

## Kaposiform hemangioendothelioma: report of a case unresponsive to usual medical treatments

Shokouh Taghipour Zahir,<sup>\*,a</sup> Seyed Soheil Benrazavi,<sup>b</sup> and Fariba Binesh<sup>a</sup>

<sup>a</sup>Assistant Professor of Anatomical and Clinical Pathology, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

<sup>b</sup>Assistant Professor of General Surgery and Pediatric Surgery, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

\*Corresponding Author E-mail: [shokouh\\_zahir@yahoo.com](mailto:shokouh_zahir@yahoo.com)

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### Abstract

Kaposiform hemangioendothelioma is an aggressive endothelial-derived spindle cell neoplasm that occurs nearly exclusively during childhood and teenage years. The lesion grows rapidly and is often associated with Kasabach-Merritt syndrome.

In this study a 24 days old male neonate who presented with an ill-defined deeply situated violaceous mass on his left arm is described. He had also anemia and life-threatening thrombocytopenia. Despite hospitalization in intensive care unit (ICU) and transfusion of platelets and packed red blood cells as well as medical managements such as oral prednisolone, intravenous (IV) methylprednisolone and interferon alpha, thrombocytopenia persisted, so surgical resection was considered. The histopathological findings were distinctive and characteristic of kaposiform hemangioendothelioma. Following surgery, the infant did not have any complications and was discharged from the hospital in good condition.

**Keywords:** Hemangioendothelioma, Sarcoma-Kaposi, Infant-Newborn, Arm, Surgery

Kaposiform hemangioendothelioma is a rare tumor of childhood often accompanied by Kasabach-Merritt syndrome and occasionally lymphangiomatosis.<sup>1</sup> A complete description of the clinical features, identification of the sites of prevalence, and coinage of the phrase “kaposiform hemangioendothelioma” were introduced in 1993 by Zukerberg et al.<sup>2</sup> The tumor is seen almost exclusively in childhood with the ages at presentation ranging from 1 month to 19 years. The lesions occur most commonly in retroperitoneum and deep soft tissues of the extremities, although some have also been reported in superficial soft tissues, chest wall, scalp, neck, and mediastinum. These tumors tend to be locally invasive, but distant metastases have not been reported. The tumors are often associated with Kasabach-Merritt syndrome, a consumptive coagulopathy associated with vascular lesions.<sup>3,4</sup> Several retrospective studies on patients who presented with Kasabach-Merritt syndrome have revealed that what was originally diagnosed as a capillary hemangioma may often be better described as a kaposiform hemangioendothelioma.<sup>5-7</sup> Although Kaposi sarcoma has been associated with human herpes virus 8, this virus has not been found in association with kaposiform hemangioendothelioma.<sup>7</sup> Kaposiform hemangioendothelioma has features common to both capillary hemangioma and Kaposi sarcoma.<sup>8</sup> It has generally been considered distinct from other vascular neoplasms. However, its rarity has precluded complete study of its immunophenotypic characteristics and long-term behavior.<sup>9</sup> Here, this condition is being reported in a neonate whose thrombocytopenia failed to respond to medical treatments and necessitated surgical intervention.

### Case Report

Twenty four days old male neonate was referred to Shahid Sadoughi general hospital, Yazd, Iran, from Bandar Abbas on April 2008. He had a red mass on his left arm which was noticed at birth as a congenital lesion measuring  $3 \times 3$  centimeters and occupying nearly 15-20% of his left arm length without any other problem. After two weeks, the lesion had become larger measuring  $8 \times 7$  cm associated with anemia (hemoglobin = 9 mg/dl) and thrombocytopenia (platelet count of  $96 \times 10^3 /\mu\text{l}$ ). The platelet count decreased day by day and reached to  $50 \times 10^3 /\mu\text{l}$  and the mass occupied about 60% of arm length and circumference ([Figure 1](#)). Magnetic resonance imaging (MRI) was not considered for the neonate because no MRI was available in the medical center and the patient's condition did not allow him to be referred to another center for MRI. He was transferred to ICU receiving oral prednisolone 5 mg/kg/day, but the platelet count didn't rise and fell below  $30 \times 10^3 /\mu\text{l}$ . He then received 15 cc/kg platelet and intravenous methyl prednisolone (60mg/50cc DW, during three hours for five days). No rising in platelet count occurred. Meanwhile, the hemoglobin dropped to 4gr/dl. Despite platelet and packed red blood cell transfusions, no improvement occurred. So, subcutaneous injection of alpha interferon (5U/kg every other day) was considered as the next step. However, it was discontinued because of lack of effectiveness. In addition, the lesion was aspirated and the bulky mass was reduced in size but after 24 hours, it returned to its previous dimensions. The aspirated fluid was bloody and the pathology report was negative for malignancy. The patient became candidate of receiving vincristine, but his parents did not permit this treatment. However, the persistence of life-threatening thrombocytopenia needed further management. The alternative opinion was operation. Finally surgery was done with meticulous gentle dissection of tissues preserving intact blood vessels and nerves. The skin overlying the mass was tried to be preserved as much as possible. The mass was successfully excised and removed. Following surgery, platelet count quickly raised to  $150 \times 10^3 /\mu\text{l}$ . On macroscopic examination, there was reddish blue skin with underlying subcutaneous tissue measuring  $8 \times 6 \times 2$  centimeters. Microscopic examination revealed dermal tumoral lesion with subcutaneous component composed of ill-defined nodular lesion containing a mixture of small capillary-sized vessels which blended with slit-like spaces and glomeruloid nests of rounded and epithelioid endothelial cells with abundant eosinophilic cytoplasm ([Figure 2](#)). Red blood cell fragments were identified between these cells ([Figure 3](#)). Atypia and mitotic figures were minimal and inconspicuous. Diagnosis was confirmed by immunohistochemical staining (IHC). The neoplastic cells strongly expressed vascular endothelial growth factor receptor-3 (VEGFR-3) and were weakly positive for von-Willebrand factor (factor VIII-associated antigen). Most of the neoplastic cells expressed CD34 ([Figure 4](#)).

The infant was discharged with good general condition two weeks after surgery (following forty five days of hospitalization). Six and twelve months follow up showed no evidence of recurrence or complications related to surgery.

## Discussion

Kaposiform hemangioendothelioma may have areas resembling juvenile capillary hemangioma. Unlike capillary hemangioma which is made up of discrete lobules of small vessels, this tumor consists of irregular rambling nodules. In addition, capillary hemangioma is positive for GLUT-1 which is negative in kaposiform hemangioendothelioma. Unfortunately, this marker was not available and it couldn't be studied by immunohistochemistry. In kaposiform hemangioendothelioma, there are areas composed of spindle cells with slitlike vascular spaces resembling Kaposi sarcoma. As in the present case, the endothelial cells are typically positive for vascular markers such as CD31 and CD34 and vascular endothelial growth factor receptor 3, but only weakly positive for factor VIII-associated antigen.<sup>10</sup> This pattern is similar to the antigen-expression profile of Kaposi sarcoma. To exclude Kaposi sarcoma, IHC staining for human herpes virus 8 is helpful,<sup>11</sup> but this marker was not available. Although both entities (kaposiform hemangioendothelioma and Kaposi sarcoma) have spindle cells with slit-like lumina, hyaline globules, hemosiderin deposition and endothelial antigen expression, kaposiform hemangioendothelioma has also areas of epithelioid endothelium often in glomeruloid nests.<sup>10</sup> In addition, high mitotic rate and nuclear atypia are not features of kaposiform hemangioendothelioma. In this case, nuclear atypia was minimal and mitosis was inconspicuous. Moreover, aside from the lymphadenopathic form seen in Africa, Kaposi sarcoma is rarely seen in children.

Lyons et al followed 22 patients with kaposiform hemangioendothelioma (age ranging from 8 months to 15

years; mean 2 years). Three of them died of disease, 8 were alive with disease, and 10 were alive without residual disease. Two patients developed regional perinodal soft tissue involvement, but distant metastasis didn't happen in any.<sup>4</sup> Their study emphasized that mortality is due to Kasabach-Merritt syndrome and not metastatic disease. Therefore, this tumor is continued to be classified as a vascular tumor of intermediate malignancy.<sup>3</sup>

The infant didn't receive vincristine and his life threatening thrombocytopenia was uncontrollable without surgery. Other treatments such as arterial embolization of the mass were not possible because MR angiography was not available in the medical center. Irradiation has no role in this lesion at this age. Following surgery, the infant was discharged in good condition. He was still in good condition 1 year after surgery and showed no evidence of recurrence or complications related to the surgery.

## Conclusions

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Kaposiform Hemangioendothelioma is a vascular tumor of intermediate malignancy. Medical treatments are similar to those used in infantile hemangioma. Those unresponsive to medical treatments benefit from other therapies such as transcatheter embolization and surgical excision.

## Authors' Contributions

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ShTZ first diagnosed the tumor, wrote the whole part and body of the article, searched the references, photographs and slides and sent the slides for IHC staining. SSB did the surgery, follow up and gave the treatment schedule. FB helped editing the article. All authors have read and approved the content of manuscript.

## Acknowledgments

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## Footnotes

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### Conflict of Interests:

Authors have no conflict of interests.

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## Figures and Tables

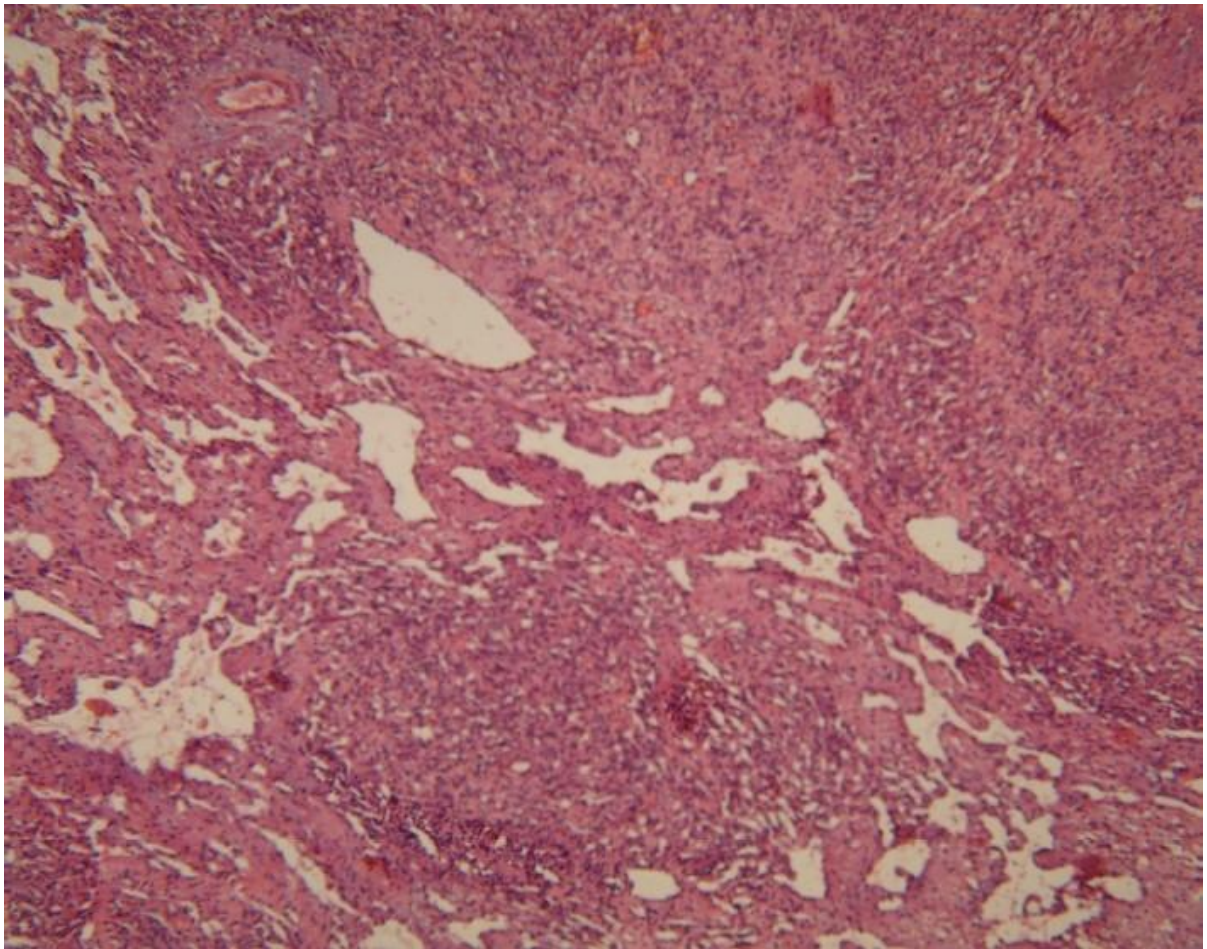
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**Figure 1**



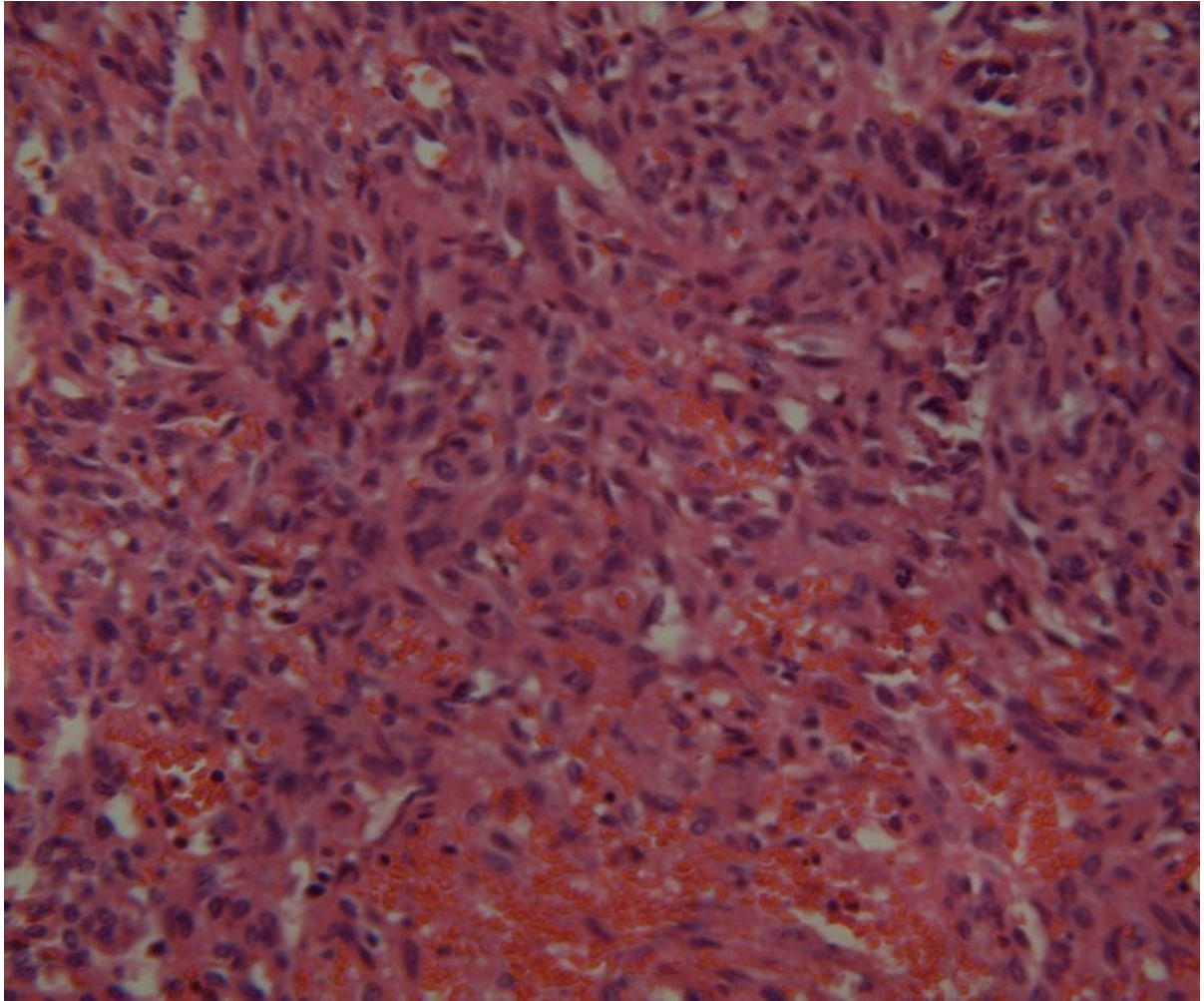
Bulky red mass on the left arm of neonate

**Figure 2**



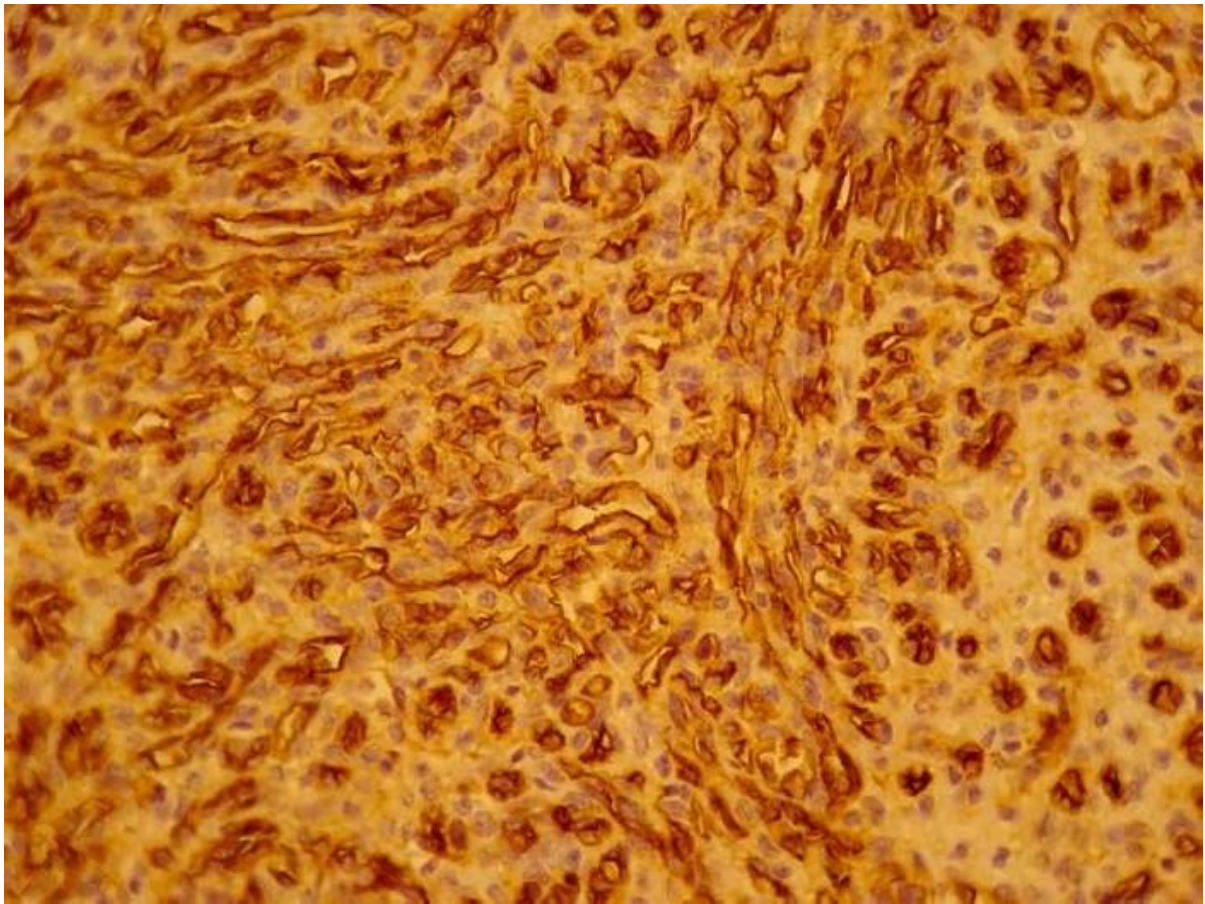
Mixture of small capillary size vessels that blend with slit-like vessels ( $\times 20$  objective)

**Figure 3**



Red blood cell fragments were identified between the spindle endothelial cells of kaposiform areas ( $\times 40$  objective)

**Figure 4**



CD34 positive endothelial cells ( $\times 40$  objective)

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