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CLINICAL REPORT

Histopathological and Immunohistochemical Characteristics of a Local Aggressive Canine Hemangiopericytoma (CHP) After Surgery

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Abstract

Case description: In the present paper, we describe the gross morphology, histopathology and immunoreactivity of a hemangiopericytoma (HP) as a PWT in a dog with recurrence after surgical excision.
Clinical findings: The mass was 3-4 cm, solitary, soft, unencapsulated, well circumscribed and grey to brown color. Cut surfaces of the mass contained discrete, round and relatively homogeneous tumors without any lobulation and liquefied foci in the centers. Histologically, the tumor was richly vascularized which arranged in staghorn vessels pattern. The neoplastic cells were uniform in appearance with mild to moderate pleomorphism and had spindle-shaped to oval/round nuclei with vesicular to hyperchromatic chromatin and eosinophilic to the amphophilic cytoplasm with variable amounts of the collagenous stroma. In the immunohistochemical evaluation, proliferating stromal and vascular cells in this tumor demonstrated strong immunoreactivity for vimentin and α-smooth muscle actin. Although, these cells were negative for S100, lysozyme, CD31, and CD34.
Treatment and outcome: Regarding to the repeated recurrence of this tumor after surgical excision, amputation of forelimb will probably be performed.
Clinical relevance: The present findings show that hemangiopericytoma in dogs can be a locally aggressive behavior with a repeated recurrence that led to the surgical amputation of limbs or even euthanasia of dogs.

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1. Introduction

Canine soft tissue sarcomas (STSs) are a heterogeneous group of tumors that comprise several neoplastic entities characterized by low metastatic potential (up to 17% of cases) and a low to moderate recurrence rate (7 to 30%) after marginal surgical excision.[1,2] STSs account for between 8 and 15% of all cutaneous and subcutaneous tumors in the dog and are especially prevalent among middle-aged to old and medium to large-breed dogs.[3] Perivascular wall tumors (PWTs) are mesenchymal neoplasms in the group of STSs and are defined as neoplasms deriving from mural cells of blood vessels, excluding the endothelial lining.[4] PWTs reported in dogs are canine hemangiopericytomas (CHP), angioleiomyomas/sarcomas, myopericytomas, angiomyofibromas, angiofibromas and glomus tumors.[5,6] CHP derives from pericytes that are capillary subendothelial lining cells that are particularly concentrated in areas of increased blood pressure such as distal extremities.[5] It was reported that CHP can show a locally aggressive behavior with repeated recurrences that led to euthanasia of dog.[7] Since, canine cutaneous PWTs have variable gross appearance[5]; they are diagnosed on the basis of specific histological growth and immunohistochemical reaction patterns.[8] Radiation therapy can result in some tumor control and longer survival times. But, chemotherapy has proven unsuccessful.[7,9,10]

The present paper described clinicopathologic and immunohistochemical characteristics of CHP associated with the prognosis in a forelimb of a male, middle-aged and medium-breed dog which the surgery was the treatment of choice for this patient.

2. Case Description and Clinical Findings

A cutaneous mass with 4-5 cm in size was observed in a forelimb of a male four year- old dog which managed with excisional surgery. After four weeks, the dog was referred to the clinic with repeated recurrence of the cutaneous mass (3-4 cm in size) (figure 1A) and the incisional biopsy was taken from the recurrent growing mass under general anesthesia using cocktail of Ketamine (5.5 mg/kg, Alfasan, The Netherlands) and Diazepam (0.3 mg/kg, Caspian, Iran). The forearm was prepped and draped appropriately. The incision was placed in the different parts of the mass and some portions of the abnormal tissue were cut without attempting to remove the entire lesion. Macroscopically, the mass was solitary, soft, unencapsulated, well circumscribed and grey to a brown color associated with superficial ulceration and secondary bacterial infection (fig 1A). Cut surfaces of the mass contained discrete, round and relatively homogeneous tumors without any lobulation and necrotic or liquefied foci in the centers. The removal cutaneous mass was processed for histopathologic and immunohistochemical evaluation. The tissue sample was fixed in 10% neutral buffered formalin and processed routinely. Sections of 5 µm in thickness were stained with hematoxylin and eosin (H&E) and examined by light microscopy. Consecutive sections to those used for the histopathological examination were subjected to immunohistochemistry for S-100 (polyclonal antibody, dilution 1:10000), lysozyme (clone h-CP, dilution 1:5000), vimentin (clone V9, dilution 1:20000), α-smooth muscle actin (clone 1A4, dilution 1:2000), CD31 (clone JC/70A, dilution 1:40), and CD34 (clone 1H6, dilution 1:30). The sections were stained using a streptavidin-biotin peroxidase complex method.[8] Negative controls consisted of substituting specific antibodies with an isotype-matched irrelevant monoclonal antibody or omitting the primary antibody. Sections were finally stained with DNA fluorochrome Hoechst 33342 (Sigma, St Louis, MO) (0.25 mg/mL, 3 minutes), washed in phosphate-buffered saline and a coverslip was applied with aqueous mounting media (Dako, Glostrup, Denmark).

3. Results

Histopathologically, this tumor was submucosal and unencapsulated associated with solid to focally whorled patterns (figure 1B). The neoplastic cells showed mild to moderate pleomorphism associated with spindle-shaped to oval/round vesicular nuclei and eosinophilic to amphophilic cytoplasm. These cells were separated by the collagenous stroma (fig 1B). Mitotic figures were inconspicuous and necrosis was absent. The tumor was richly vascularized which arranged in staghorn vessels pattern (thin-walled branching vessels) (figure 1B and C). Moreover, the inflammatory cells infiltrated which included a significant number of eosinophils and mast cells (were found close to small vessels and identified by round-single-central nucleus accompanied with numerus basophilic-cytoplasmic granules) associated with multifocal hemorrhage. According to tissue differentiation, mitotic count and quantify of necrosis[1], histologic grade of this tumor was grade II. In the immunohistochemical evaluation, proliferating stromal and vascular cells in this tumor demonstrated strong immunoreactivity for vimentin (figure 1D) and α-smooth muscle actin. The results of immunohistochemistry in these cells were negative for S100, lysozyme, CD31, and CD34.

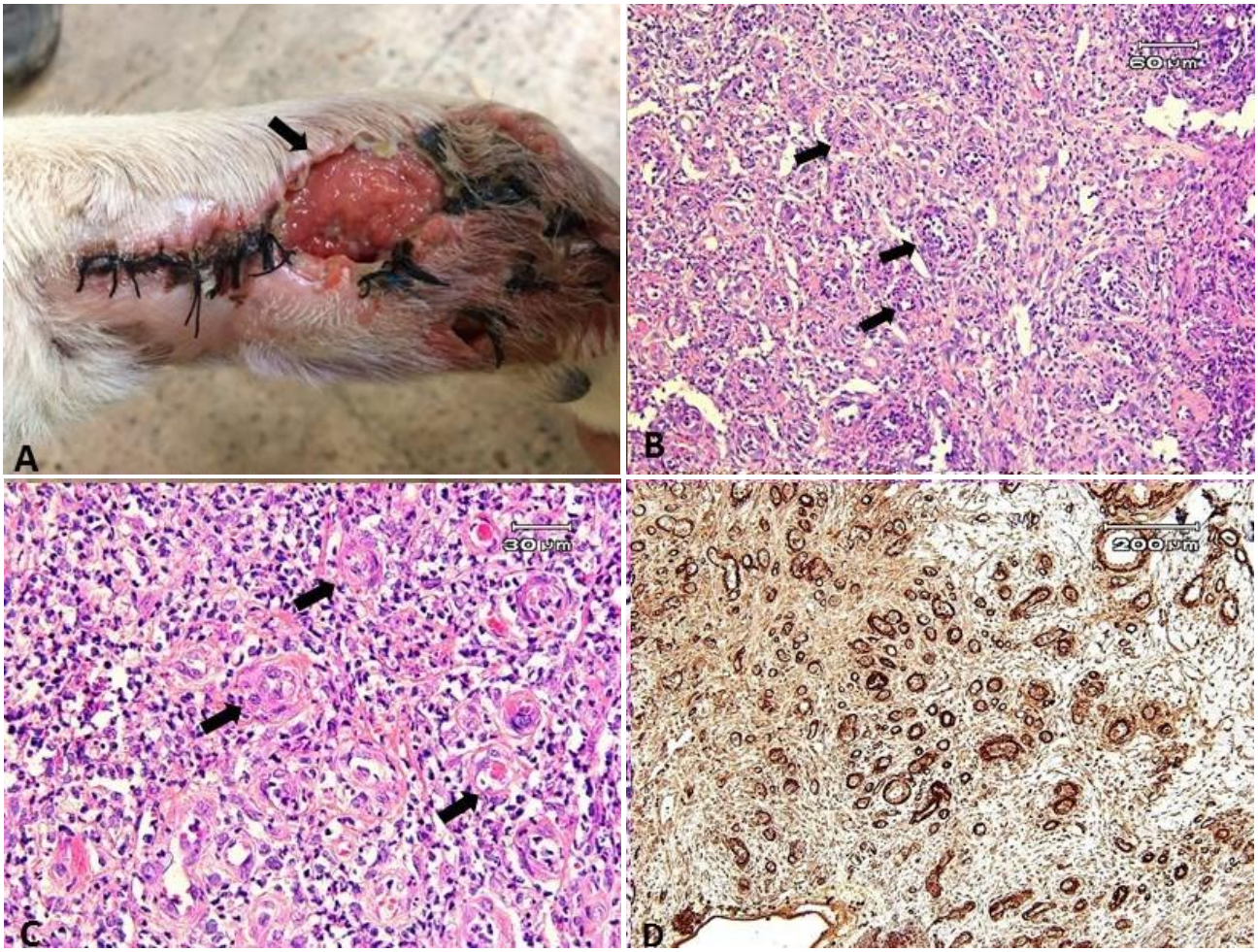

Figure 1. Hemangiopericytoma, forelimb, male four-year-old dog. The cutaneous mass with repeated recurrence in a forelimb after four weeks (A). Microscopically, the tumor showed a diffuse growth with solid to focally whorled patterns associated with richly vascularized which arranged in staghorn vessels pattern (thin-walled branching vessels) (B, C); H&E. Proliferating stromal and vascular cells in this tumor demonstrated diffuse immunoreactivity of tumor cells for streptavidin-biotin-peroxidase with vimentin antibody in cellular intermediate filaments (D); IHC.

4. Discussion

The diagnosis of canine HEP is based on the finding of major perivascular whorling pattern (as the hallmark of this neoplasm) associated with a variable and often discordant reported expression of desmin, panactin, S100, and CD34.[6] Aggressive initial surgery is considered the best treatment for PWTs and complete excision is often curative. Recent studies indicate that even marginal excision can be curative for grade 1 tumors.[8,9] In the present report, the histological pattern and immunohistochemical profile were studied in haemangiopericytoma in a dog with a high recurrence rate. Because the treatment of choice for canine cutaneous and subcutaneous STSs is surgical excision[3], this cutaneous mass was removed by surgery. However, repeated recurrence was observed. In histopathological examination, the recurrent mass consisted of layers of the spindle cells arranged in a concentric fashion around a central vessel. As mentioned previously, the observation of perivascular whorls of the spindle or fusiform cells has been stated as the hallmark of CHP.[6,8,11] Also, differential diagnosis should do with other soft tissue tumors (STTs) such as fibrosarcomas, Schwannomas, peripheral nerve sheath tumor (PNST), histiocytomas and leiomyosarcomas.[6,12] In these tumors with common H&E staining, the whorls are not arranged around vascular structures as observed in HP. Although, differential diagnosis of these tumors may be very difficult.[6,12] Therefore, immunohistochemistry examination is important and useful in ruling out of others cutaneous spindle cell tumors. The most commonly used markers for this tumor include vimentin, α-smooth muscle actin, CD34, CD31, desmin, S100, cytokeratin, Factor VIII, glial fibrillary acidic protein (GFAP) and lysozyme.[6,8,12,13]

In the present study, proliferating stromal and vascular cells were positive strongly for vimentin and α-smooth muscle actin, and were uniformly negative for S100, lysozyme, CD31, and CD34. Expression of α-smooth muscle actin has been described previously in this tumor in the dog.[6,12] Smooth muscle actin is expressed by canine pericytes of arterioles, venules and capillaries of the dermis and subcutaneous tissue.[12] Vimentin is the major member of the intermediate filament and is used primarily to discriminate between epithelial and mesenchymal tumors.[11] In the present study, positive immunostaining for vimentin confirms the mesenchymal origin of this tumor. CD31 is a transmembrane glycoprotein present in endothelial cells, megakaryocytes, macrophages and platelets.[8] However, expression of this marker has not been reported previously in CHP. According to the present results, it seems that tumor cells of CHP do not express this marker. CD34 is expressed in embryonic hematopoietic cells, vascular and lymphatic endothelial cells.[14] In the most previous studies like as the current study, expression of this marker has not been reported in CHP.[3] S100 protein is originally detected in the nervous system and is a good marker for neuroendocrine tumors. It is used in veterinary oncology mostly to distinguish schwannomas, neurofibromas, fibrosarcomas and PWTs. Numerous cells are S100-positive in schwannomas, few in neurofibromas, and none in fibrosarcomas and PWTs.[14] A recent study reported uniformly S100 protein and CD31 negative and intensely vimentin positive with a variable expression for CD34 in PWTs of dogs.[8] The expression of lysozyme suggests histiocytic differentiation. In tissues of mesenchymal origin, lysozyme is considered a histiocytic marker in dogs.[3] In the present CHP, there is no lysozyme antibody staining reaction.

The present tumor showed features consistent with grade II of CHP. Histologic grade of the CHP can be used as a diagnostic tool to predictive prognosis, recurrence and metastasis rates. Grade III usually shows a more aggressive behavior and an overall poor diagnosis. It seems that grade II can be exhibited high local recurrent rate during several weeks after surgical excision. The tumor size and quality of surgical margins have been reported to be the most important factors in predicting local recurrences due to the infiltrative behavior of CHP.[11] In the present case, because of wide excision margins and large tumor size, surgery was performed difficulty. If this tumor continues to show recurrence, amputation of the forelimb or even euthanasia like as previous report [7] will probably be performed.

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Conflict of interests

None

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چکیده

ویژگی‌های هیستوپاتولوژی و ایمنوهیستوشیمی همانژیوپریسایتوم سگ با تهاجم موضعی بعد از جراحی

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توصیف بیماری: تومورهای اطراف عروقی (PWTs) از تومورهای مزانشیمی در گروه سارکوم‌های بافت نرم (STSs) و با منشأ سلول‌های پوششی دیواره عروق خونی می‌باشند. در مطالعه حاضر، مورفولوژی ماکروسکوپی، هیستوپاتولوژی و ایمنوهیستوشیمی یک همانژیوپریسایتوم (HP) به‌عنوان یک تومور اطراف عروقی با عود مجدد بعد از جراحی در یک سگ توضیح داده شده است.

نتیجه: توده مذکور با اندازه ۳-۴ سانتی‌متر، جامد، نرم، بدون کپسول و خوب محدودشده با رنگ خاکستری تا قهوه‌ای بود. در سطح برش این توده به‌صورت محدود، گرد، هموژن، فاقد حالت لبوله و کانون‌های آبکی بود. ازنظر میکروسکوپی، این تومور غنی از عروق خونی با الگوی شاخ گوزنی بود. سلول‌های توموری دارای اشکال مشابه و پلئومورفیسم خفیف تا متوسط، هسته‌های کشیده تا گرد و بیضی وزیکولر با کروماتین هایپرکروم و سیتوپلاسم ائوزینوفیلی تا آمفوفیلی همراه با نفوذ مقادیر متغیری از استرومای کلاژنی بودند. در ارزیابی ایمنوهیستوشیمی، استرومای نفوذی و سلول‌های عروقی توموری برای مارکرهای ویمنتین و اکتین آلفا عضلات صاف به‌شدت مثبت بودند. درحالی‌که این تومور برای فاکتورهای اس-۱۰۰، لیزوزوم، سی دی-۳۱ و سی دی-۳۴ منفی بودند.

کاربرد بالینی: نتایج مطالعه حاضر نشان می‌دهد که تومور همانژیوپریسایتوم سگ می‌تواند به‌صورت موضعی رفتار تهاجمی و عود مجدد از خود نشان دهد و منجر به قطع عضو مبتلا و یا حتی آسان کشی حیوان شود.

کلمات کلیدی: تومور اطراف عروقی (PWTs)، جراحی، هیستوتوپاتولوژی، ایمنوهیستوشیمی