FILE 2

GINIGIVAL HISTIOSARCOMA WITH LYMPH NODE METASTASIS

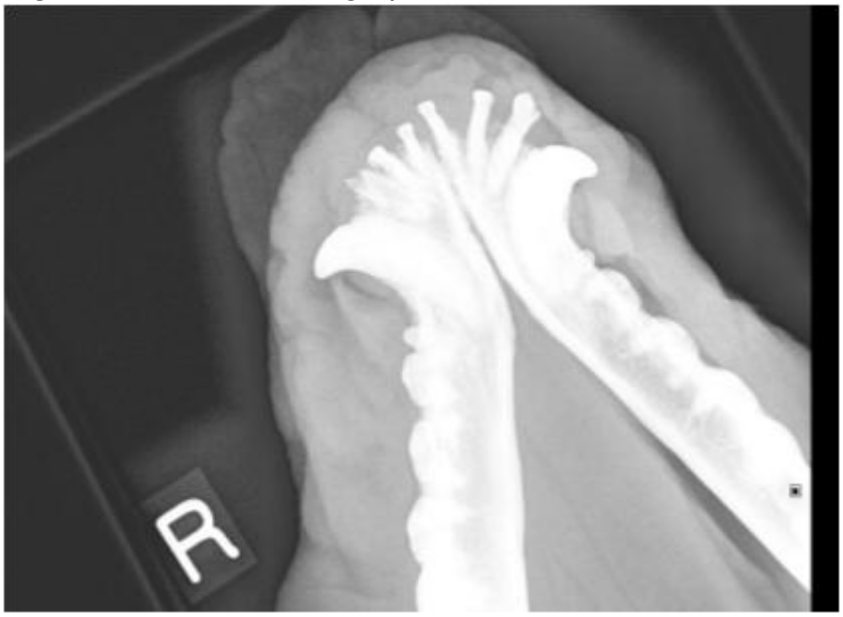
P. Monti, F. Taylor, J. Archer

The Queen's Veterinary Hospital, Department of Veterinary Medicine, University of Cambridge

HAEMATOLOGY AND BIOCHEMESTRY: All parameters were within the reference intervals.

DIAGNOSTIC IMAGING: Two intraoral radiographs of the mandible and two views of the thorax (right and left lateral views) were obtained under general anaesthesia. Radiology of the lower mandible was consistent with a minimally lytic oral mass. Horizontal bone loss was identified between all incisors and a lytic extension was identified between lower I1 and I2 in a V shape (figure 1). Radiographs of the thorax were unremarkable.

Figure 1. Intraoral radiograph of the mandible.



CYTOLOGY: The cytology of the submandibular lymph node revealed the presence of a non lymphoid round cell population. These cells occurred individually and showed moderate to marked anisocytosis and anisokaryosis. The nuclear to cytoplasmic ratio was increased. The nuclei were round, eccentrically located and the chromatin was lacy. Multiple irregular nucleoli were visible but not prominent in all cells. The cytoplasm was of moderate amount, light basophilic and occasionally contained clear punctuate vacuoles. Some multinucleated cells were noted and occasionally they displayed erythrophagia. Irregular mitotic figures were present (Figures 2 and 3). A diagnosis of metastasis to the

lymph node of a round cell tumour was made and given the location of the primary mass, an amelanotic melanoma was suggested as the most likely diagnosis.

Figure 2. Fine-needle aspirate of the left submandibular lymph node. Modified Wright's, x 100 objective.

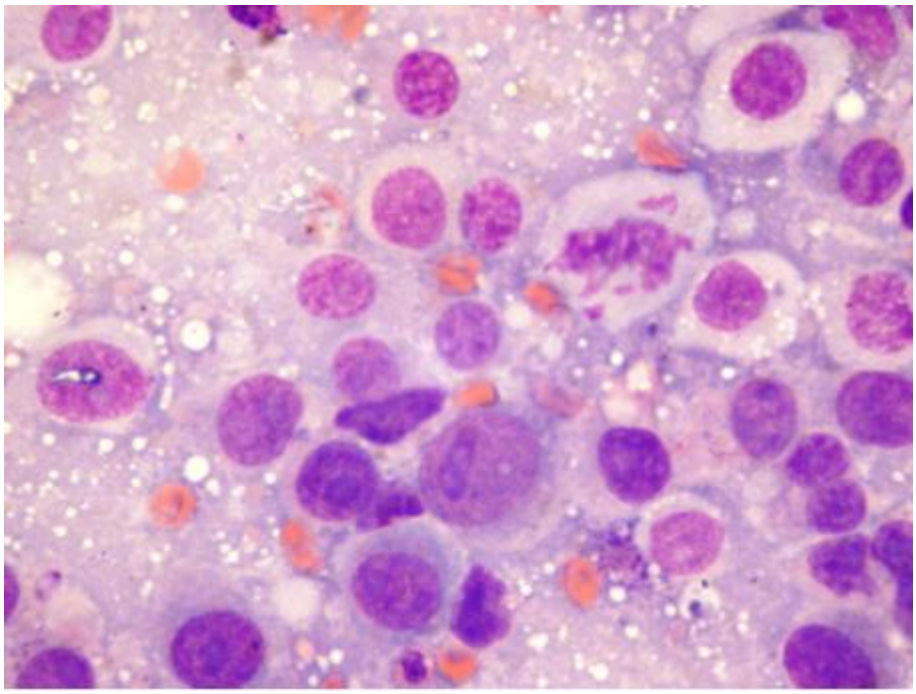
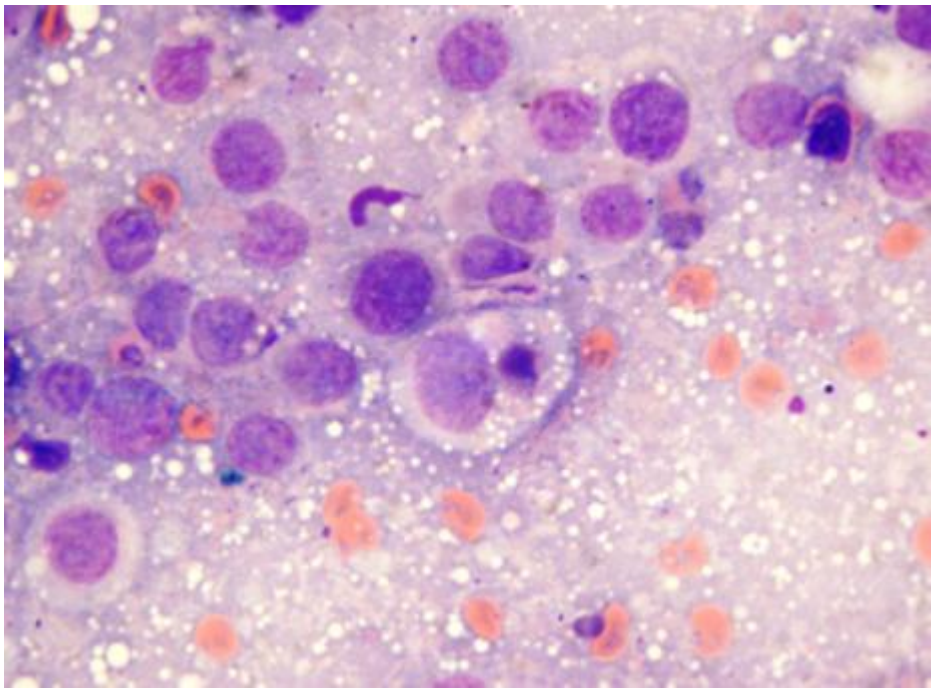


Figure 3. Fine-needle aspirate of the left submandibular lymph node. Modified Wright's, x 100 objective.



HISTOPATHOLOGY: The sample consisted of a section of gingival mucosa and underlying tissue. The epithelium was hyperplastic. Some areas appeared ulcerated and others showed a polypoid overgrowth of the underlying connective tissue covered by hyperplastic epithelium. Sometimes the epithelium appeared dysplastic but no overt signs of neoplasia were seen. The sub-epithelial tissue was heavily infiltrated with lymphocytes and macrophages and there was a lichenoid infiltration of lymphocytic type.
A histological diagnosis of gingival hyperplasia with secondary ulceration and inflammation was made, although in view of the cytological findings, further sections of the mass were cut and stained.

These revealed a small (2 mm diameter) circumscribed area containing a sheet of pleomorphic cells with polygonal and spindle forms. Numerous mitotic figures were seen, some of which had abnormal morphology. The findings suggested a neoplastic lesion of mesenchymal (sarcoma) type, although the derivation of the cells was unclear (Figures 4 and 5). Combining the cytological and histopathological findings, amelanotic melanoma and sarcoma were listed in the differential list.

Immunohistochemistry was therefore performed to further investigate the origin of the neoplastic cells and CD18, MHC II, S-100 and MAC-387 were used. The mass strongly expressed CD18 and MHC II (Figures 6 and 7) and was negative for S-100 and MAC 387. Given the lack of expression of S-100, amelanotic melanoma was ruled out.

For completeness, given the CD18 expression, CD3 and CD79a were also included in the panel. Although the mass strongly expressed CD18, it lacked expression of CD3 and CD79a therefore allowing differentiation between histiocytic disease and T and B cell proliferative disease. For differentiating between the different histiocytic diseases, MAC 387 was performed but was negative, making a dendritic cell origin more likely. A diagnosis of histiocytic sarcoma was made.

Figure 4. Section of the gingival mass. H&E, x 10 objective.

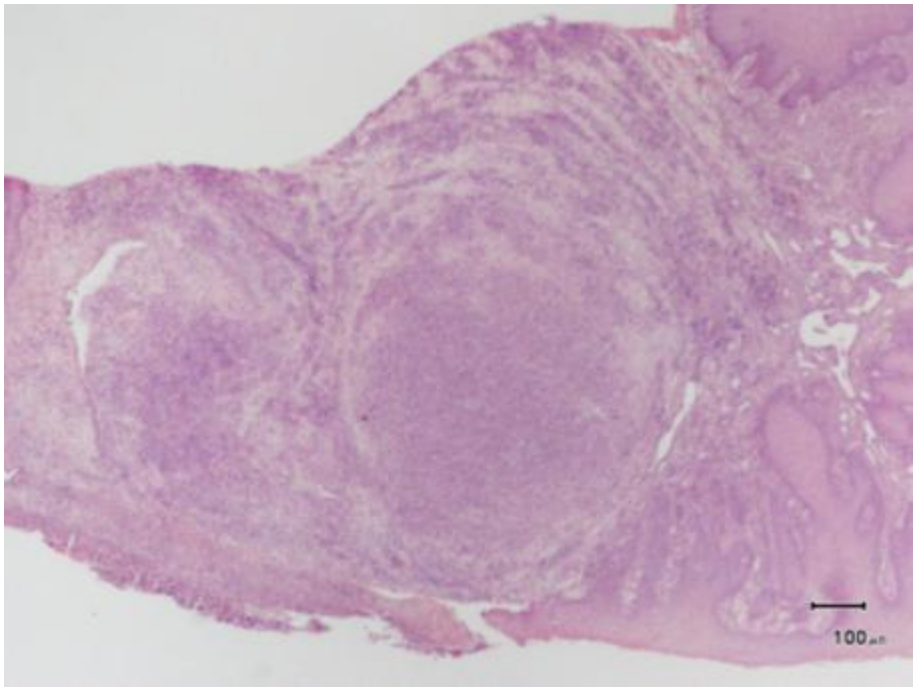


Figure 5. Section of the gingival mass. H&E, x40 objective.

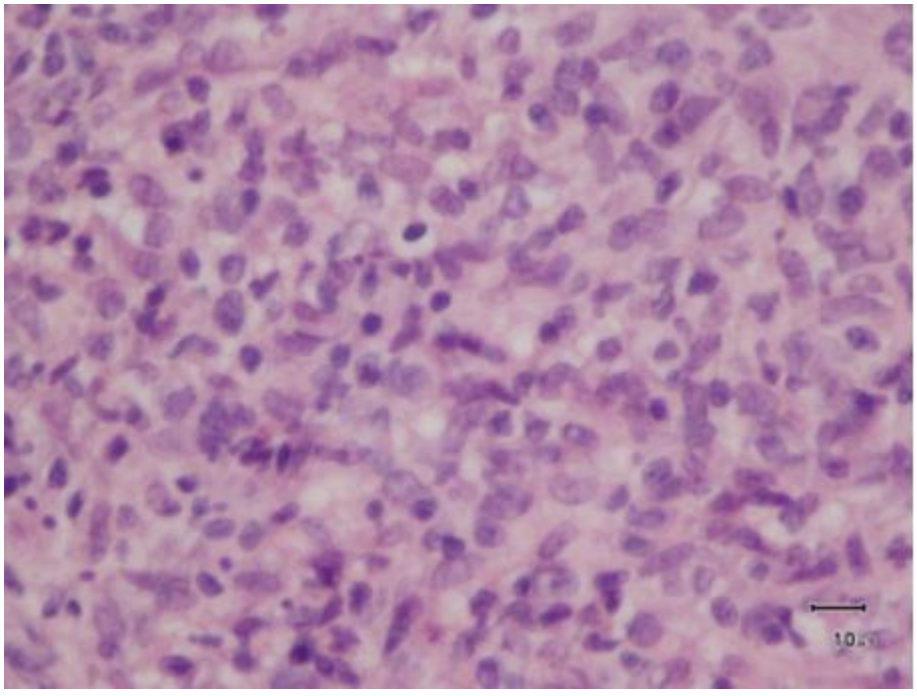


Figure 6. CD18 immunostaining. CD18 positive. X 40 objective.

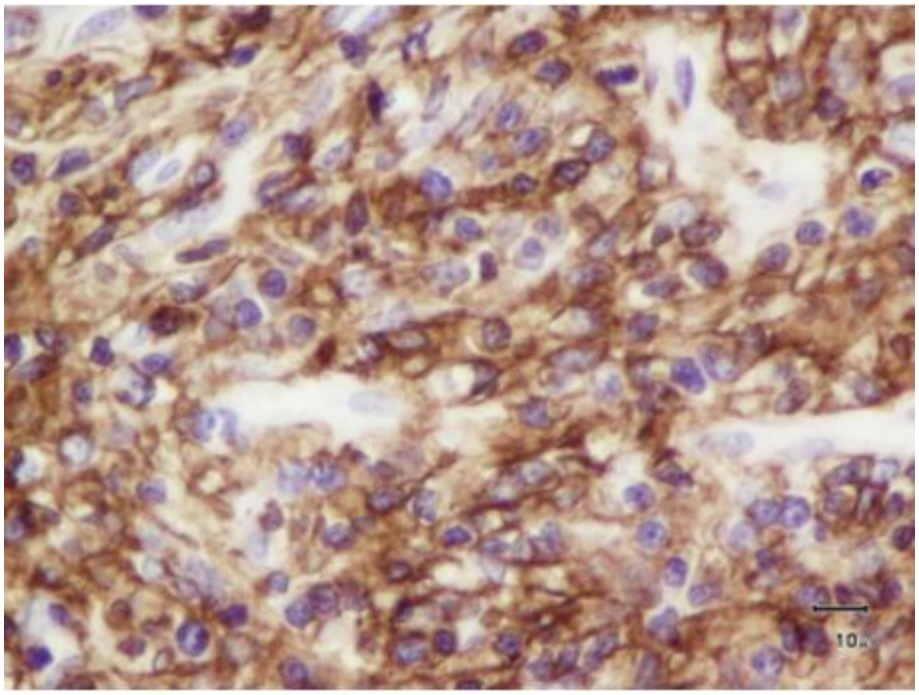
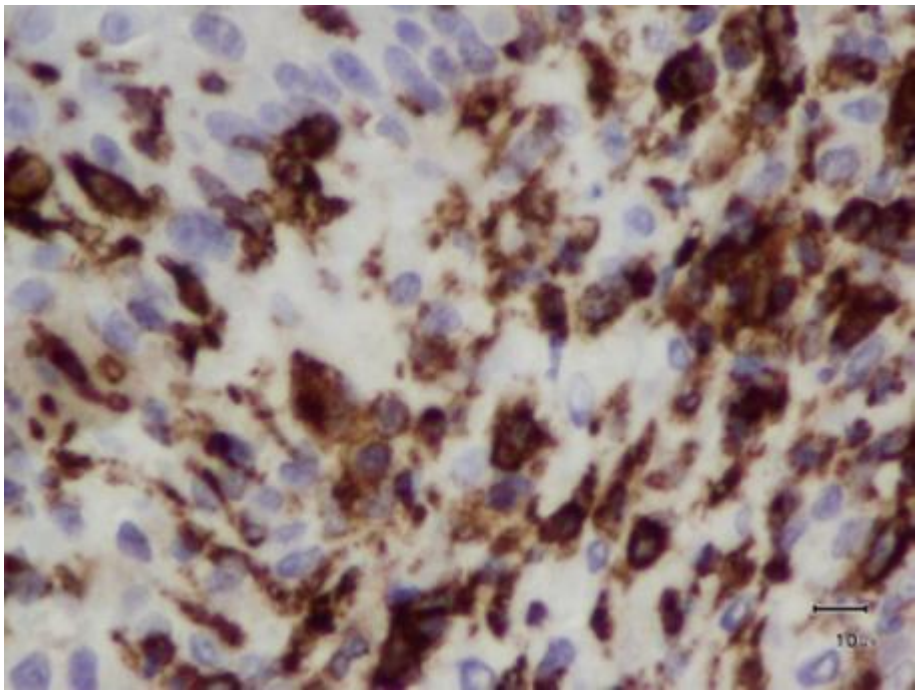


Figure 7. MHC II immunostaining. MHC positive. X 40 objective



DISCUSSION

This case describes a histiocytic sarcoma (HS) presented as an oral lesion in a dog.

Histiocytic sarcoma (HS) is an uncommon malignant neoplasm of histiocytic (dendritic cell or macrophage) origin[1]. Reported anatomical sites include lung, lymph node, liver, spleen,

stomach, pancreas, mediastinum, skin, skeletal muscle, central nervous system, bone, bone marrow, intranasal cavity and eye[2]. Two forms of histiocytic sarcomas are recognised: the localised (LHS) and the disseminated HS (DHS) [6]. LHS typically present as a rapidly growing, solitary, locally invasive soft tissue mass with high metastatic potential. This has been described in many breeds but Bernese mountain dogs, Flat coat retrievers, Labrador retrievers and Rottweilers appear to be overrepresented. Staging includes haematology, biochemistry, thoracic radiographs, abdominal ultrasound and FNA of the local lymph node. This allows differentiation between the localised and disseminated form[4]. Histopathologic diagnosis may present a challenge because routine H&E stains do not always allow differentiation of this tumour from amelanotic melanoma or occasionally from lymphocytic tumours. Therefore, immunohistochemistry is necessary for a definitive diagnosis. For this purpose, many markers have been used, although only a few of them are available for paraffin-embedded samples. Immunohistochemistry involves the use of monoclonal antibodies, and the marker most commonly used to characterise HS in formalin fixed tissues in formalin is CD18[3].

In this case, the cytology suggested as most likely diagnosis an amelanotic melanoma. The diagnosis was reached on the basis of the cellular features observed in the left submandibular lymph node but also considering the presentation of the mass. In fact, oral masses most commonly seen in dogs include melanoma (30-40%), squamous cell carcinoma (17-25%) and fibrosarcoma (8-25%)[2]. The routine histopathology did not confirm a definitive diagnosis, although it recognised the mesenchymal origin of the neoplastic lesion. The use of different markers was therefore necessary for identifying the phenotype of this neoplasm. Immunohistochemistry was able to differentiate between amelanotic melanoma and histiocytic proliferation when the markers S-100, MHC II, CD18 and MAC-387 were used. This confirmed a diagnosis of histiocytic tumour (CD18+ and MHC II+).

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To the author's knowledge, only one case of gingival HS has been previously described in literature. This was a Bernese mountain dog who was referred for evaluation of a gingival mass involving the lower right incisors which the owner noticed one week prior to presentation. Disruption of the normal position of the incisors with extensive lysis of the mandible was reported. No information was given about the draining lymph node. Further investigation revealed mild pancytopenia and multiple abdominal masses involving the spleen and the left kidney. The biopsy of the gingival mass and the aspirates of the abdominal masses and bone marrow agreed with the diagnosis of histiocytic sarcoma. No

immunophenotyping were obtained[5]. Given the distribution of this neoplasm, this can be classified as disseminated histiocytic sarcoma (DHS).

In our case, the initial staging included only thoracic radiographs and FNA of the regional lymph node because HS was not included in the initial differential list. Unfortunately the owner declined any further investigations after the diagnosis was reached.
Although no suggestion of disease dissemination was present on physical examination, further investigations including haematology, biochemistry or thoracic radiographs would be needed to subclassify this neoplasm as localised or disseminated.

This is the second reported case of histiocytic sarcoma presenting as a gingival mass in a dog. This suggests that, although this is a rare eventuality, HS should be included in the differential list any time an oral mass is presented.

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