

Kasabach-Merritt Syndrome: a case study of successful treatment with vincristine and propranolol

Aqsa Mazhar,¹ Afza Naureen Ghouse,² Saba Shahid,³ Lubna Samad⁴

Abstract

Kasabach-Merritt syndrome is a rare condition, characterised by the presence of an enlarging vascular tumour associated with thrombocytopenia, microangiopathic haemolytic anaemia and consumptive coagulopathy. The syndrome manifests in infancy, with high morbidity and mortality rates. No standard guidelines have been established for the treatment of Kasabach-Merritt syndrome to date. To existing literature we add this report of a four-month-old female child with Kasabach-Merritt syndrome who was successfully treated with propranolol and vincristine. This drug combination helped reverse the severe thrombocytopenia as well as decrease in size of her haemangioma. Management of Kasabach-Merritt syndrome continues to be a challenge, with varying response to first line drugs. Early diagnosis and initiation of treatment in a closely monitored setting is essential to ensure good outcomes. Since this is a relatively rare condition and large studies are not feasible, documenting treatment experience of single case or small series becomes even more important.

Keywords: Kasabach-Merritt syndrome, Haemangioma, Thrombocytopenia.

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Introduction

Haemangiomas are the most common paediatric neoplasm, resulting from abnormal proliferation of blood vessels¹. Although haemangiomas are typically benign, both histologically and clinically, occasionally, these tumours can cause significant complications. They can compromise breathing or feeding, obstruct vision leading to amblyopia, cause high-output cardiac failure, lead to hypothyroidism due to visceral involvement, and can

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¹Vascular Anomalies Center, Indus Hospital and Health Network, Karachi, Pakistan, ²Department of Dermatology, Indus Hospital and Health Network, ³Department of Pediatric Medicine, Indus Hospital and Health Network, Karachi, Pakistan, ⁴Interactive Research and Development (IRD), Global,

Correspondence: Lubna Samad. Email: lubna.samad@ird.global

present with painful ulceration and bleeding. Haemangiomas can also have syndromic associations, including PHACES syndrome, PELVIS syndrome, and Kasabach-Merritt syndrome (KMS)². KMS was first reported by Kasabach and Merritt in 1940³, and is characterised by giant haemangiomas, severe thrombocytopenia, and consumptive coagulopathy⁴. It is postulated that exposure of subendothelial elements or abnormal endothelium within the haemangioma results in aggregation and activation of platelets with a secondary consumption of clotting factors⁵. This disorder is found in only about 1% of children with a haemangioma, but when present, the mortality rate can be as high as 50% due to secondary complications that include disseminated intravascular coagulation, respiratory failure due to airway compression, and high output heart failure caused by large haemangiomas⁶. Since KMS is a relatively rare entity, we add to the limited literature with this report detailing the presentation and management of an affected child.

Case Report

A 4-month-old girl presented to Vascular Anomalies Center Clinic at the Indus Hospital and Health Network, Karachi, Pakistan, in October 2021 for management of a mass at the nape of the neck. She was the first child of a consanguineous marriage, born by Caesarean section. At birth, an initial flat reddish patch was seen at the nape. Over the next four months, it gradually increased and evolved into a large swelling extending to the occipital and postauricular areas. Initial examination revealed a playful child with normal developmental milestones. There was an irregular swelling extending from the postauricular area to the entire posterior aspect of the neck. The mass was firm and non-tender, without discrete margins. The overlying skin was reddish-blue and smooth with no signs of inflammation (Fig 1a). The rest of the examination was normal. A clinical diagnosis of the infantile haemangioma was made. The complete blood count at the time of initial presentation and during the course of treatment is detailed in Table 1. An ultrasound of the swelling showed an infiltrating soft tissue density lesion involving the cutaneous and subcutaneous tissues of the upper back extending up to the posterior aspect of the neck and reaching up to the right external ear,



Figure-1: The patient's images at different stages.

showing mild vascularity on colour doppler imaging, thus confirming our clinical diagnosis. MRI confirmed the ultrasound findings with extension to the right periauricular, pre and postauricular area extending down along the right side of the neck up to the supraclavicular location. The large right sided component was abutting the major vessels, parotid and submandibular glands on that side. Homogeneous contrast enhancement was demonstrated leading to a likely diagnosis of haemangioma. The hepatobiliary ultrasound scan was normal. Oral propranolol was started at 1mg/kg/day in 3 divided doses which was then increased to 2 mg/kg/day after 1 week.

Table-1: Relevant haematological investigations carried out during hospital stay and follow-up at the outpatient department.

Patient visits Weeks from on set of therapy	Investigations			Treatment Milestones
	WBC X 10 ⁹ /l	Hb gm%	Platelet X 10 ⁹ /l	
Week 1	17	11.6	74	Propranolol started 1mg/kg/day
Week 2	14.3	9.8	15	Dose of propranolol increased to 2mg/kg/day. Admitted, prednisolone started
Week 3	18.5	9.6	63	Propranolol increased to 3mg/kg/day
Week 4	26.8	9.8	6	Re-admitted, Vincristine started
Week 10	12.9	9.4	20	Prednisone tapering started
Week 14	20.8	11.5	40	
Week 18	22.8	11.5	134	Prednisolone stopped
Week 22	20.5	11.7	332	
Week 26	17.3	12.8	431	
Week 28	-	-	-	VCR stopped
Week 30	12.7	13.2	452	
Week 36	11.4	12.9	370	

After 2 weeks on medication, in Nov-2021 she presented at the emergency department with an increase in the size of the swelling and associated fever. On examination, the lesion appeared erythematous, and had extended to involve the right ear and eye (Fig 1b). Haematological parameters were repeated in which a significantly low platelet count was seen (Table 1), while PT and APTT were normal. A diagnosis of KMS was made on the basis of clinical findings and laboratory investigations. After admission, platelets were transfused, prednisolone started at a dose of 1 mg/kg/day, and the dose of propranolol increased to 3 mg/kg/day. Blood cultures drawn in the emergency department showed *Escherichia Coli* for which intravenous meropenem was started. After 4 days on this treatment regimen, platelet counts improved and the patient was discharged on oral prednisolone and propranolol.

Two weeks later, she was readmitted with high-grade fever and reappearance of erythematous patches over the lesion with a low platelet count (Fig 1c). A decision was taken to administer vincristine at a dose of 0.5 mg/m² of body surface area on weekly basis. After 2 doses of vincristine, reduction of erythema and increased platelet count were noted. She was discharged home on oral prednisolone and propranolol, coming in for weekly doses of vincristine. After 6 weeks, cushingoid features were noted, due to which oral prednisolone was tapered

and stopped. Weekly vincristine was continued for 24 weeks along with oral propranolol. The size of the swelling had reduced remarkably with haemostatic stability achieved (Fig 1d). Vincristine was stopped while propranolol has been continued to date without any side effects and child is currently doing very well (Fig 1e). Written informed consent was obtained from the parents for publication of this case report and the accompanying images.

Discussion

There are few reported cases of KMS in literature from Pakistan, and according to the best of the authors' knowledge no experience with use of oral propranolol in KMS has been reported from the country. We present a case study of a child with KMS who was managed successfully with multi-modal treatment with propranolol (3mg/kg/day), oral prednisolone (1mg/kg/day) and Vincristine (VCR) (0.5 mg/m² of body surface area weekly).

Treatment of KMS is primarily aimed at managing the coagulopathy that arises as a direct consequence of the haemangioma. Treatment options available for KMS including medical treatment (propranolol, interferon, steroids, chemotherapy), vascular embolization, radiation therapy, and surgery^{4,6}. Complete surgical resection was previously considered the gold standard of treatment, but due to high morbidity and mortality rates and the emergence of safer treatment options, surgery is now only reserved for selected cases⁶. The treating physician needs to customise management for each affected patient, choosing the most suitable treatment to achieve maximum involution of the lesion and preservation of organ function either with a single drug or combination of drugs.

In our patient, monotherapy with propranolol was initially started, but with the emergence of haematological complications, oral steroids and subsequently vincristine were added. Heisley-Royster et al. retrospectively reviewed 15 patients with KMS and reported that 11(74%) were successfully treated with a combination of corticosteroid and vincristine as first-line therapy⁷. Although literature review indicates that prednisolone can be safely continued for 3-6 months⁸, we had to stop oral corticosteroids due to appearance of cushingoid features and deterioration of clinical and haematological parameters within 4 weeks of starting prednisolone. Vincristine has been reported as a viable treatment option for steroid-resistant KMS⁹. An average treatment duration of 22-27 weeks has been reported for Vincristine⁹. Irritability, loss of deep tendon reflexes, and abdominal pain are common side effects of VCR reported in

literature, and can limit treatment options when they appear early in the course of treatment. However, our patient responded well to VCR which was administered for 24 weeks with no side effects observed. Similarly, no side effects of propranolol (bradycardia, hypotension, hypoglycaemia, rash, fatigue, and bronchospasm) were observed in our patient. We found our treatment approach to be successful based on the normalization of haematological parameters and reduction in size of the haemangioma. Propranolol will be continued for now, and the decision to taper it off will be taken after at least 2 years of age.

Conclusion

Our case report details the treatment course of a child with KMS, where multimodal treatment was started. The initiation of propranolol with subsequent addition of vincristine successfully reversed the haematological derangement and led to reduction in size of the haemangioma. Thus, combination treatment of these two drugs can be considered in management of KMS. Due to the rarity of the condition, we believe that this report adds to the literature by documenting successful management of this condition.

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