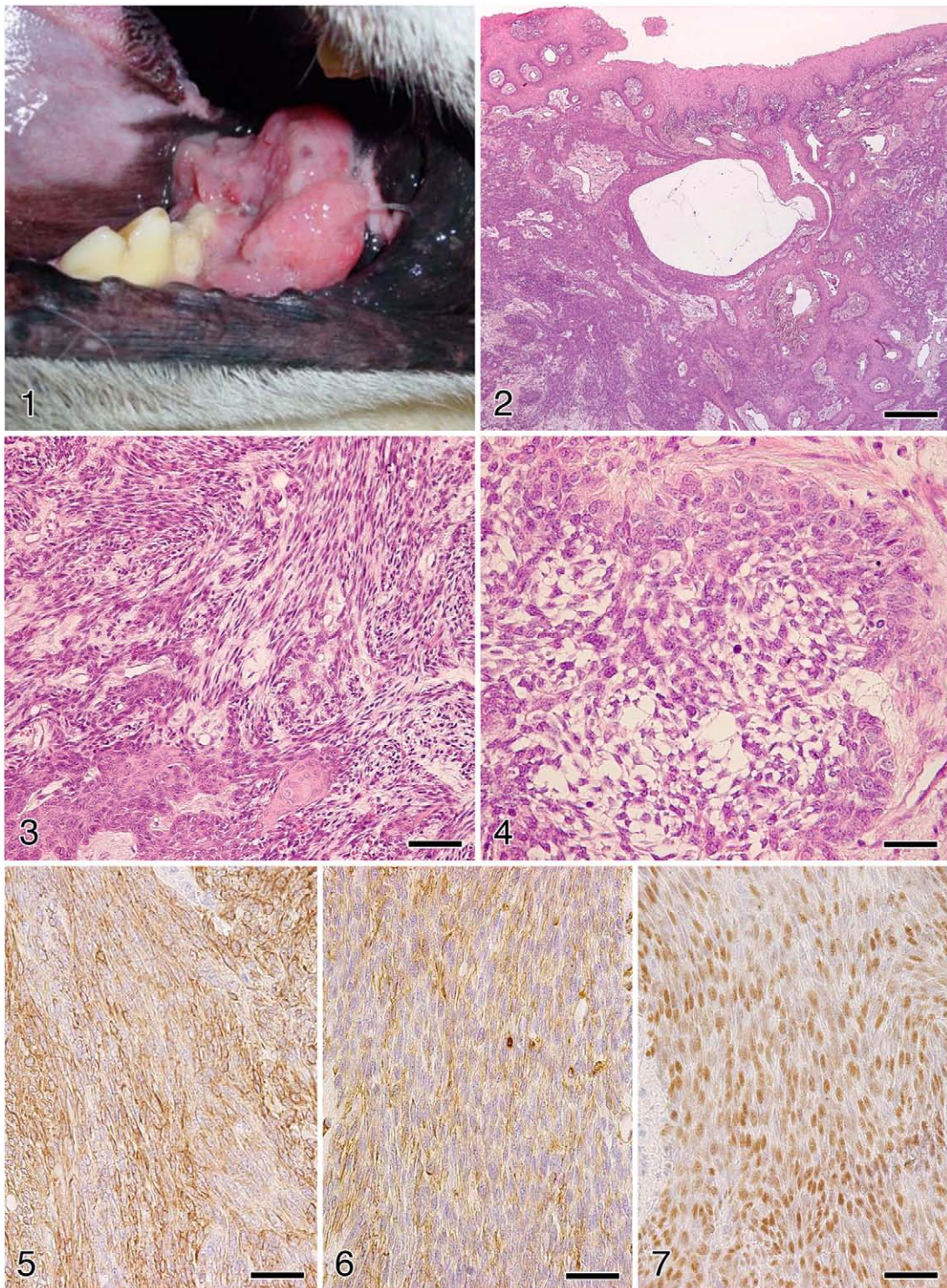


Fig. 1. A gingival mass is found caudal to the first molar of the left mandible.

Fig. 2. The neoplastic cells are occasionally continuous with mucosal epithelium, and cysts in variable size are formed. HE. Bar=330 μ m.

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 μ m.

Fig. 4. Stellate reticulum in the neoplastic cell nest. HE. Bar=30 μ m.

Figs. 5–7. Positive immunohistochemical labeling of the spindle cells for CK 14 (5), vimentin (6) and p63 (7). IHC. Bars=30 μ m.

teoid and bone tissue are sometimes detected in ameloblastoma 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 odontogenic 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 cytoplasmic clearing, and formation of long intercellular bridges typical of stellate reticulum [6]. Our case differs from ameloblastoma in atypia of peripheral cells, namely spindle shaped cells, and obvious peripheral infiltration. The World Health Organization classification of human tumors defines ameloblastic 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 ameloblastic carcinoma develops in the gingiva and displays an ameloblastoma-type histology together with keratinization [2]. Human spindle cell ameloblastic carcinoma exhibits an admixture of proliferating sarcomatoid spindle cells and ameloblastomatous 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 continuity with the oral epithelial layer, suggesting that it had a peripheral 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 odontogenic neoplasm that was characterized by the presence of spindle neoplastic cells, which were positive for epithelial and mesenchymal immunohistochemical markers.

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