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CASE REPORT

# Associated with Kaposiform Hemangioendothelioma Kassabach Merritt Syndrome - Case Report

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## Abstract

The authors describe a case of Kaposiform Hemangioendothelioma on the palate, associated Kasabach Merrit Syndrome in childhood. During corticosteroid therapy presented recurrence, being associated interferon alfa. Since then , it had no new admissions with almost complete remission of the tumor.

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## INTRODUCTION

Kaposiform Hemangioendothelioma (KHE) is a rare vascular tumor, and is present in the cutaneous and/or visceral form. It has benign histological characteristics; however, mortality is high if left untreated. Few cases have been reported in the literature since its initial description. KHE may be associated with Kasabach-Merritt syndrome (KMS), which is characterized by a consumptive coagulopathy with severe thrombocytopenia and microangiopathic hemolytic anemia[1].

Treatment of KHE is controversial and should be personalized[1-5]. A good prognosis is usually reached when KHE is not associated with KMS. This report describes the case of a preschooler male patient, with KHE in the palate associated with KMS; treatment involved corticoid and interferon-alpha therapy, and the therapeutic response was good.

## CASE REPORT

A two-year-old male patient, born and resident of Campo Florido, state of Minas Gerais, Brazil, was admitted to the pediatrics emergency room, with a productive cough and precordialgia for one week. The results of physical examination indicated the patient presented with dyspnea, a 1 x 1.5 cm hemangioma in the palate, and hepatosplenomegaly. The echocardiogram showed a pericardial effusion and later, and the results of pericardiocentesis indicated lymphocytosis.

Infectious diseases, neoplasms, and autoimmune diseases were excluded. An ultrasound of the abdomen was performed and indicated homogeneous hepatomegaly and heterogeneous splenomegaly. Corticotherapy (prednisone, 1 mg/kg/day) was initiated empirically, with the improvement of symptoms but without a specific diagnosis. Ambulatory follow-up was done but was interrupted after a few months.

One year later, the patient presented the same symptoms and was hospitalized again; the symptoms evolved to disseminated intravascular coagulation (platelets = 6000/mm$^3$, PT = 41.4 sec, INR = 1.16, and fibrinogen = 105 mg/dL), and microangiopathic hemolytic anemia (hemoglobin = 6.2, presence of schistocytes in the peripheral blood, HDL = 469).

He was treated again with corticosteroids (methylprednisolone at 1 mg/kg/day, which was later switched to prednisone at 20 mg/day) and had a hemodynamic stabilization and subtle remission of the tumor. An MRI of the abdomen showed homogeneous and discreet hepatomegaly associated with multiple vascularized splenic micronodules. These findings are observed in cases of hemangioendothelioma, which is diagnosed in infectious diseases associated with immunosuppression.

However, laboratory tests excluded infectious diseases. The patient eventually developed Cushing's syndrome, and an attempt was made to interrupt the use of corticosteroid after three years of therapy but was not successful.

In December 2012, he was hospitalized with severe pneumonia, which evolved to KMS, and was subjected to corticosteroid and interferon-alpha therapy. The patient responded well to therapy, was discharged from the hospital, and used prednisone at 20 mg/day and interferon alpha at 3,000,000 IU three times a week. This therapy was maintained for approximately three years without new hospitalizations up to this date, with gradual remission of the hemangioma in the palate (its current dimensions are 0.5 x 0.5 cm) (Figure 1).



**Figure 1.** Hemangioma in the palate, measuring 0.5 x 0.5 cm Source: Authors.

## DISCUSSION

KHE is a rare and aggressive tumor[1] with benign histological characteristics; however, it has a malignant behavior with local proliferation and often involves vascular aggression[4]. It was first described in children in 1993 by Zukerber, Nickoloff, and Weiss[6].

It occurs more frequently in children younger than two years, although it has been reported in adults[7], and its incidence in women is slightly higher than that in men. In the United States, hemangiomas occur in approximately 2.5% of newborns[4].

The most pronounced clinical manifestation is a poorly delimited plaque, purplish in color, hard, and with a radial expansion similar to a bruise[1,2]. The patient may present hepatosplenomegaly due to platelet sequestration or

intracavitary lesions. In addition, pericardial effusion secondary to anemia may occur, as observed in our patient. Hemangiomas are common in the trunk or extremities.

One in every 300 cases of hemangiomas involves coagulopathy, which is often associated with lymphangiomatosis or KMS, ulceration, and bleeding of the hemangioma[4]. In SKM, the presence of a vascular tumor triggers consumptive coagulopathy with thrombocytopenia via imprisonment of platelets and microangiopathic hemolytic anemia.

The diagnosis of KHE is histopathological in cases in which undefined multiple nodules are separated by connective tissue, and these nodules infiltrate the dermis and subcutaneous tissue. These nodules are composed of small capillaries covered by endothelial cells and fusiform clusters of epithelial cells of epithelioid aspect.

In particular, hemosiderin, intracytoplasmic hyaline bodies in the fusiform cells, and vacuoles in the eosinophilic cytoplasm of epithelioid cells are observed (Figure 2). Fusiform cells and the frequent presence of fibrin cells simulate Kaposi's sarcoma. However, the presence of epithelioid cells helps discard the occurrence of this disease[1,3].

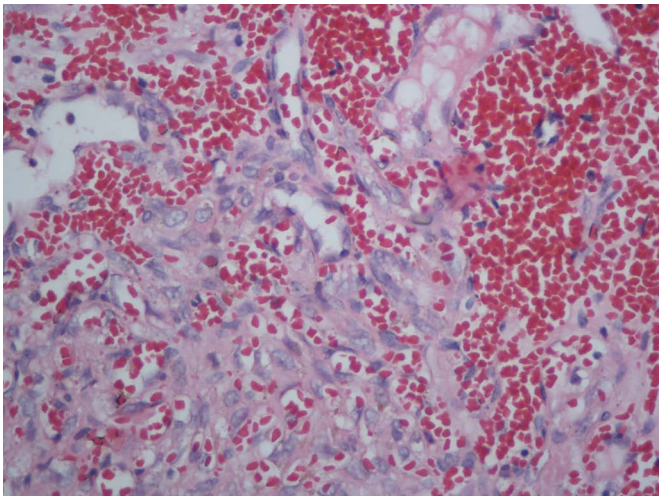


**Figure 2.** Histological examination indicated the presence of a large number of extravasated red blood cells and granular deposits of hemosiderin, with areas of sclerosis and the formation of small vascular spaces between cells. These cells were either rounded or fusiform. Source: Authors.

Coagulopathy can occur during hemangioma growth or, later, it can be associated with a contusion of the lesion. Treatment consists of supportive care and corticoid therapy as the first-line treatment until resolution of symptoms.

When corticosteroid treatment is not adequately effective, it can be associated with chemotherapeutic drugs such as vincristine, interferon alpha, and rapamycin. Interferon alpha is an immunomodulator that limits angiogenesis by decreasing the levels of fibroblast growth factor and inhibiting endothelial growth factor. Interferon alpha is not recommended for infants younger than one year because of its adverse effects on the central nervous system[8]. It is recommended in cases of life-threatening and functional risk to the patients who did not respond well to corticosteroid therapy and is more effective when initiated early[9].

Few studies have evaluated the treatment of this condition with rapamycin and vincristine; therefore, the use of interferon alpha was chosen on the basis of the reports available and the severity of this case. Our patient was empirically subjected to corticoid therapy because the possibility of an autoimmune disease was not discarded.

When follow-up was interrupted, the use of corticosteroids was also ceased, leading to the reappearance of symptoms and subsequent hospitalization and diagnosis of KHE. When an attempt was made to interrupt treatment with prednisone because of its long-term side effects, remission of symptoms occurred, and therefore, the patient was subjected to interferon-alpha therapy.

Since then, the patient did not present KMS, the hemangioma was stabilized in the palate, and a gradual remission was observed in the previous year. In cases of KHE restricted to the skin and without coagulopathy, a surgical excision can be done. KHE can be fatal in 20% of cases, usually associated with the KMS[5]. No case studies have been reported on the survival of patients with KHE associated with KMS. The disease has a good prognosis when diagnosed and treated from the onset.

## REFERENCES


1. Kamiyama SY, Almeida LM, Quattrino AD, Lopes M, Rochael MC. Hemangioendotelioma kaposiforme. Dermatol Pediatr Lat. 2008;6(3):141-4.
2. Cooper JG, Edwards SL, Holmes JD. Kaposirform hemangioendothelioma: case report and review of literature. Br J Plast Surg. 2002;55(2):163-5. PMID: 11987956 DOI: http://dx.doi.org/10.1054/bjps.2001.3769
3. Walker GM, Abu-Rajab R, MacLennan A, Hajivassiliou CA, Howatson AG, Carachi R. Kasabach-Merritt syndrome in a neonate caused by a kaposiform hemangioendothelioma. Med Pediatric Oncol. 2002;38(6):424-7. DOI: http://dx.doi.org/10.1002/mpo.1357
4. Mukai AO, Zanlochi AG, Elias CP, Holim CH, Baida LL, Tutia PC, et al. Hemangioendotelioma kaposiforme e síndrome de Kasabach-Merritt. Rev Paul Pediatr. 2008;26(2):192-6. DOI: http://dx.doi.org/10.1590/S0103-05822008000200017
5. Rodriguez Z N, Benavides J P. Sirolimus (rapamicina) en pacientes con hemangioendotelioma kaposiforme: Caso Clínico. Rev Chil Pediatr. 2013;84(5):537-44. DOI: http://dx.doi.org/10.4067/S0370-41062013000500009
6. Zukerberg LR, Nickoloff BJ, Weiss SW. Kaposiform hemangioendothelioma of infancy and childhood. An aggressive neoplasm associated with Kasabach--Merritt syndrome and lymphangiomatosis. Am J Surg Pathol. 1993;17(4):321-8. DOI:http://dx.doi.org/10.1097/00000478-199304000-00001
7. Zhang H, Luo J, Feng X. Kaposiform hemangioendothelioma in the uterine cervix of a 5-year girl. Fetal Pediatr Pathol. 2012;31(5):273-7. DOI: http://dx.doi.org/10.3109/15513815.2012.659382
8. Kai L, Wang Z, Yao W, Dong K, Xiao X. Sirolimus, a promising treatment for refractory Kaposiform hemangioendothelioma. J Cancer Res Clin Oncol. 2014;140(3):471-6. PMID: 24464150 DOI: http://dx.doi.org/10.1007/s00432-013-1549-3
9. López Almaraz R, López Gutiérrez LJ, Belendez Bieler C, Herrero Hernández A, Mateos González ME, Ramirez Villar G. Tumores vasculares en la infancia. An Pediatr (Barc). 2010;72(2):143.e1-143.e15.