Kaposiform Hemangioendothelioma

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Introduction

Kaposiform hemangioendothelioma (KHE), first described by Zuckerberg et al. in 1992, is a rare, locally aggressive vascular neoplasm that mainly occurs in children and presents common histopathologic features to both hemangiomas and Kaposi sarcoma. The incidence is estimated at 0.07/100,000 children per year. It generally originates on the skin and soft tissue, usually affecting deeper tissue by infiltrative growth. Although visceral involvement is uncommon, the occurrence of KHE within the bone and retroperitoneal or mediastinal spaces has been described. About 160 cases have been reported in the literature. In more than 70 % of cases, KHE is associated to Kasabach-Merritt syndrome (KMS) and lymphangiomatosis. KMS designs patients in which the neoplasm occur in association with profound thrombocytopenia (<20,000), consumptive coagulopathy, and hypofibrinogenemia with fibrin degradation products resulting from the localized intravascular coagulation in the tumor.

Clinical Features

KHE presents during early childhood (most often in the first years of life) with fewer than 20 adult patients reported in the literature, and it is more common in males. It appears as one or multiple violaceous subcutaneous masses with ill-defined borders and a purpuric, bruised appearance. In most cases, the tumor involves the extremities and trunk (75 % of cases). Approximately 10 % of KHE do not involve the skin. The retroperitoneum is the most frequent extracutaneous location, followed by the muscle, bone, and thoracic cavity. Over time, especially in cases associated with KMS, the tumor becomes indurated and firm with a red purple hue, ecchymoses, and petechiae.

Pathology

The features of KHE resemble both a capillary hemangioma and Kaposi sarcoma (Figs. 37.1, 37.2, and 37.3). KHE shows infiltrating sheets composed of variably spindled endothelial cells, slit-like vascular channels reminiscent of Kaposi sarcoma, microthrombi, hemosiderin deposition,

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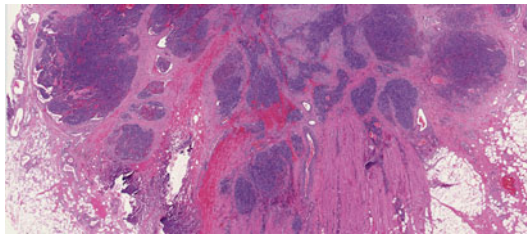

Fig. 37.1 Kaposiform hemangioendothelioma. Irregular tumor nodules growing in an infiltrative fashion and evoking a dense hyaline stromal response (Courtesy of H. Kutzner, *Friedrichshafen*)

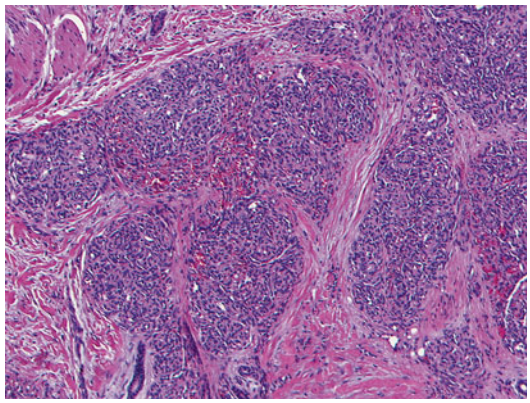

Fig. 37.2 Kaposiform hemangioendothelioma. Tumor nodules composed with well-canalized areas alternating with poorly canalized and solid-appearing areas resembling a capillary hemangioma (Courtesy of H.Kutzner, *Friedrichshafen*)

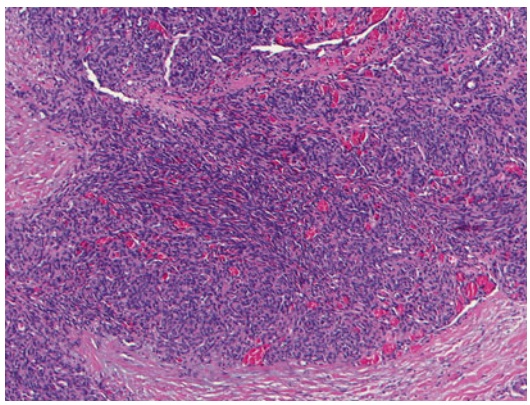

Fig. 37.3 Kaposiform hemangioendothelioma. Infiltrating sheets composed of variably spindled endothelial cells and slit-like vascular channels reminiscent of Kaposi sarcoma (Courtesy of H.Kutzner, *Friedrichshafen*)

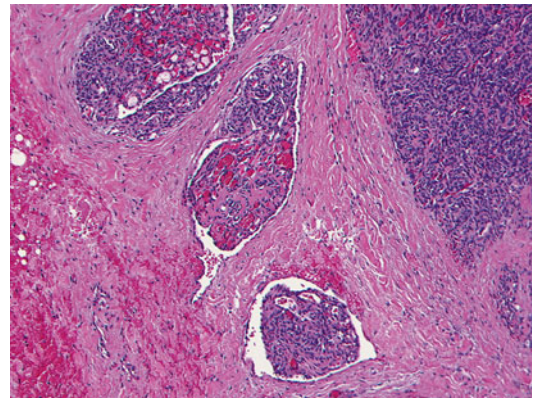

Fig. 37.4 Kaposiform hemangioendothelioma. Some areas show a glomeruloid pattern (Courtesy of H.Kutzner, *Friedrichshafen*)

edema, fibrosis with scanty inflammatory cells, and abnormal lymphatic channels. Tumor nodules surround areas that are well canalized alternating with solid-appearing areas mimicking a capillary hemangioma. Some areas may show a glomeruloid pattern reminiscent of renal glomeruli (Fig. 37.4). The rate of mitosis is variable but usually is not high. Endothelial cells in nodules are CD31, CD34, D2-40, PROX-1, and FLI1 positive but negative for GLUT1 and LeY (juvenile hemangioma-associated antigens). Focal actin positivity may be seen. HHV-8 transcripts are not identified.

Differential Diagnosis

The diagnosis is based upon the histology and on its correlation with clinical features, in particular the depth of the lesion. The relationship between KHE and tufted angioma is controversial. The "cannon ball" distribution of skin nodules and their "tufting" into ectatic spaces are characteristic of tufted angioma. In KHE, the tumor nodules coalesce, enlarge, and assume a widely infiltrative pattern within the fibroblastic stroma, a feature not observed in tufted angioma. A different pattern of expression of D2-40 has been reported as useful to distinguish the two entities. Nevertheless, the morphological overlap between KHE and tufted angioma has led to consider the

two lesions into the same disease spectrum and that tufted angioma may represent a minor form of KHE.

Prognosis

KHE tend to be locally invasive, but are not known to produce distant metastases. Several factors are associated with the outcome of patients with KHE: accessibility to surgical excision; location (cutaneous versus deep involvement); size of tumoral mass; clinical response to interferon, glucocorticoids, or propranolol; and the presence of lymphangiomatosis and KMS. The latter phenomenon is directly responsible for the significant morbidity and mortality, including hemodynamic instability, local invasion, and compression of vital structures.

Treatment

Surgical excision is the treatment of choice for tumors of limited size. However, since the margins are often poorly defined, surgical excision is often incomplete. For tumors that are not resectable, prednisone, vincristine, sirolimus, interferon alpha, propanol, and antiplatelet drugs have been used. However, no single regimen leads to the complete resolution of the tumor. The management of infants with KHE associated with Kasabach-Merritt phenomenon involves primarily the treatment of the tumor responsible for the coagulopathy and supportive measures to maintain hemostasis.

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