

Capillary haemangioma: Histopathological characterization of a rare gingival mass in a calf

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ABSTRACT

A two months old cross bred Jersey calf was presented with an irregularly oval growth (2.5 cm x 5 mm) in the mandibular gingiva. The mass was greyish-white and ulcerated. The growth was surgically removed and submitted for histopathology. Tissue sample was processed as per standard histological techniques. Microscopically, tissue revealed extensive superficial ulceration with necrosis and bacterial colonies. Underneath, abnormal proliferation of vascular endothelial cells was evident showing plump cells with mild anisocytosis, anisokaryosis and low mitotic figures. Deeper tissue revealed abnormal proliferation of vascular capillary network which were separated into lobules by meagre collagenous stroma. Interlobular stroma had loose collagen. Mast cells were scattered in the stromal components of the neoplastic capillary networks. This paper reports the histopathological features of rare case of capillary haemangioma in a two months old cross bred Jersey calf exhibiting multifocal organization of thrombi with recanalization and activity of mast cells in capillary haemangioma.

Keywords: Calf, capillary hemangioma, gingiva, mast cells

Haemangiomas are benign vascular tumours that arise due to abnormal proliferation of blood vessels¹. Congenital haemangioma is common in children² and infrequent in animals³. Haemangioma is common in dogs and rare in other domestic animals⁴. Capillary haemangioma is one among the variant of haemangiomas which occur in various organs⁵. Gingival capillary haemangioma is infrequent in calves⁶. Hereditary involvement with mutation in the GNAQ gene is proposed rather environmental cause for haemangiomas⁷. Histologically, multifocal organization of thrombi with florid intravascular proliferation of endothelial cells is a feature which underpin the subject of GNA mutations in haemangioma. Further, mast cells play crucial role as 'double-edged sword' in progression and regression of haemangiomas⁸. Quantity of activated mast cells in stromal cells of haemangioma decide the phase of the tumour⁹. This paper documents the rare gingival capillary haemangioma in a two-months-old crossbred Jersey calf with histopathological features of multifocal well-organized thrombus, exhibiting recanalization and activity of mast cells in stroma of tumour tissue.

A Jersey cross bred calf of two-months-old was presented to Veterinary Clinical Complex, Veterinary College and Research Institute (VCRI), Tamil Nadu Veterinary and Animal Sciences University, Orathanadu, Tamil Nadu with the history of growth in the gingiva of mandibular incisors. The growth was well-defined, whitish-grey and nodular. Surface showed ulceration and had focal area of haemorrhage. The mass was slightly firmer and attached with broad base over the mucosa of labial surface of gingiva of the mandibular incisors. The mass was roughly oval and measured 2.5 cm (length) x 5 mm (width) (Fig. 1). The mass was surgically removed. The tissue was fixed in 10% formalin and submitted for histopathological diagnosis to the Department of Veterinary Pathology, VCRI, Orathanadu. Biopsy tissue was processed as per standard paraffin-embedding technique¹⁰. Tissue sections of 3-4 µm thickness were prepared and stained as per haematoxylin-eosin staining protocol¹¹. Duplicate sections were stained

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with Masson trichrome stain¹², standard toluidine blue stain¹³ and Heidenhain's hematoxylin¹¹.

Microscopically, the tumour mass was dome-shaped (Fig. 2) showing extensive superficial ulceration of the mucosa, necrosis with bacterial colonies and a focal area of haemorrhage. A focal area of the mucosa with stratified squamous epithelium was evident towards lower-side of the tissue. Ulcerated areas revealed throngs of infiltrative neutrophils extending a little deep into the dermis (Fig. 3). Underneath, the tissue was highly cellular and revealed the proliferative vascular endothelial cells forming numerous variable sized channels filled with erythrocytes (Fig. 4). The vascular lining cells were

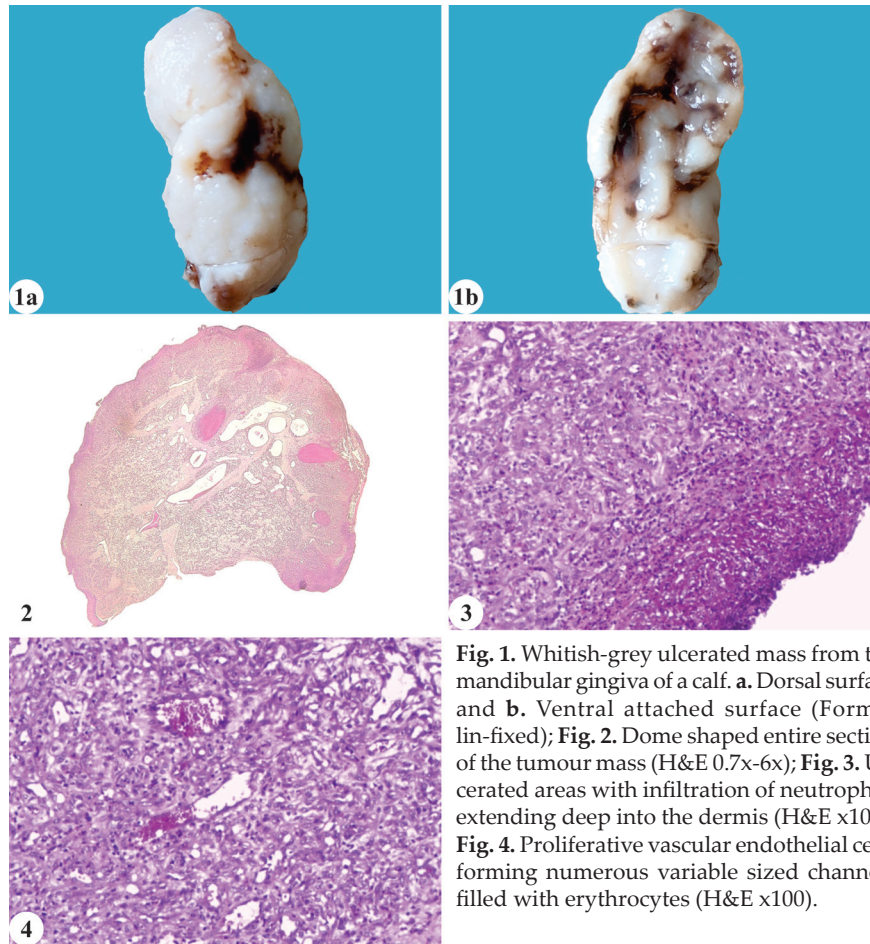


Fig. 1. Whitish-grey ulcerated mass from the mandibular gingiva of a calf. **a.** Dorsal surface and **b.** Ventral attached surface (Formalin-fixed); **Fig. 2.** Dome shaped entire section of the tumour mass (H&E 0.7x-6x); **Fig. 3.** Ulcerated areas with infiltration of neutrophils extending deep into the dermis (H&E x100); **Fig. 4.** Proliferative vascular endothelial cells forming numerous variable sized channels filled with erythrocytes (H&E x100).

rotund. These endothelial cells found to infiltrate deep into the dermis. In the transit area, the cells were corpulent and showed slight pleomorphism (Fig. 5a). These cells had prominent ovoid to spindle shaped vesicular nucleus with stippled chromatin (salt and pepper chromatin pattern) (Fig. 5b) and had very low mitotic figures (0-4/10 high power fields x400). Cells revealed mild anisocytosis and anisokaryosis. Transit area also revealed abnormal capillaries with narrow and or wider luminal area. These capillaries were either filled with blood or serous fluid. Few of these capillaries showed well-formed organized thrombus (Fig. 6). The thrombus had proliferation of endothelial cells into the thrombotic mass (Fig. 7).

Deep in the dermis, the neoplastic endothelial cells formed lobules of irregularly arranged, variable sized, closely packed vascular network. The lobules were separated by moderate collagenous stroma (Fig. 8). Vascular clusters showed irregularly anastomosing thin walled capillaries with uneven lumen (Fig. 9). Capillaries were lined by single layer of plumpy endothelial cells (Fig. 10). Lumen of the neoplastic capillaries either contained few erythrocytes or mostly empty. Some capillaries showed scattered and indistinct lumina. Lobules of capillaries were separated by moderate amount of

collagen which was evidenced on Masson trichrome stain (Fig. 11). Stroma between the capillaries contained loose, thin collagenous stroma (Fig. 12). The stroma contained scattered mast cells and plasma cells. Mast cells (MCs) were lesser in the superficial portion and scattered in the stromal elements of the deeper neoplastic capillary network (Fig. 13).

Vascular anomalies were categorized into (a) Congenital vascular malformations (hamartoma) and (b) Neoplastic transformations. Vascular neoplastic transformations (angioma) are classified into benign haemangioma and malignant haemangiosarcoma¹⁴. Further haemangioma are sorted into capillary, cavernous and epithelioid haemangioma¹⁴ on the basis of the size of the vascular channels¹⁵ and appearance of endothelial cells respectively^{16,17}.

Haemangiomas were found to be less frequent in animals¹⁸. It was reported to occur as cutaneous tumour in skin^{15,19}, subcutis³ and visceral tumour in internal organs¹⁶. The occurrence of haemangioma was rare and infrequent in oral cavity²⁰. It was reported from the tongue of a dog²¹. Vascular tumours of gums were found to be rare in animals²² and extremely rare in calves²⁰. A unique report of haemangiosarcoma of gingival tissue

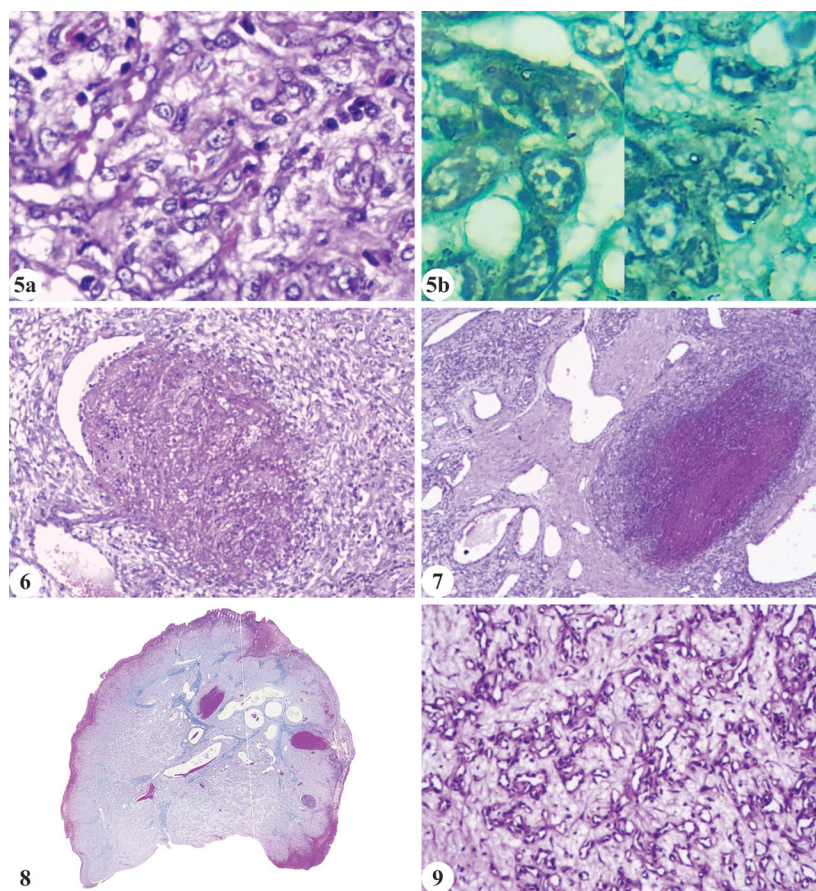


Fig. 5a. Plumpy neoplastic vascular endothelial cells with prominent ovoid to spindle shaped vesicular nucleus with stippled chromatin (H&E x400); **Fig. 5b.** Stippled chromatin (resembling salt and pepper) of proliferating vascular endothelial cells (Heidenhain's hematoxylin with light green counter stain x1000); **Fig. 6.** A neoplastic capillary with well-formed organized thrombus; **Fig. 7.** Organised thrombus exhibiting proliferation of endothelial cells into the thrombotic mass (H&E x40); **Fig. 8.** Neoplastic mass shows meagre collagen in entire tumour mass (Masson trichrome stain 0.7x-6x); **Fig. 9.** Irregularly arranged, variable sized, closely packed capillary network separated by collagenous stroma (H&E x100).

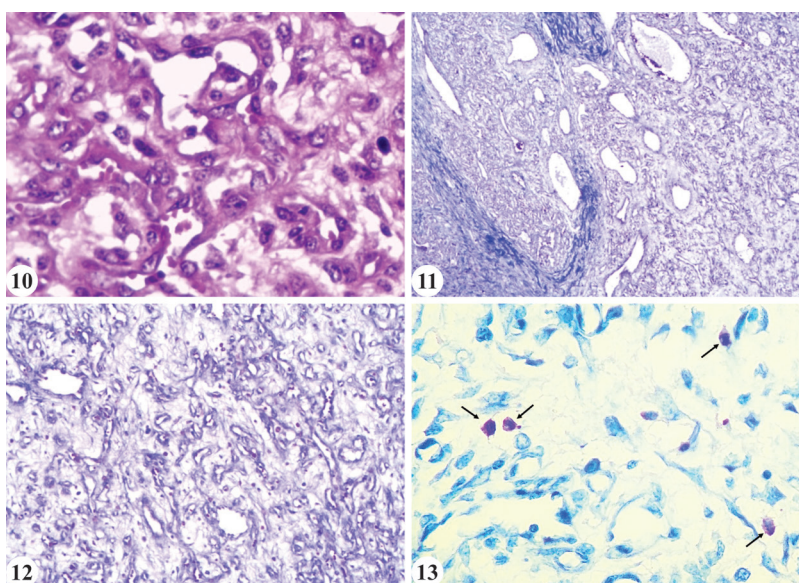


Fig. 10. Neoplastic capillaries are lined by single layer of plumpy endothelial cells (H&E x400); **Fig. 11.** Neoplastic mass shows separation of lobules with collagen bundles (Masson trichrome stain x40); **Fig. 12.** Irregular capillary network separated by loose collagenous stroma (Masson trichrome stain x100); **Fig. 13.** Scattered mast cells (arrow) in stromal tissue of capillary haemangioma (Standard toluidine blue stain x400).

was reported in a 2-months-old calf of native breed in Iran²⁰.

In the catalog of vascular tumours, the capillary haemangioma of gingiva was found to be uncommon in animals^{6,17,23,24}. Infrequently, capillary haemangioma was described in various organs/tissues in animals^{4,5,19,25}. The earlier reports documented the glossal capillary haemangioma in bovine^{6,23,24,26} and cat⁴.

Histopathological findings described in the present study was similar with the previous reports^{6,19,21,23,24,27}. The feature of capillary thrombus with recanalization recorded in the study was in-line with previous reports^{7,20}. Multifocal vascular thrombus, organization of thrombi with intravascular proliferation of endothelial cells, which were streaming into the thrombi were the distinctive features. These changes were observed immediate underneath the ulcerated area and in the transit zone composed of proliferative neoplastic cells.

The more remarkable feature was the presence of scattered mast cells (MCs) in the stroma of the neoplastic vascular stroma. These cells were lesser in superficial areas rather moderate in the deeper neoplastic tissue. Evidence of mast cells and plasma cells in the stroma of deeper neoplastic tissue of the present study might not indicate the inflammatory reaction. However, in contradictory to the observation of¹⁹ have described the inflammatory lobular capillary haemangioma in the skin of left ventral neck of guinea pig¹⁹. It was proposed that MCs plays pivotal role in progression and regression of vascular tumours²⁸. It was thought that MCs were found to be low in proliferating phase, increase in early involution phase and later on decrease in late involution phase of the haemangiomas⁹. Biological role of these MCs in haemangioma was studied by⁸. Activated MCs secrete both angiogenic and anti-angiogenic modulators in haemangioma. Among, Type III collagen and fibroblast growth factor (FGF-2) hold the key in endothelial cell proliferation during proliferation of haemangioma, whereas interferons (INF- α , β and γ) downregulate the FGF-2, endothelial cell proliferation and inhibit mitogenesis of vascular endothelial growth factor (VEGF) respectively⁸. Low number of MCs in the superficial lesion with abundant endothelial cells might indicate the proliferative phase of the tumor. The presence of scattered MCs in the stromal capillary network in deeper lesion might possibly reflect the involution phase of the haemangioma in the present study. To summarize, MCs were regarded as paradoxical in vascular tumours as documented earlier^{8,9}.

Elaborative studies on the role of MCs in haemangioma is imperative for better understanding on the biology of MCs in vascular tumours of animals. This report records the incidence of gingival capillary haemangioma with

thrombotic features in a two months old cross bred Jersey calf.

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