Volume 59 (11) : November, 2006
Irish Veterinary Journal

PEER REVIEWED

peer reviewed

Lingual haemangiosarcoma in a crossbred dog

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An eight-year-old, male neutered, crossbred dog was presented for investigation of a lingual mass of four months duration. Oral examination revealed a 7cm x 5cm soft, fluctuant mass at the caudal aspect of the tongue. Ultrasound examination of the mass demonstrated mixed echogenicity, with cavitations containing hypoechoic and anechoic regions. Lingual haemangiosarcoma was diagnosed on histopathological examination of multiple biopsy samples, with confirmation of the vascular endothelial origin of tumour cells by positive immunolabelling for factor VIII-related antigen.

Irish Veterinary Journal
Volume **59** (11) 622-625, 2006

Keywords: Dog, Tongue, Haemangiosarcoma

Introduction

The oropharyngeal region is the fourth most common site of malignant neoplasia in the dog (Dorn and Priester, 1976); however, neoplasia confined to the tongue is rare (Hoyt and Withrow, 1984). In a study by Dorn and Priester (1976), lingual tumours comprised only 4% of all oropharyngeal neoplasms in a review of 469 cases. The most common types of lingual tumour reported are: squamous cell carcinoma, granular cell myoblastoma, malignant melanoma, fibrosarcoma and mast cell tumours (Hoyt and Withrow, 1984; Beck *et al*., 1986; Srebernik and Appleby, 1991). These more prevalent tumours have been well documented in the literature as case reports and case series and their biological behaviour has been studied. Other tumour types such as haemangioma, haemangiosarcoma and rhabdomyosarcoma have been reported rarely (Culbertson, 1982; Schoofs, 1997; Lascelles *et al*., 1998; Brockus and Myers, 2004), and the clinical presentation and biological behaviour of these tumours are still largely unknown. This report describes, in detail, the clinical and pathological findings of a case of lingual haemangiosarcoma as a primary tumour in the dog.

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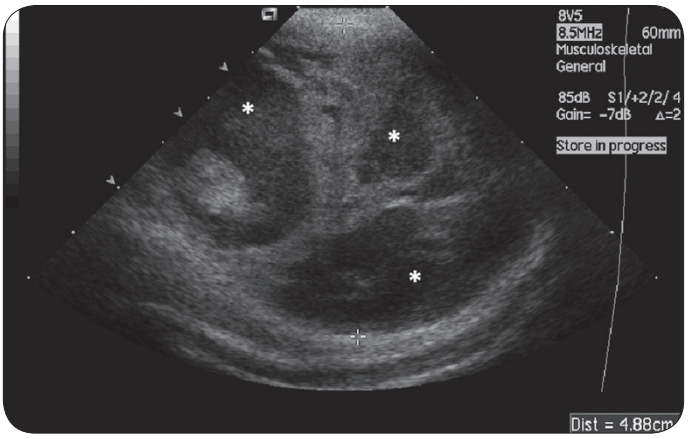

Figure 1: Sagittal image of part of the mass acquired via a ventral approach, with the transducer applied on the skin from the ventral aspect at the level of the base of the tongue (between callipers). The cavities containing echogenic material are visible within the mass (asterisks).

Case report

An eight-year-old, male neutered, crossbred dog was presented to the Queen Mother Hospital, at the Royal Veterinary College, London, for further investigation of a lingual mass of approximately four months duration. The mass appeared not to have altered in size during the preceding months of veterinary treatment and a previous incisional biopsy sample had been non-diagnostic. Referral was sought due to non-resolution of the mass and the recent development of mild dysphagia.

On presentation, the dog was bright and alert, in good body condition and weighed 14.7kg. Clinical examination was unremarkable, except for the presence of a large mass, approximately 7cm x 5cm in diameter, visible in the caudal inter-mandibular space, which was

freely mobile and painless on external palpation. On oral examination, the mass was seen to be occupying a large proportion of the caudal aspect of the tongue and the tongue could not easily be protruded from the mouth.

Initial investigations consisted of a complete blood cell count, serum biochemical profile and an ultrasound examination of the mass. Further diagnostics, including radiographs of the pharynx and thorax and a full oral examination were carried out under general anaesthesia. Routine haematology and biochemistry were unremarkable and thoracic radiographs revealed no evidence of metastases.

Ultrasound examination of the tongue revealed a mass of mixed echogenicity, with cavitations containing hypoechoic/anechoic regions (**Figure 1**). The mass extended rostrally from the base of the tongue and measured 7.5cm by 4.9cm. It was well vascularised and well marginated and evidence of foreign material was not seen. There was no evidence of invasion of the mass into local soft tissues. Lateral and dorsoventral radiographs of the skull revealed a localised, homogenous, poorly-demarcated soft tissue opacity in the oropharyngeal region. Bony abnormalities were not present.

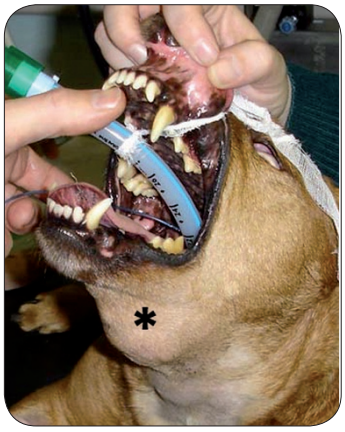

Figure 2: The mass was apparent as an intermandibular swelling (asterisk) with the tongue in a normal anatomical position.

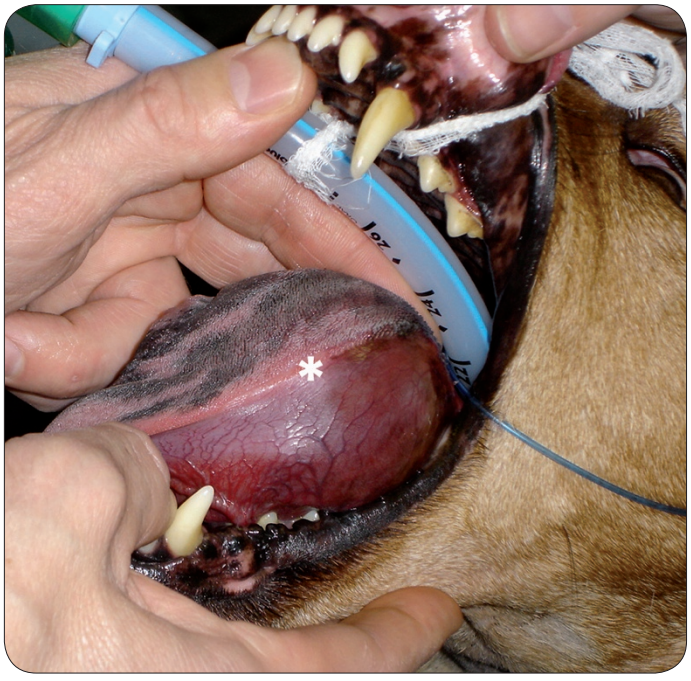

Figure 3: The extent of the mass (asterisk) revealed under general anaesthesia via oral examination and protrusion of the tongue.

A full oral examination under general anaesthesia did not reveal obvious dental or bony abnormalities, or invasion of soft tissue structures. On palpation, the mass was soft and fluctuant and was continuous with the tissue of the tongue in texture and colour (**Figures 2** and **3**). At surgery, multiple incisional biopsy specimens were taken from the mass via a single incision, from both superficial and deep areas. This incision into the mass confirmed the cavitatory nature.

Biopsy specimens were fixed in 10% neutral buffered formalin and were processed for histological examination by routine methods and were embedded in paraffin wax. Sections (5µm) were cut and mounted on glass slides and stained with haematoxylin and eosin. Further sections were dewaxed and rehydrated by routine methods for immunohistochemical staining. Antigen retrieval was accomplished by protease digestion at 37°C, and the sections were labelled with rabbit polyclonal antibody to factor VIII-related antigen (von Willebrand factor; Dako A/S, Denmark) at a 1 in 4000 dilution. Histologically, tumour cells comprising these sections were arranged in sheets and lined numerous irregularly shaped blood-filled spaces. The tumour cells were round or polygonal, with central, bulging, round nuclei. There was moderate variation in nuclear size with up to six mitotic figures per high power (X400) field (**Figure 4**). Large areas of tumour cell necrosis with haemorrhage were noted. The tumour cells showed diffuse, strong positive cytoplasmic labelling for factor VIII-related antigen (**Figure 5**). The histological and immunohistochemical findings were consistent with the diagnosis of haemangiosarcoma.

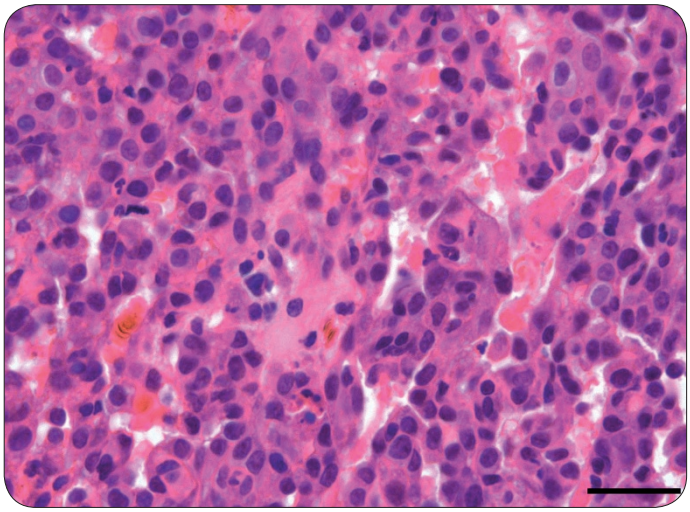

Figure 4: Haemangiosarcoma, showing plump tumour cells lining vascular spaces. (Haematoxylin and eosin X400. Bar = 250 microns.)

In view of the poor prognosis, the owner elected for euthanasia on receipt of the biopsy results. Euthanasia was carried out by the referring veterinarian and post mortem examination was declined.

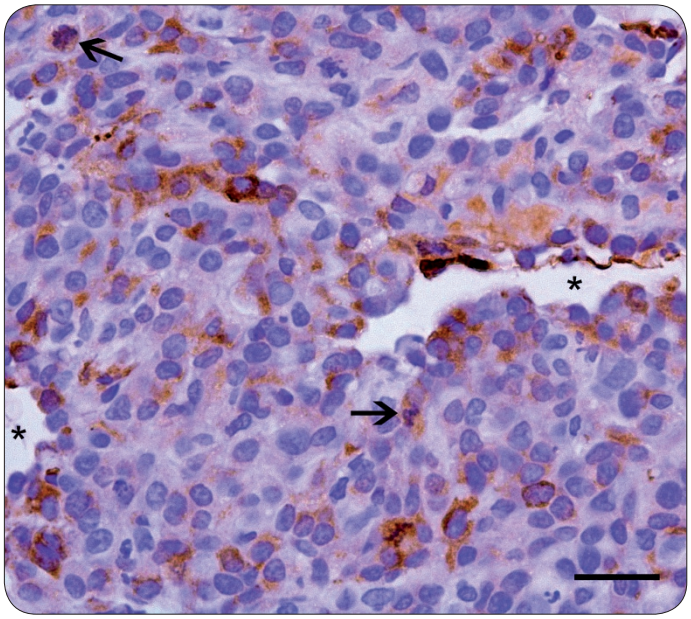

Figure 5: Tumour cells including those lining vascular spaces (asterisks) and those containing mitotic figures (arrows) show positive granular cytoplasmic staining for factor VIII-related antigen. (Two-layer indirect immunoperoxidase staining. Bar = 250 microns.)

Discussion

Haemangiosarcomas are malignant neoplasms of vascular endothelial cell origin, seen commonly in dogs (MacEwen, 2001). They have an aggressive biological behaviour and evidence of metastasis is present at time of diagnosis in up to 80% of canine patients (MacEwen, 2001; Smith, 2003). The gross appearance of these tumours is variable in both size and colour, and areas of necrosis and haemorrhage are frequently present within the mass. They are often poorly circumscribed and poorly differentiated tumours and in some cases, immunohistochemical labelling for factor VIII-related antigen is required to establish a more definitive histological diagnosis (von Beust *et al*., 1988). Haemangiosarcoma has been reported to occur in various sites in the dog, notably in the spleen, heart, liver, lungs, kidneys, skin and oral cavity (Brown *et al*., 1985; MacEwen, 2001).

Lingual haemangiosarcoma has only been reported in two previous studies, in combination with cutaneous haemangiosarcoma or other tumours at distant sites (Culbertson, 1982; Beck *et al*., 1986). Previously, documented lingual haemangiosarcoma has been located only on the dorsal surface of the rostral or middle portions of the tongue and has been of small dimensions: most less than 2cm in diameter (Culbertson, 1982; Beck *et al*., 1986). In this case, although limited staging had been performed before the owner opted for euthanasia, obvious evidence of metastasis or multicentric disease had not been demonstrated. The tumour was located, unusually, on the caudal aspect of the tongue and measured 7.5cm x 4.9cm.

The most common clinical signs reported in dogs presenting with lingual neoplasia are: haemorrhage from the mouth, oral pain, malodour, ptyalism, dysphagia, increased respiratory noise or a visual mass (Hoyt and Withrow, 1983; Beck *et al*., 1986). In a study of 57 canine tongue tumours, a visual lingual mass was the presenting complaint in 40% of cases and 25% of cases were incidental findings (Beck *et al*., 1986). In this dog, mild dysphagia was the only clinical sign related to the mass at time of referral and haemorrhage was not seen, in contrast to the frequent rupture and haemorrhage from haemangiosarcoma in other locations (Smith, 2003). The caudal nature of this tumour led to late detection of the disease, primarily due to the lack of clinical signs. It was detected only when it became prominent in the inter-mandibular space. Rostral lesions are generally associated with a better prognosis due to earlier visual detection, increased amenability to surgical therapy and potentially a decreased rate of metastasis (Withrow, 2001; Dvorak *et al,* 2004). Caudal lesions are postulated to metastasise earlier in the course of the disease, due to a richer lymphatic and blood supply (Withrow, 2001).

Staging of the disease was performed via ultrasonographic examination of the regional lymph nodes and thoracic radiographs. Following the diagnosis of haemangiosarcoma, further staging would have included abdominal ultrasound and echocardiography to check for splenic, hepatic and cardiac neoplasia. Although this was presumed to be an isolated, primary tumour due to the lack of obvious metastatic disease, involvement of the tongue in animals with multicentric disease and concurrent cutaneous lesions has been documented (Culbertson, 1982; Beck *et al*., 1986) and, indeed, it is possible that this tumour may have represented metastasis from another site.

A diagnostic tissue biopsy is essential in all cases of neoplasia, to determine treatment options and prognosis. In patients with a lingual mass, this is particularly important, because some types of lingual tumour, such as granular cell myoblastomas (GCMB), often appear large and invasive, but carry a good prognosis, rarely metastasise and surgical removal is curative (Beck *et al*., 1986; Withrow, 2001). Biopsies should be representative and deep parts of the tumour should be included.

Histological examination with routine staining is often adequate for the diagnosis of many neoplastic conditions, including haemangiosarcoma, but if the histological diagnosis is uncertain, immunohistochemical labelling can be used to confirm the tissue of origin and likely tumour type. Factor VIII-related antigen has been shown to be a positive marker of normal, reactive and neoplastic endothelial cells of vascular and lymphatic origin in the dog (von Beust *et al*., 1988; Powers, 2001). In this case, the histological appearance of the mass and the positive immunolabelling of tumour cells with factor VIII-related antigen confirmed the diagnosis of haemangiosarcoma.

Various treatment options have been described in the literature for lingual tumours. Many rostrally-located tumours are readily treatable via partial glossectomy, with the intent of cure or palliation (Beck *et al*., 1986; Schoofs, 1997; Withrow, 2001). These rostral tumours thus carry a guarded to fair prognosis. Major glossectomy in the dog has also been reported, with a relatively good success rate in terms of long-term owner satisfaction, adequate oral function and survival statistics (Dvorak, 2004), which provides evidence that surgery is still a viable option, even for a tumour of this size and location. However, the prognosis for visceral haemangiosarcoma in any location is poor, with gross or micro-metastases usually present

at time of diagnosis (MacEwen, 2001; Smith, 2003) and thus surgery was felt to be inappropriate for this dog, particularly in light of the significant initial morbidity caused by the proposed surgical procedure. Chemotherapy and radiotherapy may be used as definitive therapy, adjuvant therapy following cytoreductive surgery and palliative therapy (Hoyt and Withrow, 1984; Beck *et al.,* 1986), but it is likely that these modalities would have been relatively ineffective in managing local and distant disease in this case.

Conclusion

In summary, this case of lingual haemangiosarcoma appeared to be a primary tumour; the clinical and pathological findings have been described in detail. Very little is known about the nature, prevalence and behaviour of haemangiosarcoma in this location, due to the scarcity of case reports in the current literature. In this case, the duration of the tumour, without obvious evidence of metastasis, suggests a slow growing benign tumour, which is not a typical characteristic of haemangiosarcomas. More information is necessary before an accurate prognosis and treatment advice can be given for these cases.

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