

CASE REPORT

Kaposiform hemangioendothelioma with fatal outcome: Kasabach–Merritt phenomenon and hypercalcemia

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Abstract

Kaposiform hemangioendothelioma is a rare, borderline tumor that typically occurs during early childhood. Kasabach–Merritt phenomenon is a complication characterized by a consumptive coagulopathy resulting from the localized intravascular coagulation. Hypercalcemia generation is a rare association that was related in our case to parathyroid hormone-related protein produced by this angioma.

KEYWORDS

dermatology, hematology, pediatrics and adolescent medicine

1 | INTRODUCTION

Kaposiform hemangioendothelioma (KHE) is a rare, locally invasive vascular tumor that typically occurs during early childhood. Kasabach–Merritt phenomenon (KMP) is a rare but life-threatening complication of KHE, which is characterized by thrombocytopenia and coagulation abnormalities. Herein, we report a new rare case of KMP combined with hypercalcemia caused by KHE.

2 | CASE REPORT

A 15-day-old infant was presented with a rapidly enlarging angiomatous mass, located in the palm of the hand present since birth. It had increased in diameter size from 2

to 8 cm within 15 days reaching the dorsum of the hand. The patient was born full-term, with normal delivery and birth weight. He had presented neonatal jaundice requiring phototherapy. Physical examination showed a red to purple mass with an advancing ecchymotic rim and a brilliant telangiectatic surface with bleeding ulcerations (Figure 1). On palpation, the tumor was firm and warm with a thrill. Baseline laboratories, including platelets count, showed thrombocytopenia of $100.000/\text{mm}^3$, which later decreased to $45.000/\text{mm}^3$. Laboratory coagulation testing revealed high D-dimers ($729 \mu\text{g/L}$) (normal range: $0\text{--}500 \mu\text{g/L}$), high bilirubin value ($161 \mu\text{mol/L}$) (normal range: $5\text{--}17 \mu\text{mol/L}$), anemia (hemoglobin: 11.1 g/dl), low rate of fibrinogen, and normal rate for prothrombin as well as activated partial thromboplastin time. The diagnosis of Kasabach–Merritt phenomenon (KMP) complicating a

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vascular tumor was made. Initially, the patient was treated with oral prednisolone 3 mg/kg/day and acetylsalicylic acid 10 mg/day. Follow-up laboratory studies showed significant improvement in hematologic parameters with normalization of the platelet count and D-dimer, but the mass continued to enlarge rapidly to reach 18 cm 1 month later (Figure 2). Ultrasound revealed an arterial and venous vascular proliferation with peripheral arteriovenous microfistulas. Magnetic resonance imaging (MRI) had shown multi-lobular mass with extension to the forearm, without bone lysing. Radiographic examination had not shown elsewhere location. A skin biopsy concluded in a



FIGURE 1 Red to purple mass with an advancing ecchymotic rim and a brilliant telangiectatic surface

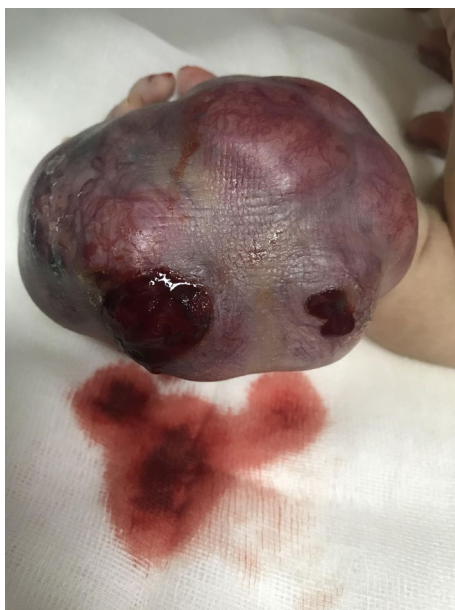


FIGURE 2 Large mass, 18 cm in diameter with bleeding ulcerations

kaposiform hemangioendothelioma (KHE) (Figure 3A–C). Immunohistochemistry was positive for CD31 and negative for CD34, factor 8, AML, and GLUT1 (Figure 3D). During his hospitalization, he presented drowsiness with diarrhea leading to discover a hypercalcemia (3.98 ml/L). Treatment includes intravenous fluids and diuretics with prednisolone. Further explorations of this hypercalcemia showed a low PTH at 3.78 pg/ml, normal 25OH vit D, increased calciuria, and stage 3 nephrocalcinosis on abdominal ultrasound, which exclude hyperparathyroidism (primary or secondary), vitamin D metabolic disorder. Also, bone infiltration was excluded. PTH-related protein secretion from tumors was suspected. Unfortunately, few days later, the patient is dead.

3 | DISCUSSION

Kaposiform hemangioendothelioma is a neoplasm of intermediate malignancy that was first designated by Zukerberg and colleagues¹ in 1993 because of its locally invasive growth, aggressive course, and “focal Kaposi-like appearance.” It mostly occurs during the first year of life, and over 50% of KHE lesions were present at birth.^{2,3} It occurs mostly on proximal arms, legs, trunk, head, and neck. It can have a deep location such as retroperitoneum. Its origin is multifactorial with genetic factors.²

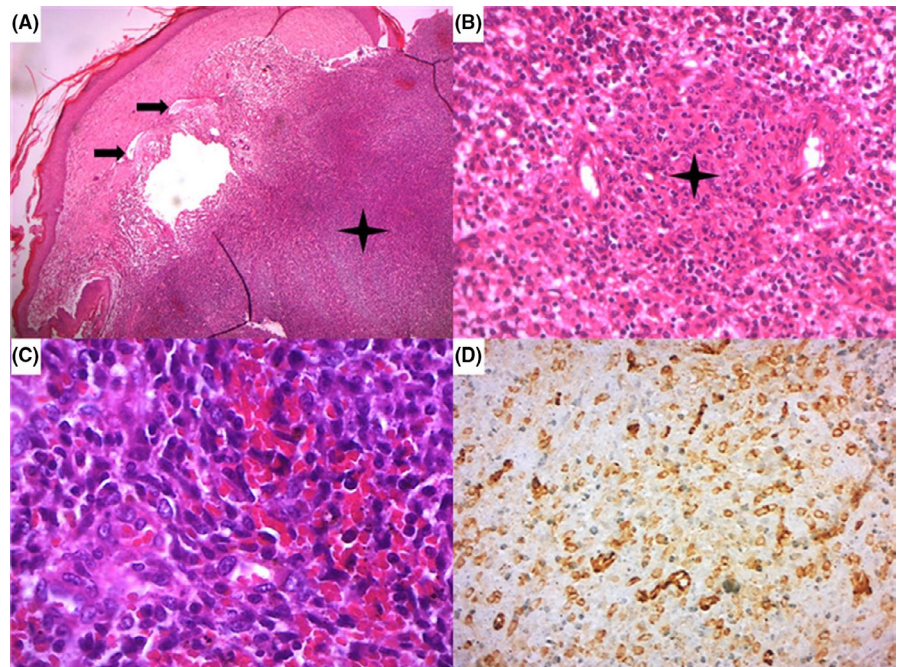
Patients with KHE may develop an aggressive locally growing associated with thrombocytopenia and consumptive coagulopathy resulting from the localized intravascular coagulation. This feature corresponds to KMP. The latter complicates KHE in 70% of cases³ and less frequently tufted angioma. Rapid tumor growth and coagulation abnormalities lead to intralesional hemorrhage, severe anemia, muscles and bone infiltration, compression of vital structures, and hemodynamic instability.⁴ The mortality rate of KHE complicated by KMP ranges from 10% to 40%.

Special KHE presentations associated with a higher incidence of KMP are retroperitoneum and intrathoracic location,² multifocality, lesion size, and deep infiltration.^{4,5}

Magnetic resonance imaging is generally a first-line assessment because the deep infiltrating nature of KHE may not be apparent on physical examination or on ultrasound. The tumors involved multiple tissue planes and had poorly defined margins with remodeling of adjacent bone.^{3,5} Biopsy should be considered if possible and safe in patients with an uncertain diagnosis.

Kasabach–Merritt phenomenon combined with hypercalcemia (HC) is reported in one case in 35-day-old infant with HEK of the upper right arm.⁶ The level of blood calcium was reduced to normal following surgery. Calcium balance is the combined effect of regulation, through parathyroid hormone (PTH), calcitonin, and active vitamin D3.

FIGURE 3 (A): Tumor shows infiltrative growth pattern of a highly cellular proliferation (asterisk) with adjacent lymphangiomatosis (arrows) (hematoxylin and eosin $\times 25$); (B): Glomeruloid structures are seen in the proliferation (asterisk) (hematoxylin and eosin $\times 200$); (C): At high magnification, the tumor is composed of bland spindle cells, resembling those of Kaposi sarcoma, surrounding slit-like spaces containing erythrocytes (hematoxylin and eosin $\times 400$); (D): immunohistochemically, spindle cells are positives for CD31 ($\times 400$)



For our patient, results from PTH and vitamin D examination showed neither primary hyperparathyroidism nor vitamin D metabolic disturbance. Since KHE is a borderline tumor, which had been previously reported in association with HC,⁶ HC generation was related to PTH-related protein (PTHrp) produced by this angioma, but the level of PTHrp cannot be measured. Surgical treatment was impossible.

Soon after the diagnosis of KMP, patients should be treated aggressively with a combined regimen. Supportive treatment includes infusion of blood components (thrombin and fibrinogen) and an anti-platelet drugs. The infusion of platelets is discouraged in the absence of acute bleeding because their VEGF content might stimulate tumor growth. Oral prednisolone (3–5 mg/kg/d) has been recommended as the first-line treatment for KHE with KMP with variable results. In case of resistance to steroids, alternative treatments, such as vincristine and interferon, should be considered. Surgical resection is the definitive treatment of KHE, but is rarely possible because of infiltration and bleeding. Radiation therapy is efficient but should not be used because of its adverse effects. Embolization is possible but rarely applicable. Recent studies have demonstrated a satisfactory efficacy of sirolimus, an inhibitor of mammalian target of rapamycin (mTOR) in the treatment of KHE.⁷

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None.

CONFLICT OF INTEREST

The authors have no potential conflicts of interest to disclose.

AUTHOR CONTRIBUTIONS

BM, RM, and BE wrote the manuscript. BS, AM, and SF contributed to the management of the patient and revised the manuscript. TM and TS wrote parts of the manuscript related to the histopathological aspects of the disease. LG and HT critically reviewed the manuscript and gave final approval. All authors have read and approved the final manuscript and agree to take full responsibility for the integrity and accuracy of the work.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

DATA AVAILABILITY STATEMENT

In accordance with the DFG Guidelines on the Handling of Research Data, we will make all data available upon request.

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