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Case Report
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A Rare Case of Cerebral Hemangioma Associated with Kasabach –Merritt Phenomenon and Extramedullar Hematopoiesis Cured with Sirolimus

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Abstract

We report the case of a 2-month-old infant with a life-threatening intracranial hemangioma and concomitant Kasabach Merritt phenomenon (KMP), who presented with pancytopenia secondary to extramedullary hematopoiesis. Because of the pancytopenia and major hemostatic disturbance, the biopsy was refuted and treatment with a combination of solumedrol and sirolimus was initiated based on the hypothesis of a kaposiform hemangioma (KHE) complicated by KMP. A complete remission of all biological (4 months), radiological (11 months), and clinical (14 months) disturbances was achieved with this treatment.

Keywords: cerebral hemangioma, newborn, Kasabach, Merritt phenomenon, extramedullar hematopoiesis, sirolimus

Introduction

There have been very few reports of intracranial hemangioma and no case of association with Kasabach-Merritt phenomenon (KMP). We report on an infant who suffered from a huge intracranial hemangioma and concomitant KMP, who presented a pancytopenia secondary to an extramedullary hematopoiesis.

Case Report

We report the case of a 4-day-old male who was hospitalized for suspected neonatal alloimmune thrombocytopenia. There was no detection of maternal alloantibodies. Clinical examination was normal except for macrocephaly attributed to an occipital caput succedaneum. Transfontanellar ultrasound was normal. At one month of age, he developed a moderate hemolytic anemia without etiological explanation. At two-month-old, he was taken to the pediatric emergencies for left-hemisphere seizures. Clinical examination showed a rapid increase in head circumference to 43 cm (> + 3 SD) from 36 cm (+ 1 SD) at birth, with a 7-cm occipital mass and massive hepatosplenomegaly attributed to extramedullary hematopoiesis in the absence of other obvious causes. Laboratory results showed pancytopenia (hemoglobin level 8 g/dl, white blood count 3.3 G/L neutrophil count 0.39 G/L), a consumptive coagulopathy (platelet counts 19 G/L, elevated fibrinogen degradation products (5 and 20 µg/ml) and hypofibrinogenemia 1.37 g/L). Bone marrow analysis was normal. Transfontanellar US demonstrated the presence of a giant highly vascular lesion. MRI showed a gadolinium-enhancing extra-axial right parieto-occipital lesion crossing the midline and measuring 10 x 8 x 6 cm in discrete hypersignal T1, hyposignal T2, with a cortical bone defect (Figure 1).

He received several transfusions of red blood cells, platelets and plasma, but his condition rapidly worsened with a persistent seizure state, respiratory distress and oliguria. He was therefore transferred to the referring neurosurgery department to investigate the possibility to biopsy this potentially life-threatening tumor.

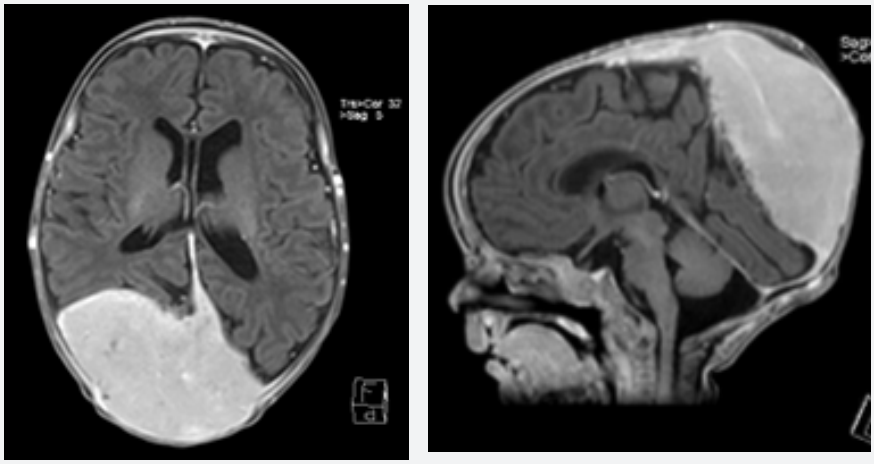

Figure 1: MRI axial and sagittal T1weighted with gadolinium at diagnosis.

Due to pancytopenia and major hemostatic disturbance, the biopsy was refuted and a treatment combining solumedrol (4 mg/kg/D) and sirolimus (0.5 mg/D) was initiated according to the hypothesis of kaposiform hemangioendothelioma (KHE) complicated by a KMP. On the 7th day of this treatment, the hemostasis disorders improved. Steroids were decreased to 2 mg/kg/D. Transfusion independence occurred on day 17 for platelets and on day 44 for red blood cells. Leucopenia normalized on day 44, platelet count and hemoglobin level on day 119. At the age of 7 months, an MRI control showed a 64% decrease in tumor volume. Steroids were then tapered while sirolimus was continued at the same dose. At week 10 after diagnosis, the volume of the KHE was greatly reduced. At 11 months of age, the tumor was in complete remission on MRI monitoring and clinical examination no longer showed splenomegaly. At the age of 14 months, the hepatomegaly disappeared and the steroids were stopped. The rest of the clinical examination was normal. A CT-scan showed a 94 x 80 mm cortical bone defect where the hemangioma was located. Subsequently, sirolimus was tapered and stopped at 31 months of age. At that time, the cortical bone defect was measured at 4 x 3 cm. Today, the child is healthy with no neurological sequelae. The MRI (Figure 2) and CTscan are normal with no bone defect. A psychomotor monitoring showed no retardation.

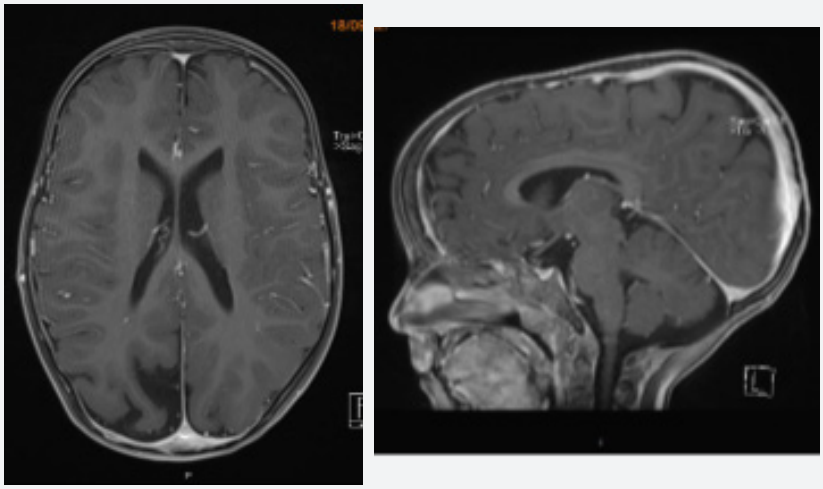

Figure 2: 49 weeks post diagnosis: MRI axial and sagittal T1 weighted with gadolinium.

Discussion

KHE are known as vascular tumors that typically occur in infancy and affect the skin and underlying tissues in other 90% of cases [1]. The most common location is the extremities, trunk, head, and neck area [1]. Only very few cases have been reported in the central nervous system [2-10] of which only 3 were reported as KHE [4,6,7]. They most often present as bulky (median size

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7.5 cm), indurated, solitary vascular tumors [1]. In the absence of biopsy and thus pathology, because of both intracranial location and life threatening consumptive coagulopathy, we assumed that this locally aggressive vascular lesion was compatible with a KHE. This is in agreement with its firm and inflammatory clinical characteristics and the destruction of the underlying bone, but in disagreement with large congenital RICH (rapidly involuting congenital hemangioma) in which coagulation disturbances have also been reported [4]. In addition, the level of thrombocytopenia observed in our case is much lower, and duration of the consumptive coagulopathy much longer than those reported for RICH [11]. It was complicated by severe anemia, due to intralesional hemorrhage, probably causing extramedullary hematopoiesis. Severe anemia was observed in 20% of cases in the series of Ji et al., but no extramedullary hematopoiesis was described [1]. KMP occurred in 69.9% of cases of KHE in this series of 146 patients, and in 79% of in the series of 153 infants of Schmid et al. [1,12]. No KMP was reported in 3 cases of intracranial KHE [4,6,7]. The mortality of vascular tumors complicated by KMP is estimated to be 10-30% [13].

Surgery is rarely proposed for KHE, aiming only to reduce consumptive coagulopathy, because of the difficulties of resecting tumors in healthy margins and without deterioration, even less in the case of KMP [1]. Because of the rarity of this disease, the multiplicity of agents tested at different times, and the unpredictability of responses, the optimal treatment remains undetermined. Steroids, vincristine and interferon-β have been used as first line therapy. However, success using corticosteroids alone was achieved in only 10-27% of all cases, in about 60% when combined with IFN- β and in 60-70% when combined with vincristine [13]. Significant benefits are not clearly described with vincristine alone in life-threatening situations [1]. In 2013, a consensus recommended steroids associated with vincristine [14]. Faced with the life-threatening condition in our case, we delivered specific treatments as soon as the diagnosis was made, without histopathology. Indeed, early treatment has been shown to be associated with reduced morbidity, mortality and better long-term outcomes [1]. A rapid and dramatic response using the mTOR inhibitor sirolimus, was first reported in 2010 in a case of KMP-complicated KHE [15]. Since then, several reports have confirmed the efficacy and low side-effects of this treatment for KMP-complicated KHE [10,13,16-21]. However, attention must be paid to the risk of infections and the development of pneumonia [21]. In the series of Kai et al. reporting six refractory KHE complicated KMP, sirolimus was effective in 100% of cases with a mean time to response of 5.3 days and a mean time to stabilization of 15.1 days [17]. Good disease control was also reported to be 100% in the series of eight cases by Tan et al. [13]. Tumor shrinkage was reported in 33/34 patients, and response in KMP in 30/31 patients in the review of Schmid et al [12]. The initial response time was 6.8 days and the time to complete platelet count stabilization was 19.1 days [13]. In our case, steroids were tapered from platelet stabilization (2 months) and discontinued when complete resolution of biological abnormalities was achieved (4 months). Sirolimus was withdrawn gradually at 14 months, when all clinical abnormalities were normalized, and discontinued at 19 months from the initial administration. In the series of Tan et al., sirolimus was administrated during 4 to 10 months [13].

To our knowledge, this case is the first to describe a child with a cerebral KHE associated with KMP and extramedullar hematopoiesis. In cases of congenital or rapidly growing scalp tumor in infancy, presenting as locally aggressive vascular lesion, we recommend not to perform a biopsy, much less in cases of KMP. Immediate institution of the association of sirolimus and steroids appears to be the most rapidly effective treatment.

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