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Short communication

Episode of Kasabach-Merritt phenomenon following Japanese encephalitis vaccination: Case report

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ABSTRACT

Kasabach-Merritt phenomenon (KMP) is a rare potentially life-threatening consumptive coagulopathy characterized by thrombocytopenia and hypofibrinogenemia occurring associated with the vascular tumors kaposiform hemangioendothelioma (KHE) and tufted angioma (TA).

A 10-month old male infant, diagnosed with KHE on his left leg, underwent a rapid increase of the lesion and severe thrombocytopenia, one day after the first dose of inactivated Japanese encephalitis (JE) vaccination. The episode of KMP was treated successfully by steroid.

KMP is a rare complication of vaccination that physicians should be aware of. Giving up the following vaccination to provide the recurrence of KMP is not recommended.

1. Introduction

In 1940, Kasabach and Merritt described an infant who had extensive purpura and severe thrombocytopenia and a "giant capillary hemangioma" on his left thigh [1]. Thereafter, the term "Kasabach-Merritt syndrome" (KMS) has been used to describe various cases which broadly fit that description. Owing to revise of vascular tumors classification and development of the histopathology in recent decades, it is now clear that KMS occur with kaposiform hemangioendothelioma (KHE) and tufted angioma (TA), not with infantile hemangioma (IH) or congenital hemangioma [2]. Now, Kasabach-Merritt phenomenon (KMP) has been used to describe the rare consuptive coagulopathy characterized by profound thrombocytopenia and hypofibrinogenemia occuring associated with the vascular tumors KHE and TA. KHE and TA are thought to be part of the same neoplastic spectrum [3,4].

The exact pathogenesis of KMP has been unclear. Researchers proposed that platelets were trapped, activated and consumed in the abnormal vascular structure [4]. The management varies widely among different academic centers, including corticosteroids, chemotherapy, surgery, compression therapy, vascular embolization, sirolimus, interferon-alpha, radiotherapy, propranolol, anticoagulants, anti-platelet agents and antifibrinolytic agents. Comprehensive treatment is recommended [4–6]. Recently, a consensus-derived first-line therapy for KHE associated with or without KMP has been proposed. For cases of KHE associated with KMP, first-line therapy with intravenous vincristine 0.05 mg/kg once weekly and oral prednisolone 2 mg/kg OR intravenous methylprednisolone 1.6 mg/kg/d is recommended [7].

We have treated a 10-month-old boy who underwent a sudden recurrence of KMP after receiving the first dose of inactivated JE vaccination. To provide his parents with an evidence-based answer regarding the possible link between the vaccination and episode of KMP and the risk of recurrence of KMP after reimmunization, we looked into the relevant literature.

2. Case report

A 10-month-old boy was sent to our department with thrombocytopenia and durative enlargement of lesion on his left leg, after receiving the first dose of inactivated JE vaccination (JEVAC®, 201312B34, Inactivated Vero cell derived JE vaccine (P-3 strain) produced by Liaoning Cheng Da Biotechnology Co., Ltd, China). The lesion has been confirmed to be KHE by pathology when he was 2-month-old (Fig. 1a–f).

Examination revealed a normal looking baby with a giant, solitary, firm tumor, involving the anteromedial and posterior aspect of left crus and anterior aspect of distal thigh, measured to be 10 * 20 cm. The lesion was ill-defined with pebbly texture and local high temperature. There were no presence of bleeding in

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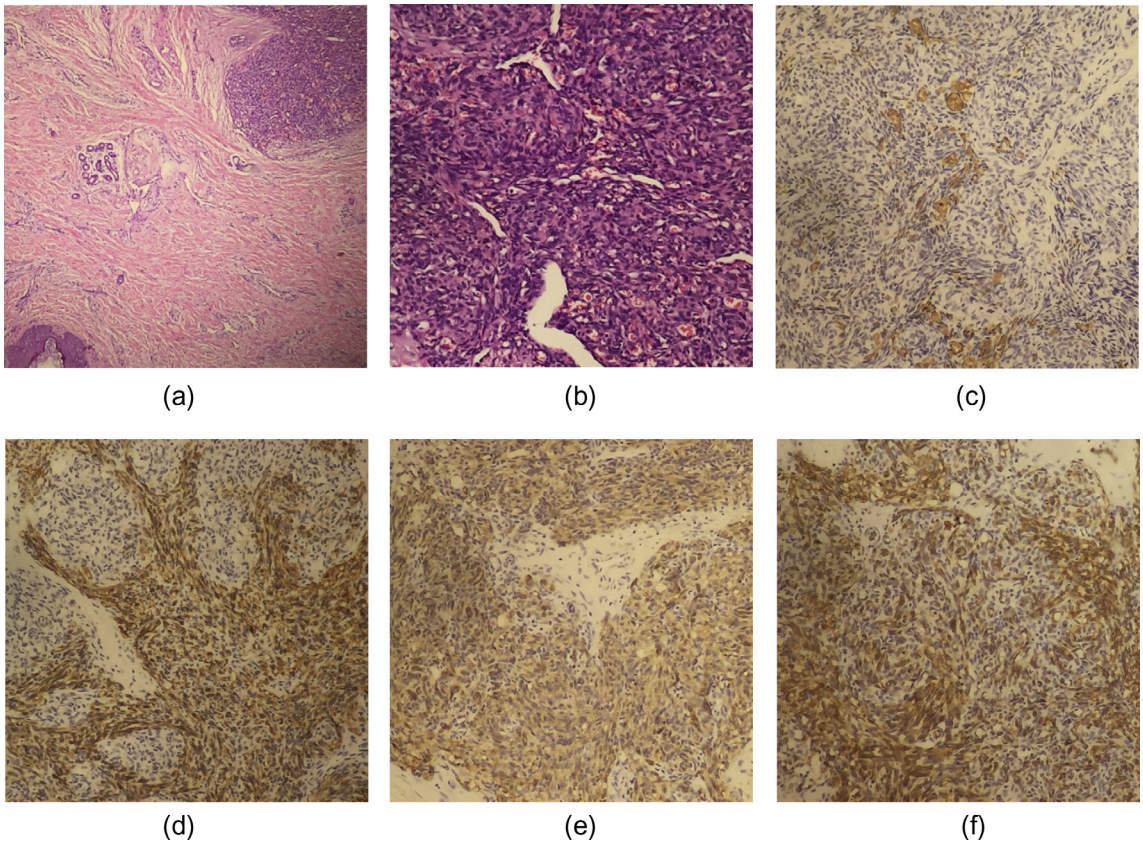

Fig. 1. (a) H-E staining revealed tumor nodule located in Dermis, 40×. (b) Slitlike channels lined with spindle endothelial cells, H-E, 100×. (c) In immunochemistry staining, Glut1 (−), EnVision, 100×. (d) Spindled endothelial cells immunopositive for D2-40. (e) The tumor showed diffuse positive staining for CD34, EnVision. (f) The tumor showed diffuse positive staining for CD31, EnVision.

the skin, mucous membranes, gastrointestinal tract, brain, urinary tract and retroperitoneum.

The past medical history showed that the boy was born with a $4 * 5$ cm firm mass at the anterior aspect of left crus with normal platelet count. The lesion biopsy demonstrated a KHE. When he was 4-month-old, he went through the first episode of thrombocytopenia and rapidly increase of the lesion without apparent triggers. Oral prednisolone 2 mg/kg/d was given and tapered when the platelet count rise to normal range. Size of the lesion and platelet counts were stable, until he received the first dose of inactivated JE vaccination (administrated by subcutaneous route at the lower edge of the left deltoid muscle). Two days before the vaccination, the complete blood count showed normal platelet count. Twelve hours after the vaccination, mild enlargement of the lesion has been noticed. The platelet count tested in the next morning when he sent to our department was $45 * 10^9$/L.

Laboratory examination findings showed prothrombin time of 11.5 s, activated partial thromboplastin time of 31.9 s, fibrinogen level of 1.58 g/L, D-Dimers of >20 mg/L, and anti-platelet antibodies were positive. Ultrasonic examination of the abdomen excluded splenomegaly. Liver and renal function test were negative.

There was no history of recent infections or drug use or blood transfusion. Family history was unremarkable and the child was fully vaccinated. Considering the complete clinical evidence, a final diagnosis of KMP was made.

The child was treated with steroid pulse therapy and compression therapy. Intravenous methylprednisolone (10 mg/kg once a day) was administrated for 3 days with a taper [8]. After 3 days of treatment, the platelet count increased to $295 * 10^9$/L, and the lesion was soften and decreased significantly. Since then, the platelet counts of this patient kept being in normal levels.

3. Discussion

3.1. Does vaccination trigger the KMP?

KMP is characterized by thrombocytopenia and consumptive coagulopathy associated with KHE or TA. Causes of thrombocytopenia can be divided into: decreased bone marrow platelet production, increased splenic sequestration, dilution, and increased peripheral platelet destruction. Ruled out the possibility of bone marrow suppression, dilution, splenomegaly, in the development of KMP, thrombocytopenia might be caused by increased destruction of platelet in the tumor.

KHE and TA got specific pathological structure, which might result in aggregation and activation of platelets. Histologically, KHE is composed of infiltration nodules. At the center of those nodules, slitlike vascular channels lined with spindle endothelial cells were observed. The newly formed basement membrane of the slitlike channel was very thin [9]. TA is consisted of tightly packed capillaries located in the mid to reticular dermis in a cannonball pattern [10]. KHE and TA have certain similar histologic feature and the transformation between them have been observed [3,4]. It's proposed that KHE and TA are part of the same neoplastic spectrum, and TA could be a "minor" form of KHE [3]. Abnormal platelet activation and aggregation may occur secondary to interaction between platelets and abnormal tumor endothelium and poorly

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