

Kaposi-Like Vascular Tumor of the Urinary Bladder in a Cow

Isabel PIRES^{1)*}, Felisbina Luisa QUEIROGA¹⁾, Filipe SILVA¹⁾, Carlos PINTO²⁾ and Carlos LOPES³⁾

¹⁾CECAV, Department of Veterinary Sciences, Universidade de Trás-os-Montes e Alto Douro, 5001–801 Vila Real,

²⁾Serviço de Desenvolvimento Agrário de São Miguel, 9500–343 Ponta Delgada and ³⁾Institute of Biomedical Sciences Abel Salazar, Largo Professor Abel Salazar, 4099–003, Porto, Portugal

(Received 16 December 2008/Accepted 29 January 2009)

ABSTRACT. Kaposiform hemangioendothelioma is a rare human vascular neoplasm. In veterinary medicine this tumor type was only recognized in the dog. Here we describe an unusual case arising in the urinary bladder of a Holstein-Friesian adult cow. Histologically the tumor presented a nodular proliferation of spindle cells, forming angular slits, often containing extravasated erythrocytes. Peripherically, well-formed vascular channels were seen. These cells were positive to vimentin and to factor VIII-related antigen by immunohistochemical stain. Based on its characteristics, it was classified as kaposiform hemangioendothelioma and as far as we know, it is the first case described in cattle.

KEY WORDS: cattle, Kaposiform hemangioendothelioma, urinary bladder, vascular tumor.

J. Vet. Med. Sci. 71(6): 831–833, 2009

In cattle, vascular tumors located in the urinary bladder are common as an element of the bovine enzootic hematuria (BEH) syndrome. The histological types mostly described are hemangioma (capillary and cavernous) and hemangiosarcoma [1].

The WHO Histological Classification of Tumors of Domestic Animals does not include the hemangioendothelioma histological type, except for the Kaposi-like vascular tumor, an extremely rare and controversial tumor of intermediate malignancy [5]. In spite of this lack in the WHO classification, the presence of hemangioendothelioma in the brain [3] and in the urinary bladder [1] of cows has been described.

In humans, hemangioendotheliomas are classically tumors of “intermediate” or “borderline” malignancy and are classified into spindle cell, retiform, polymorphous and kaposiform hemangioendotheliomas [2, 6]. The Kaposiform hemangioendothelioma (KHE) is a rare vascular tumor found almost exclusively in early childhood with a wide anatomical distribution. It is a locally aggressive, non-metastasizing endothelial-derived spindle cell neoplasm with features of capillary hemangioma and Kaposi sarcoma [10]. In domestic animals, to our knowledge, this histological type has only been described in the dog (one case published) [10].

Here we report an unusual case arising in the urinary bladder of an adult female Holstein-Friesian cow, coming from São Miguel Island, Portugal, where BEH is endemic. The tumor was collected at a slaughterhouse, from an animal with a clinical history of hematuria. Macroscopically, the urinary bladder presented one submucosal reddish nodule with 0.5 cm. The tissue had been routinely fixed in 10% neutral buffered formalin and embedded in paraffin, sec-

tioned at 3 μ m and stained with hematoxylin and eosin (HE), Periodic acid-Schiff (PAS) and Gomori's reticulin silver impregnation for conventional light microscopical observation. For immunohistochemical studies representative sections were examined by the streptavidin-biotin-peroxidase complex method. Antibodies to the following antigens were applied: collagen IV (68–124, Chemical Credential[®]), factor VIII-related antigen (A0082, Dako[®]), CD31 (JC/70A, Dako[®]), CD34 (NCL-END, Novocastra[®]), vimentin (NCL-Vim-V9, 1:100, Novocastra[®]), alpha smooth muscle actin (NCL-SMA, 1:50, Novocastra[®]), keratin (Z0622, 1:800, Dako[®]) desmin (D33, 1:50, Dako[®]), proliferating cell nuclear antigen (PCIO, 1:100, Dako[®]) and Ki-67 (MIB-1, 1:100, ImmunoTech[®]). The chromogen was diaminobenzidine tetrahydrochloride and the counterstain was Mayer's hematoxylin. Negative controls were prepared by omitting the primary antibodies and replacing them with PBS. Tissue sections known to express the corresponding antigens served as positive controls.

On histological examination, we observed a proliferation of spindle-shaped tumor cells that contained eosinophilic cytoplasm and elongated nuclei with finely distributed chromatin without conspicuous nucleoli. These fusiform cells were associated with slitlike vascular spaces (Fig. 1 and Fig. 2). Well-formed capillaries were present at the periphery of the tumor. Nuclear atypia was minimal or moderate and mitotic figures were averaging 2 to 5 in 10 high-power fields. Focal hemorrhagic areas were seen and necrosis was absent. PAS positive hyaline globules were not seen. Gomori's reticulin silver impregnation and immunostaining for collagen IV demonstrated the presence of multiple small vascular channels even in fusiform areas (Fig. 3). Immunohistochemically, the cells stained positively for vimentin in the well-formed capillaries and in fusiform areas. Factor VIII-related antigen was positive although its distribution varied significantly in the tumor. In adjacent normal vessels and in tumoral cells, in well-formed capillaries, the positiv-

* CORRESPONDENCE TO: PIRES, I., Department of Veterinary Sciences, Universidade de Trás-os-Montes e Alto Douro, 5001–801 Vila Real, Portugal.
e-mail: ipires@utad.pt

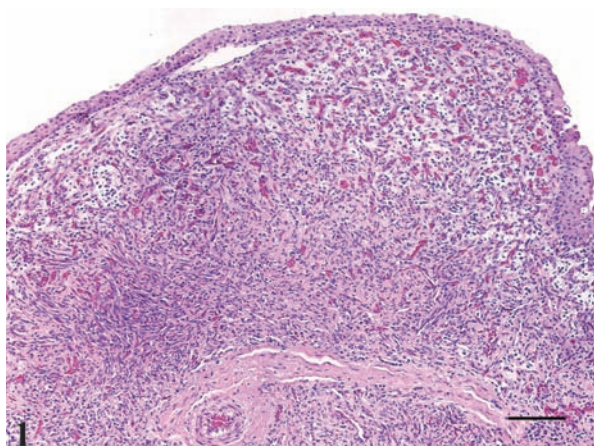


Fig. 1. Urinary bladder. Holstein-Friesian cow. Kaposiform hemangioendothelioma with features of capillary hemangioma in the periphery and proliferation of spindle cells. HE. Bar=120 μ m.

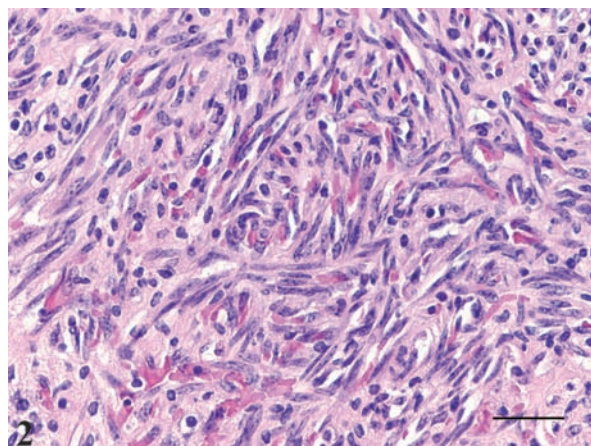


Fig. 2. Urinary bladder. Holstein-Friesian cow. Proliferation of spindle cells, associated with slitlike vascular spaces. HE. Bar=30 μ m.

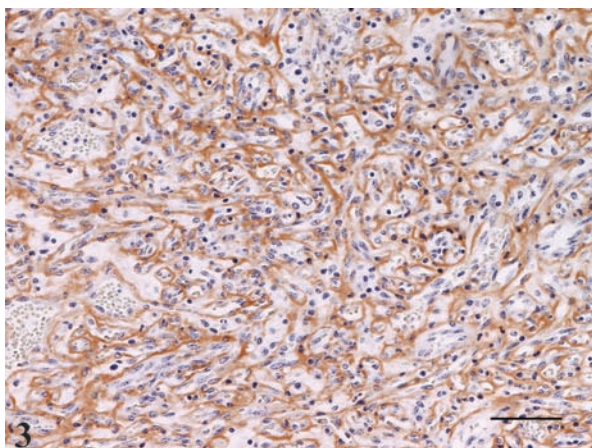


Fig. 3. Urinary bladder. Holstein-Friesian cow. Type IV collagen immunostaining reveals vasoformative nature of tumor even in spindle cell areas. Streptavidin-biotin immunoperoxidase method, Mayer's hematoxylin counterstain. Bar=60 μ m.

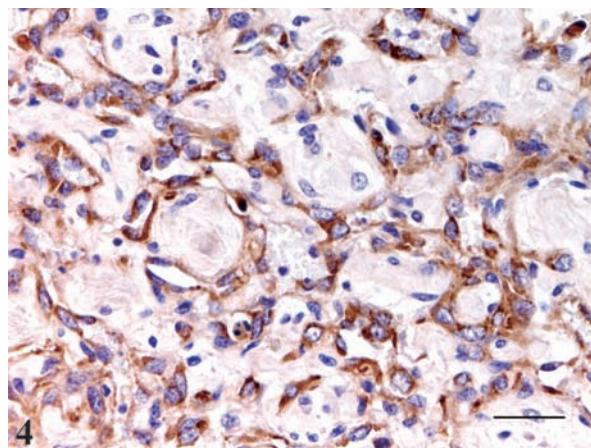


Fig. 4. Urinary bladder. Holstein-Friesian cow. Factor VIII-related antigen immunostaining in endothelial tumor cells. Streptavidin-biotin immunoperoxidase method, Mayer's hematoxylin counterstain. Bar=30 μ m.

ity was diffuse and intense. In fusiform areas the immunolabeling was focal (Fig. 4). The endothelial markers CD31 and CD34 did not exhibit any reaction in the cattle specimens used. A periendothelial focal positive staining for alpha smooth muscle actin was noted. The tumor cells were negative for keratin and desmin. Proliferating cell nuclear antigen was detected in 43% of the tumoral cell population and Ki-67 in 7%.

The KHE is a rare and poorly recognized tumor in animals. In the WHO Classification of Skin and Soft Tissues Mesenchymal Tumors in Domestic Animals, a Kaposi-like vascular tumor is described, only in the dog, usually involving tongue and/or skin [5]. However, in the WHO Classification of Tumors of the Urinary System of Domestic Animals, this histological pattern is not referred [7]. In humans, KHE is also a rare endothelial-derived spindle cell neoplasm, affecting children and early adolescents with fea-

tures common to capillary hemangioma and Kaposi sarcoma [10].

In our case, the histological appearance of the tumor had remarkable resemblance of the spindle cell proliferation of dog and human KHE [5, 6]. The vascular origin was confirmed by its histological appearance with evident blood vessels (which contain numerous erythrocytes) and by its positivity to factor VIII-related antigen, a universally accepted marker for endothelial cells, also expressed in bovine endothelial cells [4]. Gomori's reticulin silver impregnation and immunostaining for collagen IV also demonstrate vasoformative structures. Microscopically, KHE should be distinguished from capillary hemangioma, epithelioid hemangioendothelioma, spindle cell hemangioendothelioma, and Kaposi's sarcoma [9]. In the present case the diagnosis of capillary hemangioma was excluded because of the presence of spindle cells, forming angular

slits. The epithelioid hemangioendothelioma is characterized by the presence of cells that contain intracytoplasmic vacuoles with erythrocytes not seen in our case. Spindle cell hemangioendotheliomas has excluded by the absence of characteristic cavernous vascular spaces usually at the periphery of the lesion. The lack of PAS-positive hyaline globules in the cells, the absence of a characteristic lymphoplasmacytic infiltrate and a less diffusely infiltrative pattern exclude a diagnostic of Kaposi's sarcoma.

The tumor was classified as a kaposiform hemangioendothelioma and as far as we know this is the first report of KHE in cattle. Additionally, to our knowledge this histological type has never been reported in animal urinary bladder.

ACKNOWLEDGMENT. We thank Mrs. Lígia Bento for expert technical assistance.

REFERENCES

1. Carvalho, T., Pinto, C. and Peleteiro, M. C. 2006. Urinary bladder lesions in bovine enzootic haematuria. *J. Comp. Pathol.* **134**: 336–346.
2. Dhawan, S. S. and Raza, M. 2007. Spindle cell hemangioendothelioma. *Cutis* **79**: 125–128.
3. Finnie, J. W., Leong, A. S. and Swift, J. G. 1993. Two haemangioendotheliomas in a bovine brain. *J. Comp. Pathol.* **108**: 393–398.
4. Gulbahar, M. Y., Yuksel, H and Aslan, L. 2003. Angiokeratomatous papilloma associated with papillomavirus in a calf. *Vet. Pathol.* **40**: 582–586.
5. Hendrick, M.J., Mahaffey, E.A., Moore, F.M., Vos, J. H. and Walder, E.J. 1998. Histological Classification of Mesenchymal Tumors of Skin and Soft Tissues of Domestic Animals. pp. 1–62. *In: WHO International Classification of Tumors of Domestic Animals, 2nd Series, volume II* (Schulman, F.Y.S. ed.) Armed Forces Institute of Pathology, Washington, D.C.
6. Mentzel, T., Mazzoleni, G., Dei Tos, A. P. and Fletcher, C. D. 1997. Kaposiform hemangioendothelioma in adults. Clinicopathologic and immunohistochemical analysis of three cases. *Am. J. Clin. Pathol.* **108**: 450–455.
7. Meuten, D. J., Everitt J., Inskeep, W., Jacobs, R. M., Peleteiro, M. and Thompson, K. G. 2004. Histological classification of Urinary System of domestic animals. pp. 1–70. *In: WHO International Classification of Tumors of Domestic Animals, 2nd Series, volume XI*. (Schulman, F.Y.S. ed.) Armed Forces Institute of Pathology, Washington, D.C.
8. Pinto, C., Januário, T., Geraldles, M., Machado, J., Lauren, D. R., Smith, B.L. and Robinson, R.C. 2004. Bovine Enzootic Haematuria on São Miguel Island – Azores. pp. 564–574. *In: Poisonous Plants and Related Toxins* (Acamovic, T., Stewart, C.S. and Pennycott, T.W. eds), CABI Publishing, Wallingford, U.K.
9. Vincek, V., Zaulyanov, L. and Mirzabeigi, M. 2004. Kaposiform hemangioendothelioma: the first reported case in a non-human animal species. *Vet. Pathol.* **41**: 695–697.
10. Wilken, J. J., Meier, F. A. and Kornstein, M. J. 2000. Kaposiform hemangioendothelioma of the thymus. *Arch. Pathol. Lab. Med.* **124**: 1542–1544.