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NEOPLASTIC DISEASE

A Non-joint Tissue Biphasic Synovial Sarcoma in a Dog

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Summary

A subcutaneous tumour was identified in the malar region of a 14-year-old neutered female mixed breed dog. The dog was humanely destroyed and necropsy examination was performed. The tumour did not invade neighbouring tissues and no metastasis was found. Microscopically, the tumour showed a range of features including the presence of multinucleated giant cells, chondrocyte differentiation and cystic or slit-like structures. All of these features are consistent with previously reported descriptions of synovial sarcomas in dogs. Mesenchymal cells accounted for the majority of the tumour, but cytokeratin-positive epithelioid components were also confirmed by immunohistochemistry. The tumour was diagnosed as a biphasic type of synovial sarcoma. Synovial sarcoma in man may develop in tissues unrelated to joints and this is the first report of a non-joint synovial sarcoma in a dog.

Keywords: biphasic tumour; dog; immunohistochemistry; synovial sarcoma

Synovial sarcomas arise in joints and have been reported in dogs, cats, cattle and ferrets (Tremblay *et al.*, 2000; Oyamada *et al.*, 2004). Canine synovial sarcomas occur mainly in the elbow or stifle and rarely involve the hip or jaw (Griffith *et al.*, 1987; Karayannopoulou *et al.*, 1992). Microscopically, synovial sarcomas are categorized into four subtypes: (1) spindle cell dominant, monophasic fibroblastic type, (2) epithelioid cell dominant, monophasic epithelioid type, (3) biphasic type and (4) poorly differentiated type. Of these subtypes, the fibroblastic type is predominant in animals (Fox *et al.*, 2002). Although synovial sarcomas have several characteristic histological features, they are difficult to distinguish from other tumours such as malignant fibrous histiocytomas, fibrosarcomas, peripheral nerve sheath tumours, melanomas, chondrosarcomas and giant cell tumours of the soft tissue (Loukopoulos *et al.*, 2004). Despite the term 'synovial' sarcoma, the tissue of origin of these tumours remains controversial. In some reports, these tumours were derived from primitive mesenchymal precursor cells, which are located outside of the synovial membrane and have the ability to differentiate into epithelioid or fibroblastic cells (Mitchell and Hurov, 1979; Vail *et al.*, 1994). In the present paper, we report a tumour of the jaw, unrelated to the joint, but with histological characters of a synovial sarcoma.

A 14-year-old neutered female mixed breed dog was referred to a veterinary hospital for swelling of the left mandibular region. The swelling had enlarged markedly over a period of several months and the presence of the mass had prevented the dog from closing its left eye for the past 3 months. The clinical condition of the dog had worsened as the size of the tumour increased. Four months after the consultation, the dog was humanely destroyed. Post-mortem

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examination revealed a multilobulated, pale white mass (15 × 12 × 11 cm) in the subcutaneous tissue of the left cheek, extending to the base of the left ear. The mass did not invade the mandibular joint. No metastasis was found in any other tissues. A small amount of serous fluid leaked from the tumour on gross sectioning.

The mass was fixed in 10% neutral buffered formalin and embedded in paraffin wax. Sections were stained with haematoxylin and eosin (HE) and Masson's trichrome stain. Immunohistochemistry (IHC) was performed using a VECTASTAIN® Elite ABC Kit (Vector Laboratories Inc., Burlingame, California, USA). The primary antibodies used were: anti-cytokeratin AE1/AE3 (CK AE1/AE3; clones AE1/AE3, mouse monoclonal, 1 in 50 dilution; Dako, Glostrup, Denmark), anti-cytokeratin (clone MNF116, mouse monoclonal, 1 in 50 dilution; Dako), anti-vimentin (clone V9, mouse monoclonal, 1 in 50 dilution; Dako), anti-chromogranin A (CGA; rabbit polyclonal, 1 in 3,000 dilution; Yanaihara Institute Inc., Shizuoka, Japan), anti-S100 protein (rabbit polyclonal, 1 in 400 dilution; Dako), anti-neuron-specific enolase (NSE; clone BBS/NC/VI-H14, mouse monoclonal, 1 in 100 dilution; Dako), anti-ionized calcium-binding adapter molecule-1 (Iba-1; rabbit polyclonal, 1 in 250 dilution; Wako Pure Chemical Co., Osaka, Japan), anti-glial fibrillary acidic protein (GFAP; clone 6F2, mouse monoclonal, 1 in 50 dilution; Dako), anti-α-smooth muscle actin (α-SMA; clone 1A4, mouse monoclonal, 1 in 100 dilution; Dako), anti-desmin (clone D33, mouse monoclonal, 1 in 2 dilution; Dako), anti-von Willebrand factor (vWF; rabbit polyclonal, 1 in 500 dilution; Dako), anti-melan-A (clone A103, mouse monoclonal, 1 in 25 dilution; Dako) and anti-osteocalcin (clone OC4-30, mouse monoclonal, 1 in 100 dilution; GeneTex Inc., Los Angeles, California, USA). Antigen retrieval was performed by either microwaving in 10 mM citrate buffer (pH 6.0) at 90°C for 10 min (NSE, GFAP and vWF), autoclaving in 10 mM citrate buffer (pH 6.0) at 121°C for 10 min (CK AE1/AE3, CK MNF116, vimentin, Iba-1, α-SMA and melan-A), incubating in a hot water bath in 10 mM citrate buffer (pH 6.0) at 60°C for 20 min (chromogranin A) or covering sections with Proteinase K and incubating for 10 min at 37°C (S100 and osteocalcin). No antigen retrieval methods were performed for the desmin IHC. Sections were treated with H_2O_2 0.3% in methanol for 30 min to block endogenous peroxidase activity. The sections were blocked with normal goat or horse serum at room temperature for 30 min. Each section was incubated with primary antibody at 4°C overnight and then with a secondary antibody against mouse or rabbit immunoglobulin (Ig) G applied at room temperature for 30 min. The ABC reagent was applied at room temperature for 30 min. Antibody-binding was 'visualized' with 3, 3′-diaminobenzidine (DAB) chromogen and counterstaining with haematoxylin.

Microscopically, the tumour was composed of round and spindle cells with an oval to round nucleus and eosinophilic cytoplasm with ill-defined borders. Mitotic figures were frequently observed (mitotic index 11.2 per 10 ×40 objective fields), particularly in cells that surrounded blood vessels or formed slit-like spaces (Fig. 1). A large area of necrosis was present. Between the neoplastic lobules, there was a large amount of collagen. Tumour cells with chondroid differentiation or multinucleated giant cells were also observed (Fig. 2). In some regions, there were cystic structures with neoplastic cells within the cystic space.

The tumour cells near blood vessels and those forming slit-like structures were positive for CK AE1/AE3 and all other cell components expressed vimentin (Figs. 3 and 4). Iba-1-positive cells, consistent with macrophages, were scattered throughout the tumour. These cells were negative for all other antibodies.

Cystic or slit-like structures and multinucleated giant cells are commonly documented in animal synovial sarcomas (Lipowitz *et al*., 1979; Silva-Krott *et al*., 1993; Slayter *et al*., 1994; Pool and Thompson, 2002; Yamate *et al*., 2006). In addition, the presence of chondroid differentiation has also been reported in the dog (Griffith *et al*., 1987). Similar findings were also observed in the present case, leading to a diagnosis of synovial sarcoma. The tumour was formed of both cytokeratin-positive epithelioid and vimentin-positive mesenchymal components, but was negative for the other antibodies tested. These

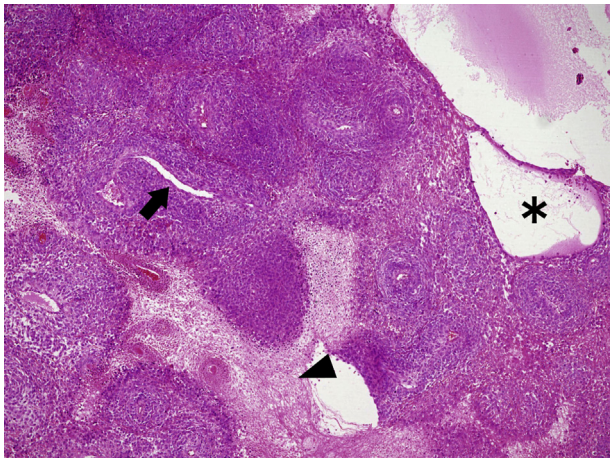

Fig. 1. Neoplastic cells proliferating around blood vessels or slit-like spaces (arrow). Necrotic areas (arrowhead) and cystic structures (asterisk) are also present. HE. ×40.