Canine biphasic synovial sarcoma: case report and immunohistochemical characterization

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Introduction

Tumors affecting joints are rare, and most are malignant rather than benign. Those reported in the veterinary literature are almost exclusively synovial sarcomas affecting dogs [2,37]. Synovial sarcoma has been reported infrequently in cats, cattle, horses and other species [33], although it accounts for about 8% of all soft-tissue sarcomas in humans [33]. In dogs, it most frequently involves the stifle and elbow, although other sites, including, for example, a rare case with bilateral hip joint involvement, have been reported [17].

Despite the assumed mesenchymal origin of the tumor and a morphological similarity with normal synovial tissue lining joints and tendon sheaths, the histogenesis of synovial sarcoma is not clearly defined [10,18,23]. Microscopically, it may be characterized by a monophasic or biphasic cellular pattern; the biphasic pattern is diagnostically more distinct and comprises of a sarcomatous component and an epithelioid component, which may form clefts and pseudoacini [25]. Synovial sarcoma may therefore resemble malignant fibrous histiocytoma, fibrosarcoma, giant-cell tumor of soft tissue or other tumors [5,31]. Consequently, it may present a diagnostic challenge for some pathologists and may be underdiagnosed, particularly atypical or monophasic variants, without the classic biphasic features, or cases with metaplastic bone formation or calcification zones. It is particularly important to differentiate synovial sarcomas from osteosarcomas, a defining feature of which is osteoid production by the malignant cells, because the latter tend to metastasize to the lungs and lymph nodes later in the clinical course of the disease [25,32].

Similarly, while the possible role of certain oncogenes and tumor suppressor genes [5], such as β-catenin [14] and p53 [28], in the pathogenesis of human synovial sarcoma has been reported, the molecular pathology of canine synovial sarcoma has not studied extensively or understood.

A specific immunohistochemical profile for canine synovial sarcoma has not been clearly defined previously, and reports on various epitopes are sparse [1]. The
development of such a profile may provide clues to the histogenesis of the phenotypically mesenchymal and epithelial elements of the tumor, while, at the same time, it may be of value in the differential diagnosis of challenging cases, decreasing the risk of under- and mis-diagnosis. Immunohistochemical detection of Epithelial Membrane Antigen (EMA), for example, may allow the identification of epithelioid components of human synovial sarcoma [27], although immunoreactivity to EMA has not been reported in canine tissues.

In the case presented here, the clinical, radiological and pathologic features of a biphasic synovial sarcoma in a young dog are described, the tumor is characterized using immunohistochemistry and histochemistry, and the immunohistochemical profile of the tumor is discussed in relation to the histogenesis, pathogenesis and differential diagnosis of canine synovial sarcoma.

Materials and Methods

A two-year-old male Rottweiler was referred to the University Veterinary Hospital, Universiti Putra Malaysia for evaluation of progressive lameness of the left forelimb of 4 months duration. Clinical, cytological and radiological examinations, and following the animal's euthanasia, the post mortem and histopathological examination were performed in a routine fashion.

Immunohistochemistry was performed on formalin-fixed, paraffin-embedded, silane-coated slides employing a streptavidin-biotin-peroxidase protocol as described previously [15,21], counterstained with haematoxylin. The antibodies used were: vimentin (V9 antibody, 1:400 dilution), cytokeratin (MNF116, 1:800), S-100 (1:400), Proliferating Cell Nuclear Antigen (PCNA, PC-10, 1:800), Epithelial Membrane Antigen (EMA, E29) (all DAKO, Carpinteria, USA), p21 protein (NCL-W AF1, 1:30), Retinoblastoma susceptibility gene protein (NCL-Rb, 1:50, both Novocastra), and p53 protein (CM-1 antibody, 1:75, Signet Laboratories, USA). The slides were subjected to ten minutes of microwave heating (low setting) in a citrate buffer, pH 6. Positive controls were neoplastic or normal tissues known to contain the relevant epitope [7,36]. The primary antibody was substituted with non-immune sera or Tris buffer in the negative controls.

Results

History and clinical examination
A two-year-old male Rottweiler was referred to the University Veterinary Hospital, Universiti Putra Malaysia for evaluation of progressive lameness of the left forelimb of 4 months duration. It had no history of trauma and many veterinarians had treated it with different types of non-steroidal anti-inflammatory drugs, without improvement of the lameness. Upon physical examination, the dog was depressed, and having non-weight bearing lameness of the left forelimb. Severe muscle atrophy of the limb was observed. Pain was evident upon palpation and manipulation of the elbow joint. There was also evidence of soft tissue swelling around the joint. Neurological examination revealed no abnormalities.

Initial radiological examination
The mediolateral radiograph of the left elbow revealed generalized reduced density of the distal humerus and also the proximal radius and ulna. The trabecular pattern of the olecranon is ill defined. Note the cortical destruction of the cranial border of the medial epicondyle, the cranial border of lateral epicondyle, and the cortical destruction of the proximal cranial border of the radius.

Management
Following this, fine needle aspiration was carried out, but, unfortunately, only numerous erythrocytes and few leucocytes were observed on cytological examination. No conclusive diagnosis was made. The tentative diagnoses at this point included synovial sarcoma, deep fungal infection and metastatic neoplasia. Recommendations to the owner included core biopsy of the lesion, amputation of the limb or...