Case Report: Kasabach-Merritt phenomenon in a 7-month-old Cambodian infant

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April 13, 2023

Abstract

Introduction. Kasabach-Merritt phenomenon (KMP) is a rare condition associated with vascular tumors such as kaposiform hemangioendothelioma and tufted angioma; it can be life threatening, due to its consumptive coagulopathy. Thrombocytopenia and hypofibrinogenemia are characteristic of KMP, and anemia and raised d-dimer levels can also be detected. Here, we report a 7-month-old Cambodian with the condition. Case Presentation. The infant was admitted to the National Pediatric Hospital in Phnom Penh because of a mass on the right side of the neck that had been progressively enlarging. The patient had severe thrombocytopenia (8,000/μL), anemia (Hb 7.6g/dL) and reduced fibrinogen level (1.5g/L). CT scan and histology of the lesion confirmed a diagnosis of hemangioma. Kasabach-Merritt phenomenon was diagnosed, and the infant was treated with platelets and fresh frozen plasma infusions, prednisolone (2mg/kg/day) and propranolol (2.5mg/kg/day). After eight weeks of therapy, platelets raised to 102,000/μL. The infant developed Cushing's syndrome after 6 months of treatment and prednisolone was scaled down to a maintenance dose of 0.5mg/kg/day. Fibrinogen levels went back to normal (2.14g/L) after seventeen months of treatment, and the tumor shrinked significantly. Conclusion. This case report shows that a combination of prednisolone and propranolol has been effective for KMP and kaposiform hemangioendothelioma. Timely recognition and treatment of Kasabach-Merritt phenomenon's are essenti

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propranolol has been effective for KMP and kaposiform hemangioendothelioma. Timely recognition and treatment of Kasabach-Merritt phenomenon's are essential.

1. Introduction

A case of capillary hemangioma with extensive purpura was first described by Kasabach and Merritt in 1940 [1]; subsequently, the disease was named after them. Kasabach-Merritt phenomenon (KMP) is a rare condition that can be life threatening because of its consumptive coagulopathy. It is associated with rare vascular tumors, particularly kaposiform hemangioendothelioma (where it occurs in up to 70% of cases) [2] and (less frequently) tufted angioma [3]. Thrombocytopenia and hypofibrinogenemia characterize the condition; anemia and raised d-dimer levels can also be found [3]. Kaposiform hemangioendothelioma, in particular, generally affects the extremities, trunk or cervicofacial region [2,4,5]; Kasabach-Merritt phenomenon occurs more frequently if the depth and infiltration of the tumor are higher, and retroperitoneum or thorax are involved [2]. We report a case observed in a Cambodian infant.

2. Case Presentation

A 7-month-old male infant was admitted to the Surgical Ward of the National Pediatric Hospital in Phnom Penh, Cambodia because of a mass on the right side of the neck that had been progressively increasing in volume over 4 months (Figure 1a). A CT scan confirmed a mass compatible with a hemangioma, of 105mm x 112mm x 136mm on the right side of the neck; the surrounding bones were intact. The patient weighted 6 kg; his height was 63cm. Respiratory rate was 28/min, pulse 115/min, temperature 36.3 ºC, SaO_2

97% 6kg 63cm, no BP level. He had severe thrombocytopenia (8,000/μL), and anemia (Hb 7.6g/dL); the fibrinogen level was reduced (1.5g/L). Liver enzymes (AST 28 IU/L, ALT 32 IU/L) and kidney function tests were normal (urea 14mg/dL, creatinine 0.6mg/dL). Glucose level was not measured. An abdominal ultrasound ruled out a liver hemangioma, and histology of the lesion confirmed a hemangioma. A diagnosis of Kasabach-Merritt phenomenon was made, and the patient received two doses of platelets infusion (10mL/kg) and one dose of fresh frozen plasma (10 ml/kg over 2hrs) for active bleeding at the biopsy site. Prednisolone (2mg/kg/day) and propranolol (2.5mg/kg/day) were started. One month later, platelets were 120,000/μL and fibrinogen was 1.5g/L. After eight weeks of treatment, platelets were 102,000/μL (prednisolone dose had been reduced because of side effects). The infant developed Cushing's syndrome after 6 months of therapy and prednisolone was scaled down by 0.5mg every month until a maintenance dose of 0.5mg/kg/day was reached. Fibrinogen levels became normal (2.14g/L) only after 17 months of therapy. The tumor has shrinked considerably (Figure 1b).

Figure 1A

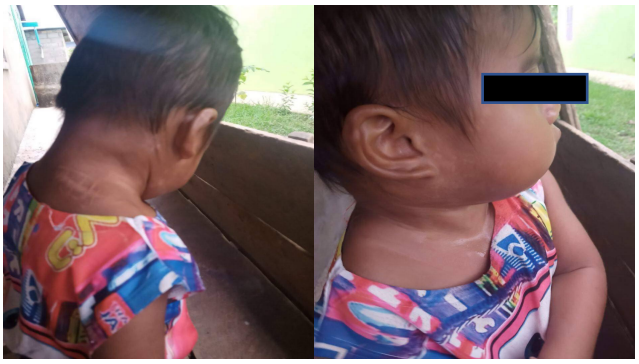

Figure 1B

3. Discussion

We have reported the second case of Kasabach-Merritt phenomenon in a Cambodian infant (the first was described a few months ago) [6]. Kasabach-Merritt phenomenon is characterized by a marked thrombocytopenia, likely due to intralesional platelet trapping [5], and is often associated with kaposiform hemangioendothelioma, which may involve different tissue planes from dermis into subcutis, fascia, muscle, and bone [2].

Treatment of KMP is based on a few drugs. In 2013, a regimen of systemic corticosteroids and weekly intravenous vincristine was recommended by a multidisciplinary expert panel in North America [7,8]; in the same year, the results of a phase II study of sirolimus which had included 10 patients with kaposiform hemangioendothelioma and KMP were published, and showed a complete and rapid resolution of KMP in all patients [9]. In Spain, vincristine, aspirin, and ticlopidine have been used with good reported outcomes [10,11]. Vincristine has numerous potential side effects, including constipation, peripheral neuropathy, irritability, and syndrome of inappropriate antidiuretic hormone secretion. Sirolimus can cause mucositis and dyslipidemia, and decreases immune responses. Corticosteroids also have important side effects, as shown in our case, and aspirin may cause Reye syndrome. Propranolol promotes regression of cutaneous infantile hemangiomas [12,13]; the response to this drug of kaposiform hemangioendothelioma, tufted angioma, and Kasabach-Merritt phenomenon is reportedly variable [14]. The side effects of propranolol include bradycardia, hypotension, bronchospasm and hypoglycemia. In our case, a combination of prednisolone and propranolol was effective

Platelet transfusions are often ineffective and can cause tumor engorgement [2]; besides, platelets have shorter half-life in KMP [15,16]. We infused platelets because of active

bleeding from the biopsy site; however, the biopsy itself might perhaps have been avoided due to the high bleeding risk.

Data Availability

All data relevant to the case are included in the case report.

Conflicts of Interest

Authors declare no conflicts of interest.

References

[1] H.H. Kasabach, and K.K. Merritt, ‘’Capillary hemangioma with extensive purpura: Report of a case,’’ *American Journal of Diseases of Children*, vol. 59, no. 5, pp. 1063–1070, 1940.

[2] S.E. Croteau, M.G. Liang, H.P. Kozakewich et al., “Kaposiform hemangioendothelioma: atypical features and risks of Kasabach-Merritt phenomenon in 107 referrals,” *Journal of Pediatrics*, volume 162, pp. 142-147, 2013.

[3] P. Mahajan, J. Margolin, and I. Iacobas, “Kasabach-Merritt Phenomenon: Classic presentation and management options,” *Clinical Medicine Insights: Blood Disorders,* volume 10, pp. 1-5, 2017.[4] M. Sarkar, J.B. Mulliken, H.P. Kozakewich, R.L. Robertson, and P.E. Burrows, “Thrombocytopenic coagulopathy (Kasabach-Merritt phenomenon) is associated with kaposiform hemangioendothelioma and not with common infantile hemangioma,” *Plastic and Reconstructive Surgery*, volume 100, pp. 1377–1386, 1997.

[5] L.L. Lyons, P.E. North, F.M-M. Lai, M.H. Stoler, A.L. Folpe, and S.W. Weiss, “Kaposiform hemangioendothelioma: a study of 33 cases emphasizing its pathologic, immunophenotypic, and biologic uniqueness from juvenile hemangioma,” *American Journal of Surgical Pathology*, volume 28, pp. 559–568, 2004.

[6] C. Chap, and S. Bin, “Kasabach-Merritt syndrome: a rare cause of swelling thigh in a Cambodian newborn,” *Oxford Medical Case Reports*, volume 2, pp. 52-53, 2022.

[7] B.A. Drolet, C.C. III Trenor, L.R. Brandão et al., “Consensus-derived practice standards plan for complicated Kaposiform hemangioendothelioma,” *Journal of Pediatrics*, volume 163, pp. 285–291, 2013.

[8] B.E. Tlougan, M.T. Lee, B.A. Drolet, I.J. Frieden, D.M. Adams, and M.C. Garzon, “Medical management of tumors associated with Kasabach-Merritt phenomenon: an expert survey,” *Journal of Pediatric Hematology/Oncology*, volume 35, pp. 618–622, 2013.

[9] D.M. Adams, C.C. Trenor, A.M. Hammill, et al., “Efficacy and safety of sirolimus in the treatment of complicated vascular anomalies,” *Pediatrics*, volume 137, e20153257, 2016.

[10] I. Fernandez-Pineda, J.C. Lopez-Gutierrez, G. Ramirez, and C. Marquez, “Vincristine-ticlopidine-aspirin: an effective therapy in children with Kasabach-Merritt phenomenon associated with vascular tumors,” *Pediatric Hematology and Oncology*, volume 27, pp. 641–645, 2010.

[11] I. Fernandez-Pineda, J.C. Lopez-Gutierrez, G. Chocarro, J. Bernabeu-Wittel, and G.L. Ramirez-Villar, “Long-term outcome of vincristine-aspirin-ticlopidine (VAT) therapy for vascular tumors associated with Kasabach-Merritt phenomenon,” *Pediatric Blood & Cancer*, volume 60, pp. 1478–1481, 2013.

[12] C. Leaute-Labreze, E. Dumas de la Roque, T. Hubiche, F. Boralevi, J.B. Thambo, and A. Taleb, “Propanolol for severe hemangiomas of infancy,” *New England Journal of Medicine*, volume 358, pp. 2649-2651, 2008.

[13] P. McGee, S. Miller, C. Black, and S. Hoey, “Propranolol for infantile haemangioma: A review of current dosing regime in a regional paediatric hospital,” *Ulster Medical Journal*, volume 82, pp.16-20, 2013.

[14] Y.E. Chiu, B.A. Drolet, F. Blei et al., “Variable response to propranolol treatment of kaposiform hemangioendothelioma, tufted angioma, and Kasabach-Merritt phenomenon,” *Pediatric Blood & Cancer*, volume 59, pp.934-938, 2012.

[15] M.A. Koerper, J.E. Addiego, A.A. de Lorimier, H. Lipow, D. Price, and B.H. Lubin, “Use of aspirin and dipyridamole in children with platelet trapping syndromes,” *Journal of Pediatrics*, volume 102, pp. 311–314, 1983.

[16] J.B. Mulliken, S. Anupindi, R.A.B. Ezekowitz, and M.C. Jr. Mihm, “Case 13-2004: a newborn girl with a large cutaneous lesion, thrombocytopenia, and anemia,” *New England Journal of Medicine*, volume 350, pp. 1764–1775, 2004.

Consent Statement:

We, the authors, confirmed that we obtained the written consent form in Khmer Language on 2nd January 2023. The mother signed the consent form on behalf of her child because the patient was less than 2 years old at the time of doing the consent.