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CASE REPORT

## Hemangioendotelioma Kaposiforme: Relato de Caso

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### Abstract

Kaposiform hemangioendotelioma is considered a benign vascular tumor, with locally invasive characteristics and histological similarity to Kaposi sarcoma. It is related to complications with varying degrees of morbidity and mortality. The definitive diagnosis is made by histological examination and the treatment course can be either surgical or drug therapy, which varies according to patients clinical indication. The aim of the research is to publish a case of Kaposiform Hemangioendotelioma admitted to a pediatric hospital in Santa Catarina, in 2022. Clinical, epidemiological and laboratory data were obtained by consulting the patients medical record; the reported case data were compared with what is described in the current literature about the disease, discussing their similarities and differences and, finally, confirming the diagnosis, through the anatomopathological exam. Despite the fact of little knowledge between physicians and pediatricians, Kaposiform Hemangioendotelioma is a disease of relevance in the medical field, since its differential diagnoses are the most common vascular tumors of childhood, infantile hemangioma and congenital hemangioma. The purpose of the study is to describe a Kaposiform Hemangioendotelioma case and alert health care professionals the recognition of diseases signs and symptoms and the need to carry out a differential diagnosis in such patients.

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## INTRODUCTION

Described for the first time in 1993 by Zukerberg and collaborators, Kaposiform Hemangioendothelioma is a benign vascular tumor that typically appears in the first years of life, characterized by an erythematous mass, locally invasive growth, aggressive course and histological similarities to Kaposi's sarcoma<sup>1,2</sup>. Data from international literature suggest a prevalence of 0.91 cases per 100,000 children<sup>2</sup>.

Due to its aggressive pathogenesis, it can lead to complications, such as Kasabach-Merritt Phenomenon, musculoskeletal disorders, lymphedema and compression of vital structures. It consists of an important differential diagnosis with Infantile Hemangioma and Congenital Hemangioma, mainly due to the phenotypic similarity of the lesion and age range of involvement<sup>2</sup>.

Regarding treatment, surgical resection of the lesion is considered curative; however, when this is not possible, drug treatment is chosen<sup>3</sup>.

This article describes a case of Kaposiform Hemangioendothelioma affecting a school-age patient undergoing outpatient care at a tertiary hospital in Santa Catarina, with the aim of alerting healthcare professionals about this diagnosis, its possible complications and its important differential diagnoses.

## REPORT

A 9-year-old male student was referred to the Pediatric Dermatology outpatient clinic due to a lesion on his face, which had been growing progressively for around 2 years. Initially, the lesion was described as a purplish stain, which gradually evolved into a plaque with an irregular appearance, with an increase in size and volume, associated with pain, itching and recurrent, minor and self-limited local bleeding. Two other similar injuries appeared months after the first, just centimeters apart. The minor had no other complaints and there was nothing significant in his health history.

On physical examination, the largest lesion was described as a warty appearance, brownish-purple in color, measuring 2.5 cm x 1.8 cm, in the left malar region; 2 other lesions of similar appearance, smaller in volume and diameter, were located in the temporal region and left ear pinna (figure 1).

For etiological investigation, a punch biopsy was performed, the report of which was suggestive of verrucous hemangioma; however, Kaposiform Hemangioendothelioma cannot be ruled out.

With the persistence of intermittent bleeding in a lesion in the left malar region, magnetic resonance angiography was requested to assess its extent and plan its excision. The examination revealed 3 nodules in the left region of the face, with intense contrast enhancement, extending to the subcutaneous plane. A complete resection

of the lesions was performed, using a local flap, without complications.

The anatomopathological examination showed atypical spindle cells, containing hyaline globules in their cytoplasm, extending into the hypodermis (figure 2); the peripheral margins of the lesion were free, but with deep margins compromised. Immunohistochemistry revealed positivity for CD31, CD34 and Ki-67 markers, in addition to a negative test for Human Herpesvirus 8 in the cells evaluated, confirming the diagnosis of Kaposiform Hemangioendothelioma.

The patient has maintained outpatient follow-up since his diagnostic investigation in 2022 until the time of publication of this article, with good postoperative evolution and no recurrence of the injury or complications associated with the reported disease.



**Figure 1.** lesions located on the face, on the left.

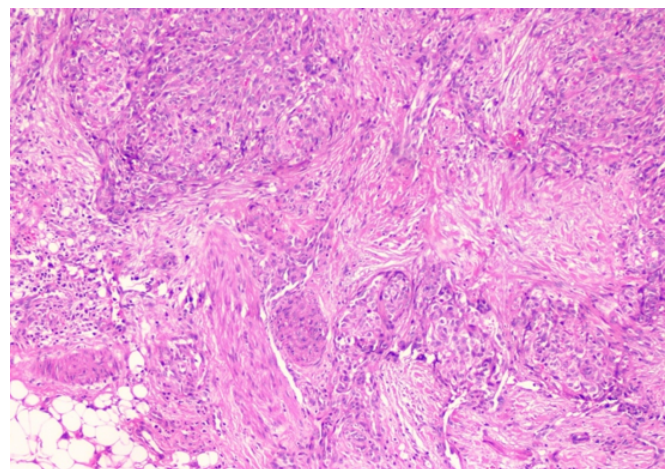


**Figure 2.** Hematoxylin&Eosin (H&E), 100x: spindle-shaped tumor cells, arranged in nodules.

## DISCUSSION

In 1993, Zukerberg and colleagues first described the benign vascular tumor that is now known as Kaposiform Hemangioendothelioma (KHE). Until its description, KHE was commonly classified as Infantile Hemangioma; however, both pathologies differ in terms of locally invasive growth, aggressive course and histological similarity to Kaposi's sarcoma, characteristic of KHE<sup>1-3</sup>.

In the United States, in one of the few studies on the epidemiology of the disease, a prevalence of 0.91 cases per 100,000 children was found. Of these, 60% of cases manifested during the neonatal period and up to 90% in the first year of life. It is believed that its prevalence is underestimated, as small, asymptomatic KHE lesions can be mistakenly diagnosed as Infantile Hemangioma<sup>2,4</sup>.

Despite appearing in a school-age patient, the vascular tumor in the reported case appears in accordance with what is described in the literature, as it is characterized by nodular, firm and progressively growing skin lesions.

Around 88% of the cases found are cutaneous involvement, located mainly on the extremities, head and neck. Although rare, deep and multiple tumors have also been described, located in different locations, such as the retroperitoneum, mediastinum and bones. If left untreated, these lesions rarely regress spontaneously<sup>2,3,5</sup>.

Infantile Hemangioma (IH) and Congenital Hemangioma (CH) are important differential diagnoses, due to the phenotypic similarity of the lesions on physical examination. IH is the most prevalent vascular tumor in children and is marked by the expressive and abrupt growth of a disorganized mass of blood vessels between 3 and 5 months of life, in addition to spontaneous involution beginning at the end of the first year of life. CH, on the other hand, is characterized by a cutaneous vascular tumor completely formed at birth – similar to 60% of cases of KHE, present at birth or in the neonatal period – and can be differentiated by the fact that CH potentially evolves in the first year of life. Exams are rarely necessary for diagnostic definition; however, upon immunohistochemical examination, IH is positive for Glut-1 and CH for WT-1, CD31 and CD34<sup>2,5,6</sup>.

KHE investigation requires clinical suspicion, imaging examination, histopathological and immunohistochemical analysis. Ultrasound is the initial examination for small and superficial lesions, whereas magnetic resonance imaging is indicated for the evaluation of deep lesions or those not apparent on physical examination. They show a nodule with well-defined margins, involvement of adjacent planes and diffuse contrast enhancement<sup>2</sup>.

Even with a physical examination that could suggest a vascular tumor, the reported patient was initially investigated with punch biopsy because his presentation was not compatible with infantile hemangioma - the likely diagnosis, as it is the most common vascular tumor in children -; since the tumor appeared at a school age, showing progressive

growth for more than 1 year, without involution and with an invasive appearance.

Without a clear etiological definition with the initial biopsy, the investigation was expanded with magnetic resonance angiography and a surgical procedure was scheduled for complete resection of the lesion and histopathological evaluation - this being considered the gold standard diagnostic test. The following lesions are suggestive of KHE: infiltrative, well-defined margins, composed of atypical spindle-shaped endothelial cells that align to form misshapen blood and lymphatic vessels, favoring the formation of platelet microthrombi, accumulation of hyaline globules and extravasation of hemosiderin deposits. On immunohistochemistry, these cells are positive for markers CD31, CD34, VEGFR-3, D2-40 and Prox-1 and negative for Glut-1 (marker of hemangiomas) and staining for Human Herpesvirus 8 (related to Kaposi's sarcoma)<sup>2,6,7</sup>.

Among the possible complications associated with KHE are musculoskeletal disorders and lymphedema, caused by the invasion of adjacent tissues by KHE<sup>2</sup>.

The Kasabach-Merritt phenomenon (KMP) is another associated complication, occurring in up to 70% of patients with KHE. Considered a coagulopathy, the phenomenon is characterized by the entrapment of platelets in misshapen blood vessels, formation of microthrombi, microangiopathic hemolytic anemia, consumption of fibrinogen and coagulation factors. It is related to tumor size, being a rare manifestation in small tumors - such as the case reported, without description of the phenomenon - and frequent in tumors that are more than 8 cm in diameter<sup>3,8</sup>.

Clinically, the phenomenon can be manifested by a rapid increase in volume, engorgement, pain and darkening of the tumor color. It is evident on physical examination in skin lesions, but it is rarely diagnosed clinically in deep lesions. Vital signs are usually altered by coagulopathy, resulting in hemodynamic instability. Furthermore, when in deep locations, the phenomenon can lead to a secondary complication - compression of vital structures<sup>2,7,8</sup>.

The evaluation of KMP requires laboratory tests, shows thrombocytopenia, increased prothrombin activity time, activated partial thromboplastin time, hypofibrinogenemia and increased d-dimer. Considered serious, it can lead to the death of up to 30% of those affected. Treatment is supportive, using cryoprecipitate transfusion in case of active bleeding and red blood cell transfusion in symptomatic anemia<sup>2,7,8</sup>.

Regarding the treatment of KHE, in line with what current articles state, the patient was treated with total surgical resection of the lesion - an option considered curative. However, it is not always possible to perform, since it has contraindications routinely found in patients with KHE, such as: extensive lesions, in places where complete resection would result in mutilation or functional impairment, as well as lesions with active KMP<sup>3,8</sup>.

Regarding pharmacological treatment - indicated when surgery is impossible - to date, there are no large clinical trials that point to a drug of choice. A group of experts from different areas in the management of KHE was brought together in 2013 to discuss commonly used pharmacological regimens and choose the best pharmacological options. For isolated KHE, the use of corticosteroids at an immunosuppressive dose was indicated; and a clinical response with a decrease in the volume of the lesion is expected within a period of 2 weeks. For KHE associated with KMP, the combination of corticosteroids and vincristine is recommended; this being a chemotherapy drug with a response rate of more than 70% in controlling KMP<sup>2,8,9</sup>.

More recent studies point to sirolimus as an effective medication for reducing tumor size, normalizing the number of platelets and, in some cases, reducing musculoskeletal pain. It is prescribed in combination therapy with corticosteroids, when combined treatment with corticosteroids and vincristine fails<sup>2</sup>.

Although little known among doctors and pediatricians, Kaposiform Hemangioendothelioma is a disease of relevance in the medical field due to its important differential diagnosis with Infantile Hemangioma and Congenital Hemangioma – the most common vascular tumors of childhood. In addition to the need for an assertive diagnosis, it is important to ensure clinical monitoring and adequate treatment for the patient with KHE, given the possibility of an aggressive course and high morbidity and mortality, related to its clinical complications.

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