Case Report

Outcome of Kasabach-Merritt Phenomenon: The Role of Vincristine as Monotherapy: Report of A Case

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Kasabach-Merrit phenomenon (KMP) is a rare disorder of pediatric hematological malignancies which is previously referred to Kasabach-Merrit syndrome (KMS). The disorder is characterized by prominent vascular mass resulting from abnormal proliferation of blood vessels, consumption coagulopathy and thrombocytopenia. The diagnosis is based upon three basic findings as above. The authors describe a 6-month-old girl with a huge ecchymotic mass at left buttock who is found to have thrombocytopenia and consumption coagulopathy. The clinical and imaging studies strongly suggested the diagnosis of KMP. Vincristine was administered after a trial of corticosteroids was failed to show clinical and laboratory improvement. After 2 weeks, the patient showed that the platelet count and fibrinogen level become to be normal without blood transfusion and gradually decreased in tumor size without any surgical procedure in 4 weeks and disappeared in 5 months without any complications. In the present report, the authors present the findings from successfully specific treatment with vincristine alone and supportive treatment for life-threatening hemorrhage with platelet concentrate and cryoprecipitate should be the best management in our situation.

Keywords: *Kasabach-Merritt phenomenon, Vincristine, Outcome*

J Med Assoc Thai 2012; 95 (Suppl. 5): S181-S185
Full text. e-Journal: *http://jmat.mat.or.th*

Kasabach-Merrit phenomenon (KMP), a benign tumor of vascular lesions, is characterized by significant thrombocytopenia, consumption coagulopathy and possible hemolytic anemia which are accompanied by rapidly enlarging vascular lesions included extremities, retroperitonium, visceral abdomen, and sometimes located in the skin also which associated with anemia and bleeding. The incidence of KMP is found only 1% of population. The diagnosis is based upon clinical and radiological findings as many lesions are too extensive to be resected surgically without high morbidity. If KMP is not treated properly, it can be life threatening with high mortality. We describe an infant who had complete remission of KMP with a huge retroperitoneal vascular lesion and successful treatment with vincristine.

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Case Report

A 6 month-old infant presented with a huge ecchymotic mass at left buttock and numerous hematoma and purpura over the skin of the lower extremities. Her parents reported that they did not notice any abnormality until the red palpable mass suddenly became visible at the left buttock in 3 days. She was referred to our hospital for an associated complication by disseminated intravascular coagulation (DIC). Physical findings on admission revealed a dark purple tumor of about 8x 12 cm in size at the left buttock (Fig. 1A). The head, neck heart, lungs were normal but purpura and multiple petechiae on the lower limbs. There was no hepatosplenomegaly. Peripheral pulses were palpable and the results of a neurologic examination showed no abnormalities. There were no other abnormal physical findings. Laboratory tests demonstrated anemia, severe thrombocytopenia and consumption

coagulopathy. Her hemoglobin level was 7.6 g/dL, her white blood cell count was 8,100/ul and her platelet count was 17,000/ul. The peripheral blood smear was found fragmented cell and decreased platelet number (Fig. 1B). In addition, coagulation parameter revealed the activated partial thromboplastin time (APTT), prothrombin time (PT) and thrombin time (TT) were in 100 sec, 120 sec and 100 sec retrospectively. The fibrinogen level was 65 mg/dl and D-dimer was 34.16 ug/ml. During admission, the liver function tests and urine examination did not show any abnormalities. Because of severe thrombocytopenia and consumption coagulopathy, platelet concentrates 0.2 unit/kg and substitution of fibrinogen by cryoprecipitate was given once a day to improve signs of significant bleeding. Computed tomography of the abdomen and pelvis showed an extensive soft tissue mass at left side of ischiorectal fossa about 12 cm displacing rectum to the right. Liver was enlarged but showed homogeneous density and no mass involvement (Fig. 1C). The above clinical and imaging findings, plus signs of DIC strongly suggested the diagnosis of Kasabach-Merritt phenomenon. Prednisolone was started at a dose of 2 mg/kg/day divided in 3 doses a day. During this treatment, patient still required platelet concentrates once daily. On the one week after steroid therapy, patient developed hypertension and gastrointestinal bleeding with no clinical improvement and need to stop steroid eventually. A magnetic resonance imaging (MRI) examination and blood pool scan byTc-99m RBCs was carried out for qualitative confirmation of this phenomenon. The present study revealed a hyper-vascularized soft tissue mass at left gluteus muscle with infiltration into left ischiorectal fossa and extended to bilateral paravertebral and psoas muscles (Fig. 1D) and Tc-99m was showed increased vascular flow in dynamic and delayed stage to the mass at posterior aspect of left lower back (Fig. 2). Because of refractoriness with corticosteroid as well as the critical clinical status of the patient, we decided to start vincristine at initial dose 0.625 mg/kg weekly. Two weeks after the start of vincristine, the platelet count gradually increased until stopped blood transfusion (Table 1). The vincristine, in the same dose, was continued for another 2 weeks, the regression of tumor size was observed. Then, it was given monthly interval via central access through 5 months until the mass was disappeared. At present, the patient's clinical and hematologic parameter remains in complete remission and there were no any side effects of vincristine for 12 months after discontinuation of vincristine.

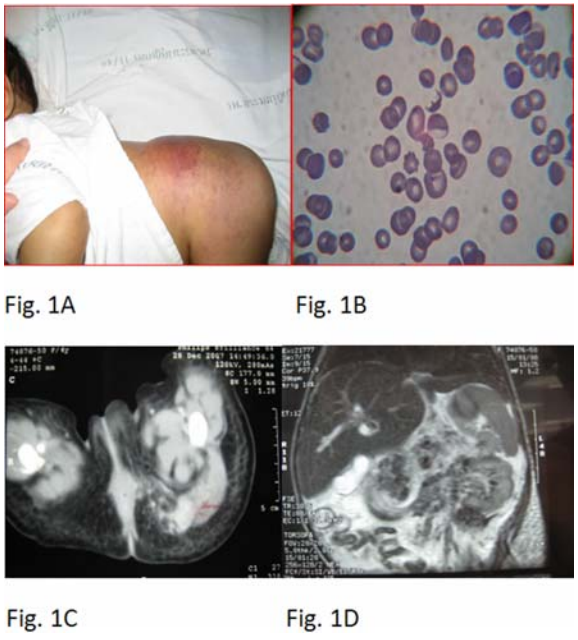

Fig. 1 Appearance of the soft-tissue mass: Findings of the physical examination to imaging studies at the time of onset

Discussion

Kasabach-Merritt phenomenon (KMP) is the one of phenomenon which requires aggressive treatment and is associated with a high mortality rate. Our case fits within the common age and phenomenon found for KMP.

When the tumor is in retroperitoneal location which most such lesions are not treated surgically, the mortality is very high[1]. In this situation, systemic corticosteroid is a mainstay in the treatment. Daily dose of 2 mg per kilogram of body weight is usually given, even using high doses of intravenous methylprednisolone to treat life-threatening

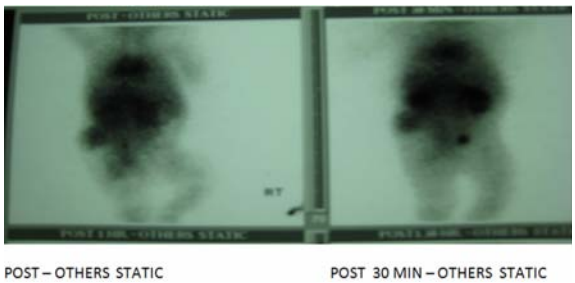

Fig. 2 Result of Tc-99mm RBCs after 7 days of treatment with corticosteroid at immediate and post 30 minutes

Table 1. Hematological parameters at onset and during treatment

Treatment	Blood component support	Hematological parameters			
		Hb (gm %)	Platelet (ul)	Coagulogram (sec)	D-dimer (ug/ml)
At onset	No			PTT = 100, PT = 120 TT = 100, Fibrinogen = 65 mg/dl	34.16
Prednisolone (1 week after)	Yes	6.5	42,000	PTT = 40, PT = 12 TT = 10, Fibrinogen = 120 mg/dl	29
Vincristine (1 week after)	Yes	8.9	52,000	PTT = 25.8, PT = 11.8, TT = 7.2	-
(3 weeks after)		9.4	176,600	PTT = 23.7, PT = 11.7 TT = 5.4, Fibrinogen = 210 mg/dl	-
(8 weeks after)	No	9.9	23,200	PTT = 29.1, PT = 11.3, TT = 7	
(6 months after)	No	10.8	357,000	-	-

condition[2]. Although the mechanism of action is unknown[3,4] but this treatment may results in dramatic shrinkage of the hemangioma[5], usually within days, can be used with a tapering schedule over 4 weeks for patients with life-threatening situation[6].

However, this treatment failed to have any effect on our patient and had side effects including hypertension, and gastrointestinal bleeding. Although earlier report support the use of steroid, many studies indicated that steroid is not effective in some cases. There is a study with interferon alpha as, an antiangiogenesis agent, is successful in 50%-60%[7] and reserved for critically ill infant patients in whom corticosteroid therapy has failed. However, the interval between the administration and the response of this treatment ranges from a few weeks to several months and particularly common side effect, spastic diplegia, has been reported in 20% of patients[8]. Haisley-Royster C et al[9] suggested that vincristine is a safe and effective treatment in the management of KMP with an average onset of response of 4 weeks and increased platelet count after the initiation of vincristine therapy. Vincristine is a vinca alkaloids which interferes the mitotic spindle microtubules binding to tubulin which induces apotosis of tumor and vascular endothelial cells and is applied in the treatment of acute lymphoblastic leukemia (ALL)[10], idiopathic thrombocytopenic purpura (ITP). It also considered to has an effect in patients with KMP by strongly suppressing angiogenesis[11].

Although vincristine as single therapy has not been proven to be of significant benefit in life-threatening patients, there is a report by Hauer J et al[12] using vincristine, combined with cyclophosphomide, actinomycin D and methotrexate for six cycles which has been maintained for 5 months. Particularly in Thailand, Wananukul S et al[13] reported using interferon-alpha-2b (IFNalpha2b) as second therapy for steroid-resistant cases for 12 months. However, the experience using vincristine in the present study was limited.

In the present report, the authors selected vincristine as monotherapy plus supportive platelet transfusion and cryoprecipitate in this case. Patient showed that the platelet count and fibrinogen level come to be normal without blood transfusion in 2 weeks and gradually decreased in tumor size without any surgical procedure in 4 weeks and disappeared in 5 months. The side effects of viscristine such as constipation, irritability and loss of deep tendon reflexes were not found in this case.

Kasabach-Merritt phenomenon (KMP) shows wide results in life-threatening hemorrhage regarding to thrombocytopenia and coagulopathy especially hypofibrinogen which is usually reserved for patients with documented isolated hypofibrinogenemia. Acute management with cryoprecipitate has been controversial for DIC and there are few prospective trial data to define the optimal use of cryoprecipitate. Although cryoprecipitate is a source of fibrinogen, VWF (von willebrand factor), FVIII, FXIII and fibronectin but not a source of all coagulation factors. However, the present report showed that the main depletion of coagulation factor is fibrinogen and can correct coagulopathy after

giving cryoprecipitate plus giving platelet transfusions for the control of active bleeding.

In conclusion, the authors reported the case of a 6-month-old infant who developed Kasabach-Merritt phenomenon based on a large retroperitoneal mass that did not respond to corticosteroid. Our patient was successfully treated with vincristine alone and supportive treatment for life-threatening hemorrhage with platelet concentrate and cryoprecipitate. The authors consider that vincristine at standard dose of 0.625 mg/kg/week (initial phase) until a sustained increase in the platelet count or gradually decreased in tumor mass and taper to 0.625mg/kg/month until disappearance of tumor mass should be the best management in our situation.

Potential conflicts of interest

Pramongkutklao Hospital's Foundation under Her Royal Highness Princess Maha Chakri Sirindhorn's Patronage.

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บทบาทของยา vincristine ในฐานะยาเดี่ยวในการรักษา Kasabach-Merrit phenomenon (KMP)

ชาญชัย ไตรวารี, รัชฎาภะ ลำกูล, กิตติ ต่อจรัส, ไตรโรจน์ ครุธเวโช, ทิพย์ ศรีไพศาล

Kasabach-Merrit phenomenon (KMP) เป็นกลุ่มโรคซมะเร็งในเด็กที่พบค่อนข้างน้อยหรือที่เรียกกันในอดีตว่า Kasabach-Merrit syndrome (KMS) โดยจะพบลักษณะความผิดปกติประกอบด้วยการที่มีก้อนที่เกิดจากความผิดปกติของเส้นเลือดซึ่งมีลักษณะสีเขียวคล้ำ ร่วมกับความผิดปกติของการแข็งตัวของเลือดและเกร็ดเลือดต่ำ โดยการวินิจฉัยจะขึ้นกับสิ่งที่พบดังกล่าวข้างต้น ในรายงานฉบับนี้ได้รายงานผู้ป่วยเด็กหญิงไทยอายุ 6 เดือน ที่มาพบแพทย์ด้วยก้อนสีเขียวคล้ำที่บริเวณสะโพกด้านซ้าย ร่วมกับพบมีเกร็ดเลือดต่ำและความผิดปกติของการแข็งตัวของเลือดจากอาการทางคลินิกและผลรังสีวินิจฉัยยืนยันการวินิจฉัย KMP โดยได้ทำการรักษาด้วยยาวินคิสติน (vincristine) หลังจากผู้ป่วยไม่ตอบสนองต่อการรักษาด้วยยาสเตียรอยด์ (corticosteroid) หลังจากนั้น 2 สัปดาห์ ผู้ป่วยเริ่มตอบสนองต่อการรักษาโดยเกร็ดเลือดและระดับไฟบริโนเจน กลับมาปกติโดยไม่ต้องได้รับส่วนประกอบของเลือดและขนาดของก้อนยุบลงภายใน 5 เดือน โดยไม่ต้องได้รับการผ่าตัดใดๆ โดยรายงานนี้ผู้เขียนได้กล่าวถึงการรักษาด้วยยาวินคิสติน (vincristine) เพียงอย่างเดียวร่วมกับการรักษาประคับประคองเพื่อป้องกันภาวะเลือดออกด้วยเกร็ดเลือดเข้มข้นและไครโอพริซิพริเตท (cryopreciptate) น่าจะเป็นอีกวิธีการหนึ่งที่เหมาะสม