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

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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

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Kaposiform hemangioendothelioma is a rare tumor of childhood often accompanied by Kasabach-Merritt syndrome and occasionally lymphangiomatosis.[1] 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.[2] 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.[3,4] 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.[5–7] Although Kaposi sarcoma has been associated with human herpes virus 8, this virus has not been found in association with kaposiform hemangioendothelioma.[7] Kaposiform hemangioendothelioma has features common to both capillary hemangioma and Kaposi sarcoma.[8] 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.[9] 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 × 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 × 7 cm associated with anemia (hemoglobin = 9 mg/dl) and thrombocytopenia (platelet count of 96 × 10^3 /µl). The platelet count decreased day by day and reached to 50 × 10^3 /µl 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 × 10^3 /µl. 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 150×10^3 /µl. 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).

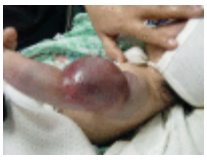

Figure 1
Bulky red mass on the left arm of neonate

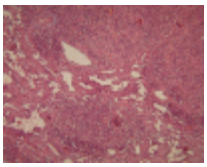

Figure 2
Mixture of small capillary size vessels that blend with slit-like vessels (×20 objective)

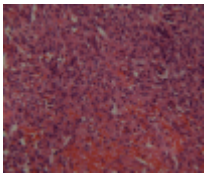

Figure 3
Red blood cell fragments were identified between the spindle endothelial cells of kaposiform areas (× 40 objective)

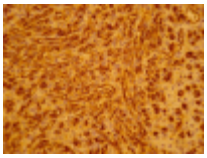

Figure 4
CD34 positive endothelial cells (× 40 objective)

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.[10] 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,[11] 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.[10] 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.[4] Their study emphasized that mortality is due to Kasabach-Merritt syndrome and not metastasic disease. Therefore, this tumor is continued to be classified as a vascular tumor of intermediate malignancy.[3]

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

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

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.

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Footnotes

Conflict of Interests:

Authors have no conflict of interests.

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References

1. Enjolras O, Picard A, Soupre V. Congenital hemangiomas and other rare infantile vascular tumors. *Ann Chir Plast Esthet.* 2006;51(4-5):339–46. [PubMed]

2. 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. [PubMed]

3. Beaubien ER, Ball NJ, Storwick GS. Kaposiform hemangioendothelioma: a locally aggressive vascular tumor. *J Am Acad Dermatol.* 1998;38(5 pt 2):799–802. [PubMed]

4. Lyons LL, North PE, Mac-Moune Lai F, Stoler MH, Folpe AL, Weiss SW. Kaposiform hemangioendothelioma: a study of 33 cases emphasizing its pathologic, immunophenotypic and biologic uniqueness from juvenile hemangioma. *Am J Surg Pathol.* 2004;28(5):559–68. [PubMed]

5. Burk CJ, Bangert J, Scott K, Hansen R. Vascular neoplasm in a newborn male. *Pediatr Dermatol.* 2007;24(5):570–1. [PubMed]

6. Krafchik BR, Hendricks L, Faguet GB, Kuthiala S. Kasabach-Merritt syndrome. 2007. Available at: http://www.medscape.com/article/202455-overview .

7. Martinez AE, Robinson MJ, Alexis JB. Kaposiform hemangioendothelioma associated with nonimmune fetal hydrops. *Arch Pathol Lab Med.* 2004;128(6):678–81. [PubMed]

8. Brasanac D, Janic D, Boricic I, Jovanovic N, Dokmanovic L. Retroperitoneal kaposiform hemangioendothelioma with tufted angioma-like features in an infant with Kasabach-Merritt syndrome. *Pathol Int.* 2003;53(9):627–31. [PubMed]

9. Enjolras O, Wassef M, Mazoyer E, Frieden IJ, Rieu PN, Drouet L, et al. Infants with Kasabach-Merritt syndrome do not have "true" hemangiomas. *J Pediatr.* 1997;130(4):631–40. [PubMed]

10. Weiss SW, Goldblum JR. Hemangioendothelioma: vascular tumors of intermediate malignancy. In: Weiss SW, Goldblum JR, editors. *Enzinger and Weiss's soft tissue tumors.* 4th ed. Philadelphia: Mosby; 2001. p. 901. (940).

11. Wananukul S, Nuchprayoon I, Seksarn P. Treatment of Kasabach-Merritt syndrome: a stepwise regimen of prednisolone, dipyridamole and interferon. *Int J Dermatol.* 2003;42(9):741–8. [PubMed]