Case Report

Kaposiform Hemangioendothelioma with Kasabach–Merritt Phenomenon in a Neonate – Role of Dual Therapy: A Case Report and Review of Literature

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INTRODUCTION

Definition and classification of vascular tumors continue to evolve. Kaposiform hemangioendothelioma (KHE) has been classified as an intermediate type of vascular tumor with propensity for local involvement (International Society for the Study of Vascular Anomalies).

Kasabach–Merritt phenomenon (KMP) has long been described to be associated with large hemangioma and resultant near-fatal consumptive coagulopathy. Investigators in 1997 demonstrated that these lesions were not true hemangiomas, but rather associated with vascular lesions, diagnosed histologically as KHE or tufted angiomas (TA).[1] Associated with KMP, these lesions can be fatal in 12% and 50% of cases.[1]

A number of therapies have been reported in the management of KHE with KMP but none have been uniformly effective.[1]

We discuss the successful management of an infant with KHE and associated KMP with vincristine and prednisolone. Difficulties encountered in establishing IV access, response to propranolol, and role of platelet transfusions are also discussed.

CASE REPORT

A 45-day-old girl presented to us with progressive swelling of the left arm since birth. An ultrasound (Doppler) evaluation at day 2 of life had shown a high flow vascular malformation involving the subcutaneous region over the left elbow.

Her antenatal scans were normal. Platelet count on day 2 of life was 1.26 lakhs/cumm which decreased to 43,000/cumm by day 5 of life.

Child was started on propranolol which resulted in an increase in size and induration of the left arm. There was also a further drop in platelet count to 17,000 cells/cumm.

As no improvement was seen with further increasing in swelling, the child was referred to us.

At presentation, the child was afebrile, with indurated left arm swelling and had a platelet count of 17,000 cells/cumm [Figure 1a].

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Review of the magnetic resonance imaging (MRI) was suggestive of KHE [Figure 2]. Urinary D-dimer was >1. As the child had worsening of the lesion with propranolol, decision was taken to start dual therapy with vincristine and methyl prednisolone.

Due to low platelet count and possibility of worsening of lesion with platelet transfusion, establishing a successful central venous access for vincristine therapy was challenging. We were able to establish a central venous access through femoral vein without platelet transfusion.

Vincristine was started at 0.05 mg/kg as weekly once dosage. Methyl prednisolone was started as intravenous infusion at 1 mg/kg once daily. This was continued for 3 weeks following which this was changed to oral prednisolone at 2 mg/kg/day.

At the time of institution of vincristine, the child’s platelet count was 6000 cells/cumm. The treatment planned was to give a total of 20 doses of vincristine (20 weeks) with tapering of steroids over 4–6 weeks as per Consensus Recommendation for cases of KHE associated with KMP.\(^1\)

After 4 cycles of treatment with vincristine, platelet counts increased to 59,000 cells/cumm. The child was given weekly dose of vincristine on outpatient basis with complete blood count monitoring. The central venous access was maintained for a period of 6 weeks, following which administration of vincristine was done by peripheral veins after consulting with oncologist.

There was a progressive increase in the platelet count after 14 weeks of therapy, with associated decrease in the arm swelling. There was also change in the intensity of the lesion with progressively clearing to normal skin tone [Figure 1b]. At 1-month follow-up after completion of 20 cycles of vincristine, the child had normal platelet count of >200,000 cells/cu mm and no increase in the size of the left arm. The child has been on follow-up for 4 years with no clinical or radiological recurrence of the lesion [Figure 1c].

**DISCUSSION**

KHE is a rare, potentially life-threatening vascular tumor often occurring as a solitary lesion involving skin and subcutaneous tissue. They are indurated having ill-defined margins with or without telangiectasia. They occur mainly on the neck, extremities, or axilla. Organ involvement has also been described.

KHE lesions may have episodic engorgement, purpura, and pain often triggered by local trauma, infection, or transfusion of blood products as was seen in our case. The tumor may spontaneously decrease in size with time; however, complete regression is uncommon.

KMP was first described by Haig Haigouni Kasabach and Katharine Krom Merritt in 1940.\(^1\) This is characterized by thrombocytopenia and hypofibrinogenemia. The thrombocytopenia is due to the platelet trapping that occurs within vascular channels with associated local fibrinogen consumption and can be severe with counts ranging from 6000 to 98,000 cells/cumm.

Another laboratory hallmark is hypofibrinogenemia with elevated markers of coagulation activation such as D-dimers or fibrin degradation products with fibrinogen levels <100 mg/dL and D-dimers levels <1.\(^1\) This was also documented in our case.

Ultrasound examination is the initial radiological evaluation. It can show the location, depth of involvement, echogenic, and vascular pattern. However,
ultrasound and computed tomography are of limited usefulness in evaluation of KHE.

MRI with gadolinium contrast is the imaging of choice. MRI findings include varying degrees of dermal and subcutaneous thickening, infiltrative and ill-defined margins extending into adjacent muscles, surrounding edema-like pattern, and ectatic high-flow vessels. The skin thickening and edema-like pattern, often described as “stranding,” are best seen on T2 fat-saturated sequences and most likely represent a combination of ectatic adjacent lymphatic channels and tumor. Signal voids consistent with hemosiderin deposits are often noted on MRI [1] [Figure 2].

The overall mortality rate is between 12% and 50% with death occurring from severe hemorrhage related to disseminated intravascular coagulation, local invasion of vital structures, high output cardiac failure, multiorgan failure, or sepsis.[3]

A number of therapies have been reported in the treatment of KMP, including steroids, interferon, antifibrinolytics, and chemotherapeutic agents such as cyclophosphamide, vincristine, and actinomycin.

The first line of management has been with steroids and vincristine.[1] With the recent success of propranolol in the management of hemangiomas, it has been reported to be used with limited success. In our case, there was worsening of the lesion.

Steroid is a good initial choice because of its ease of use, inhibits fibrinolysis, and increases platelet count in addition to its action on vascular malformation. However, it is only effective in 30%–50% of patients with KMP.[3]

Intravenous vincristine, an inhibitor of endothelial proliferation, has been used for the treatment of KMP and is an excellent choice as a first-line drug along with steroids in the treatment of KHE combined with KMP.[1]

However, administration of vincristine may not be immediately possible because of lack of central venous access or other factors. In those situations, corticosteroid therapy should be started immediately so that therapy is not delayed.

Vincristine requires time to become therapeutically active; average time to normalize the platelet count has been reported to be about 5 weeks.[1] In our case also, the platelet count normalized after 14 cycles (14 weeks) of vincristine.

Vincristine therapy cannot avoid hemangioma relapse but has been reported to result in prolonged reduction in tumor growth.[4]

We used dual therapy of vincristine and methyl-prednisolone because of the high failure rates with monotherapy.[1]

Another main concern in these infants is establishing a central venous access, which can be really challenging. The risk of bleeding due to low platelet or increasing tumor size if given platelet transfusion and maintaining the central line till the desired platelet and tumor response is achieved (5–6 weeks) add to the challenges in managing these children, especially in acute settings.

We were able to establish a femoral venous access on cutdown. The parents were educated about the care of the central line at home, and we were able to maintain the central line for 5 weeks.

Systemic interferon therapy, effective in only 50%–60% of steroid-resistant patients, is not recommended in patients aged <1 year, except when other treatment methods are ineffective and the patient’s condition is life-threatening.[1]

In 2008, Leaute-Labreze et al. reported regression of infantile hemangiomas with propranolol. Variable response to propranolol treatment of KHE, TA, and KMP was described by Chiu et al. who in their series of 11 patients treated with propranolol for KHE and TA, six of whom also had KMP.[1] In our patient, there was a paradoxical increase in the tumor size starting propranolol.

Surgical resection can be definitive treatment for Kasabach–Merritt syndrome (KMS), but in most cases is not possible because of the location and size of the vascular tumor.

Another option is transarterial embolization, and successful treatment of KMP with embolization has been reported with several embolic materials, such as coils, polyvinyl alcohol, and onyx.[1]

The principle of management of coagulopathy in KMS is to treat patients not the numbers.[1] Platelet transfusions should be reserved for active bleeding or in preparation for surgery or procedures. Infused platelets have been noted to rapidly increase the size of the tumor and even exacerbate KMS.[1]

**Conclusion**

KHE is a rare vascular tumor often associated with KMP, a rare consumptive coagulopathy characterized by profound thrombocytopenia and hypofibrinogenemia. Patients often present in a critically ill stage, and treatment remains challenging. These children should be treated aggressively with combination regimen (vincristine and steroids, in our case) rather than with single drug.
Furthermore, because of the complex clinical behavior of KHE associated with KMP, interdisciplinary management is important to minimize morbidity and mortality and improve the long-term outcomes of these children.

**Declaration of patient consent**
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**
There are no conflicts of interest.

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