Pathol. Oncol. Res. (2011) 17:969–972
DOI 10.1007/s12253-010-9331-1

CASE REPORT

Kaposiform Hemangioendothelioma of the Spleen in an Adult: An Initial Case Report

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Received: 18 August 2009 / Accepted: 26 October 2010 / Published online: 29 December 2010

Abstract Kaposiform hemangioendothelioma (KHE) is a rare locally aggressive vascular neoplasm characterized by infiltrating nodules and sheets of spindle cells, and unmistakable resemblance to Kaposi's sarcoma. KHE occurs mainly in newborns and infants and presents most commonly in the skin, deep soft tissue, and bone. We report a case of KHE in a 36-year-old female who presented with a spleen mass and underwent splenectomy. Macroscopic examination revealed a large, dark-red, firm mass in the spleen. Histologically, the tumor consisted of irregular, infiltrating nodules of densely packed spindle-shaped tumor cells closely associated with small slit-like and sieve-like blood vessels, which were separated with hyalinized hypocellular fibrous stroma. Immunohistochemically, both spindle and epithelioid cells were positive for CD34, CD31, and vimentin, but negative for EMA, cytokeratin, CD21, CD35, CD1a, and S-100 protein. The well-formed capillaries and mature vessels but not spindle tumor cell showed reactivity for factor VIII- related antigen. Alpha-Smooth muscle actin was detected in pericytes surrounding small round or slit-like capillaries. The final histologic diagnosis was KHE. Follow-up 6 month after operation revealed no sign of recurrence or metastasis.To the best of our knowledge, this is the first report of KHE arising in the spleen.

Keywords Kaposiform hemangioendothelioma · Kasabach–Merritt phenomenon · Vascular tumor · Immunohistochemistry · Spleen

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Introduction

Kaposiform hemangioendothelioma (KHE) is a rare locally aggressive vascular tumor of the skin, deep soft tissue, and bone that occurs mainly in children, often associated with Kasabach-Merritt phenomenon (KMP) and occasionally lymphangiomatosis. This name was coined for its distinctive morphology, characterized by infiltrating nodules and sheets of spindle cells, and unmistakable resemblance to Kaposi's sarcoma (KS) [1, 2]. Many comparisons with similar vascular tumors including KS, capillary hemangiomas, tufted angioma, and juvenile hemangioma have been made in the past. However, recent immunochemical studies have revealed that KHE is a distinct entity [3]. In contrast to most vascular tumors occurring in childhood are benign, KHE shows a highly locally aggressive behavior with a low tendency to resolve spontaneously, but lacks distant metastasis [4], for this reason, it has been classified as an intermediate malignancy between capillary hemangioma and KS [2, 3]. Only 165 such cases have been reported so far [5].

KHE typically occurs in infancy and the first decade of life with the ages ranging from 1 month to 19 years, and a nearly equal sex ratio [3, 5], an increasing number of cases in adults have been reported [4]. These lesions most commonly located in the retroperitoneum and deep soft tissue of the extremities, although some have also been reported in superficial soft tissues, scalp, neck, chest wall, and mediastinum [2–4], however, visceral origin of KHE is extremely rare. KHE involving spleen has not been described previously. We report a case of KHE in a 36-year-old woman who developed a solitary spleen mass, and underwent a splenectomy. Pathological examination of the spleen showed the mass to be KHE, not associated with KMP despite its size.

Clinical History

A 36-year-old woman referred to a local hospital for the uncomfortable upper abdominal symptoms. Colour doppler flow imaging (CDFI) shows the presence of a hypervascular mass, measuring 12.6×10.1×11.0 cm, suggestive of hemangioma. Laboratory findings, including complete blood count, blood biochemistry, fibrinogen and fibrin-split products and urine analysis were all within normal ranges. The HIV and HHV8 were seronegative. The patient underwent splenectomy.

The spleen weighed 350 g, measured 16.0×11.0×10.0 cm, contained a roughly lobulated, elastically hard, and ill-circumscribed hemangioma-like mass, measuring 12.6×12.3×10 cm in diameter. The cut surface showed a purplish to crimson discoloration, separated by lipofibrous tissues.

Material and Methods

The tissues were fixed in 4% formalin and embedded in paraffin wax. Tissue sections of 5-μm thickness were stained with hematoxylin and eosin for histopathologic examination. Additional sections were used for immunohistochemistry with the Dako EnVision System (Peroxidase, DAB) after antigen retrieval with EDTA. The primary antibodies used in this study include alpha-smooth muscle actin (α-SMA, 1A4, 1:50), CD1a (O10, 1: 50), CD3 (F7.2.38, 1:300), CD20 (L26, 1:200), CD21 (2G9, 1:100), CD31 (JC/70A, 1:50), CD34 (QBEnd/10, Ready-to-Use), CD35 (Ber-MAC-CDR, 1:20), CD68 (PG-M1, 1:100), CD163 (10D6, 1:100), cytokeratin (AE1/AE3, 1:50), epithelial membrane antigen (EMA , E29, 1:50), Factor VIII-related antigen (FVIII-Rag, F8/86, 1:150), Ki-67 (MIB-1), S-100 protein (polyclonal, 1:300), and vimentin (V9, 1:200). All primary antibodies were mouse monoclonal antibodies and the DakoCytomation products (Dako, Carpinteria, CA, USA) unless otherwise stated.

Results

Histologically, the tumor consisted of dense spindle cells closely associated with tightly packed small round or slit-like capillaries in a nodular growth pattern, which was separated by hypocellular hyalinized fibrous bands that contained small and medium-size, irregularly dilated lymphatic channels (Fig. 1a). This feature can be clearly demonstrated by immunohistochemical staining for CD31 (Fig. 2a), CD34 (Fig. 2c), or vimentin. The tumor cells were more often uncanalized and showed fascicular arrangement (Fig. 1b), and may appear epithelioid with glomeruloid capillary proliferation and formation of microthrombi, or focally exhibit slit-like and gaped lumen containing red blood cells (Fig. 1c). At the periphery of the lesion, well-formed capillaries appeared dilated and had a thin endothelial lining, frequently containing fibrin thrombi, sometimes filled with congealed blood (Fig. 1d). The tumor cells showed no significant cytologic atypia, nuclear pleomorphism, and mitotic activity. Areas of hemorrhage, hemosiderin deposits, and infiltration by lymphocytes but not plasma cells were seen. The splenic architecture was entirely effaced by the lesion with depletion of lymphocytes.

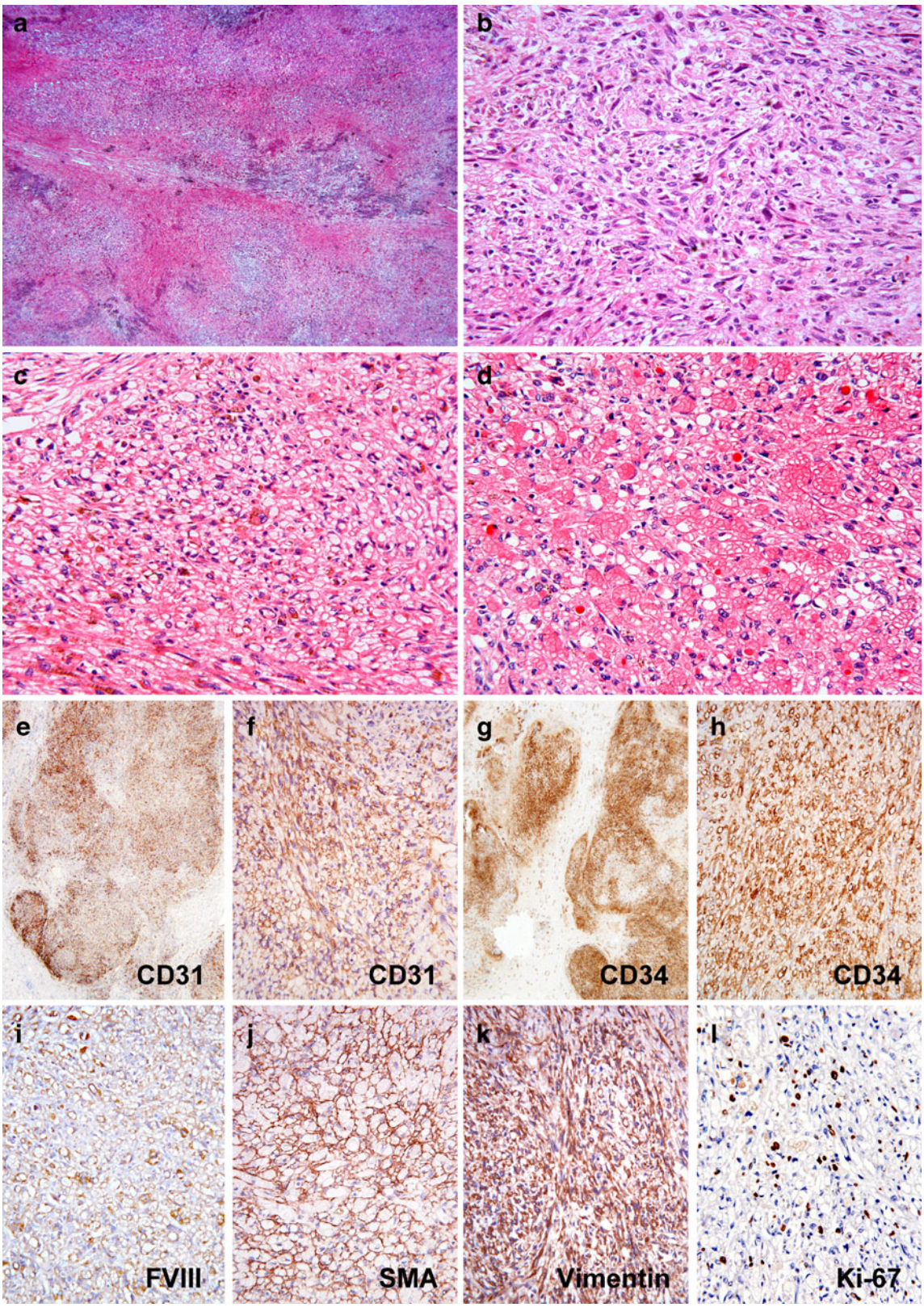
Immunohistochemically, the tumor cells, whether epithelioid or spindled, showed strong positivity for CD31 (Fig. 1e, f) and CD34 (Fig. 1g, h), while only well-formed capillaries and mature vessels showed reactivity for FVIII-Rag (Fig. 1i). In contrast, many spindle cells, presumably pericytes, were stained positively for α-SMA around the vascular spaces (Fig. 1j). The tumor cells were immunoreactive to vimentin (Fig. 1k), but not EMA, AE1/AE3, CD21, CD35, CD1a, CD68, CD163 or S-100 protein. Scattered lymphocytes within and around the tumor were primarily mature T cells positive for CD3 and negative for CD1a. Occasional B cells were demonstrated with CD20 antibody. Approximately 5% of nuclei stained for MIB-1 (Fig. 1l).

Based on these histopathological and immunohistiochemical findings, a diagnosis of KHE was made, and then the patient was referred for chemotherapy. Follow-up 6 month after operation revealed no sign of recurrence or metastasis. The followed-up is ongoing.

Fig. 1 Histopathological and immunohistochemical features of KHE. **a** Low power view of tumor tissue shows irregular infiltrating lobules or sheets of poorly formed small vascular channels surrounded by dense hyaline fibrous septa. **b** The tumor shows fascicles of spindle cells admixed with small round vascular channels or slit-like lumen containing erythrocytes and lined by flat endothelia interrupted the spindle area, which is characteristic of KHE. **c** Lobules composed of glomeruloid nests of epithelioid cells and densely packed plump spindle cells. **d** Glomeruloid nests of epithelioid cells contain hyaline globules and intracytoplasmic lumina with abundant hemosiderin pigment deposition. **e** CD31 staining delineates a distinct architecture of the lesion which shows an irregular, nodular growth pattern of tumor cell infiltrating. **f** High power view shows the spindle cells are diffuse reactivity for CD31. **g** CD34 staining pattern in KHE is similar to CD31 but more interstitial capillaries are stained. **h** The spindle cells and epithelioid cells show strong reactivity with CD34. **i** The well-formed capillaries and mature vessels but not spindle tumor cells show reactivity for FVIII-RAg. **j** α-SMA immunostaining in a cribriform pattern highlights variable member of spindle pericytes around vascular channels. **k** Spindle cell and epithelioid cells show strong reactivity with vimentin. **l**. MIB-1 labeling shows lower proliferative activity. Hematoxylin & Eosin staining. **a**, ×100; **b**, **c**, and **d**, ×400. Dako Envision peroxidase detection system. **e** and **g**, ×100; **f**, **h**, **i**, **j**, **k**, and **l**, ×400

Discussion

In this report, we describe an extremely rare case of splenic KHE in a 36-year-old female without KMP. This tumor



showed a rather typical morphology of KHE, an infiltrative nodular growth of spindle cells with slit-like vascular lumen, surrounded by dense fibrous septa, unmistakable resemblance to KS [1, 2, 4], but no significant cytologic atypia and mitoses. Typically, high mitotic rate and nuclear atypia are not features of KHE [2, 3]. By immunohistochemistry, both epithelioid and spindle tumor cells expressed endothelial markers CD31, and CD34, but not

FVIII-RAg, which is only positive in mature capillaries and vessels, while α-SMA and vimentin was expressed only by pericytes that outlines tumor spindle cells, but not by these spindle cells, results that are consistent with the earlier observations [1, 3]. Despite its unusual site, the aggressive clinical course, typical histopathologic and immunohistochemical features in our case favor a diagnosis of KHE. To our knowledge, our case is the first report of KHE involving the spleen, not associated with KMP.

A variety of vascular tumors that are histologically similar to KHE should be considered in the differential diagnosis, particularly in patient presence of KMP. These may include cellular capillary hemangioma (cellular juvenile or infantile hemangioma), KS, tufted angioma, spindle cell hemangioma (hemangioendothelioma), and epithelioid hemangioendothelioma. These tumors can be differentiated from KHE by their lack of one or more clinpathologic features observed in typical KHE, including a nodular or lobular growth pattern of spindle cell, forming slit-like spaces and gaped vascular lumen with hyaline globules and hemosiderin deposition, surrounded by broad hyalinized fibrous septa [1–6].

KHE is often associated with KMP, a consumptive coagulopathy associated with vascular lesions, characterized by profound thrombocytopenia, life-threatening hemorrhage, and lymphangiomatosis [2, 3, 7]. Generally, younger patients are more likely to have KMP (77% vs 11%) when comparing age of presentation before and after the age of 4 years [7]. Most of the adult patients showed KHE without an association with KMP but local or distant lymphangiomatosis [2, 3]. For patients without KMP and cutaneous manifestations, it would be difficult to consider the diagnosis of KHE prior to surgery [3]. However, neither of KMP and lymphangiomas was identified in our case.

Therapeutic protocols for KHE have been limited by far by a lack of experience due to the relative rarity of this neoplasm. The most effective therapy of KHE is complete excision, but for not respectable and extensive lesion with KMP [1, 3]. Treatment with corticosteroids, alpha-interferon, embolization, ticlopidine plus aspirin, chemotherapy, and radiation therapy have all been reported, with varying success [8, 9]. Several case reports have described positive patient outcomes with multimodality and chemotherapeutic regimens, however, the overall mortality remains high for retroperitoneal and mediastinal neoplasms [10].

The prognosis of KHE is mainly related to the size, anatomic site, and extent of the neoplasm, and greatly influenced by associated coagulopathy [2–4]. These tumors tend to be locally invasive, scarcely regional lymph node metastases, but are not known to produce distant metastases [2–4], while many have died as a result of extensive disease and severe coagulopathy rather than tumor recurrence [3, 8]. By comparison, retroperitoneal lesions or visceral forms are associated with a worse prognosis, with a reported mortality of up to 24%, because of bleeding or tumor invasion into vital organs [9].

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