Kasabach–Merritt phenomenon and prenatal counseling: a case series

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Kasabach–Merritt phenomenon (KMP), first described by Kasabach and Merritt in 1940, is characterized by profound thrombocytopenia associated with “giant hemangioma” [1]. Coagulopathy can be associated with aggressive presentations. It is now clear that KMP occurs exclusively with kaposiform hemangioendothelioma (KHE) or tufted angioma (TA) [2]. Occasionally, a lesion will have features of both types suggesting that they may be part of a continuum [3, 4]. In prenatal period, KMP complicating KHE or TA may be suspected by the sudden growth of a distinctive solitary vascular tumor. Cardiac failure as well as nonimmune fetal hydrops may appear secondarily. Magnetic resonance imaging (MRI) is the imaging of choice for prenatal diagnosis and follow-up. Since congenital presentation of KMP is in most cases a severe condition, its prenatal diagnosis may eventually lead to discussion of therapeutic abortion [5]. Recently, a consensus-derived practice standards plan for complicated kaposiform hemangioendothelioma (occurring after birth, or during childhood), was published by a multidisciplinary, multi-institutional expert panel [6]. However, no such consensus exists for prenatal management.

The aim of this case series was to report on two perinatal cases, including one prenatal case leading to therapeutic abortion and one neonatal case, successfully treated by a multimodal therapy. Prenatal counseling should include the possibility of neonatal multimodal treatment that can lead to favorable outcomes.

Key Clinical Message
Kasabach–Merritt phenomenon can be encountered in the perinatal period. No consensus exists regarding prenatal management. We report one prenatal case leading to therapeutic abortion and one neonatal case, successfully treated by a multimodal therapy. Prenatal counseling should include the possibility of neonatal multimodal treatment that can lead to favorable outcomes.

Keywords
Kasabach–Merritt phenomenon, perinatal period, prenatal counseling.

Case 1
A 27-year-old woman without any personal or family history was referred to a Multidisciplinary Center of Fetal Medicine at 26 weeks and 4 days of gestation. A routine ultrasonography (US) performed 1 week earlier (25 weeks of gestation), revealed a large soft tissue lesion on the right thigh of the fetus. Through US, the lesion was found...
to be homogeneous, diffusely hyperechoic, and infiltrating the soft tissue. A pelvic extension was suspected. The Doppler study showed hypervascularization of the mass. An MRI study (Fig. 1), showed a dermo-hypodermic extension, where the underlying muscles where spared. The lesion infiltrated the paravesical region and a significant edema of the limb was observed. At 26 weeks, US showed that the lesion had significantly increased in size, responsible for a marked increase in the circumference of the thigh. The lesion appeared more heterogeneous and still highly vascularized. The fetus also presented with echographic signs of cardiac failure (cardiomegaly, mitral insufficiency, pathologic Doppler flow of the ductus venosus, and pulsatile umbilical venous flow), fetal hydrops as well as severe anemia (increased velocity in the middle cerebral artery). Those imaging features, together with rapid extension and hemodynamic complication, were consistent with KHE complicated with KMP. After a multidisciplinary discussion, termination of pregnancy was proposed to the parents, due to the rapid extension, the hemodynamic degradation, and the young age of the fetus. The parents elected for pregnancy termination at 27 weeks of gestation. A pathological exam confirmed KHE.

**Case 2**

A 1-day-old, full-term infant was referred to our neonatal intensive care unit (NICU) in Lyon for further investigation of a marked hypertrophy of the left leg, with purple-brownish discoloration of the skin, sensitive to palpation (Fig. 2). No anomaly had been detected during pregnancy, and high-resolution ultrasound did not reveal fetal abnormalities or malformations. No hemodynamic disorder was observed for the neonate. Profound thrombocytopenia ($14 \times 10^{9}$/L) and severe anemia (82 g/dL) were evidenced upon the patient’s arrival. Activated partial thromboplastin time (46 sec) was minimally elevated. As well, hypofibrinogenemia (40 mg/dL) appeared secondarily after 3 days. An MRI showed a dermal and subcutaneous thickening with ill-defined margins extending into adjacent muscles of the limb and perineum. Cardiac ultrasound was normal. Clinical presentation, biological abnormalities, and imaging features were highly indicative of combined KHE with KMP. After discussing the patient’s results at a multidisciplinary meeting which included a neonatologist, oncologist, radiologist, and dermatologist, methylprednisolone was started at a 3 mg/kg/day basis and vincristine on a 0.05 mg/kg weekly basis. Initial follow-up showed a rapid tumor extension to perineum and chest wall, complicated by respiratory distress requiring continuous airway pressure support. Ticlopidine and aspirin were added after 1 week of treatment. Due to profound anemia, the neonate was treated with recurrent red blood cells. Platelet transfusion was avoided, in order to limit platelet consumption and subsequent worsening of KMP.

Platelets were lowest at $3 \times 10^{9}$/L during the first week. Progressive improvement was observed after a 3-week-period, including tumor involution, lightening of the reddish coloration, and stepwise biological marker normalization.
(platelets $30 \times 10^9$/L). With the exception of frequent vomiting, no treatment side effects were apparent. Corticosteroids and ticlid were diminished and stopped after 1 month as aspirin and vincristine were maintained. The limb was wrapped with compressive bandages, and daily physiotherapy was introduced to improve mobility of the leg. Platelet normalization was obtained after 1 month and a half, and tumor stabilization occurred after 3 months (Fig. 3). However, vincristine was maintained for 2 years as local recurrence occurred as soon as the treatment was stopped. At this point, the patient’s psychomotor development was perfectly normal, even though eating disorders persisted from birth until the age of two. Follow-up was maintained until the age of five.

KMP is characterized by severe thrombocytopenia due to platelet trapping within the tumor in contrast to venous or lymphaticovenous malformations where the platelet count is minimally depressed. Hypofibrinogenemia and fibrinolysis are secondary. Prothrombin time and activated partial thromboplastin time are normal and anemia is caused by the sequestration of red blood cells in the tumor [7].

These lesions can be extremely fast-growing and locally invasive. In the perinatal period, KMP may be associated with cardiac failure or nonimmune fetal hydrops [5]. The mortality rate ranges from 20% to 40% according to world literature [2,8]. On pathology, KHE or TA can be distinguished from infantile hemangioma, because of negative endothelial GLUT 1 marker [9].

MRI is the imaging modality of choice for prenatal diagnosis and follow-up for such condition. Heterogeneous soft issue infiltration demonstrating increased T2 intensity, decreased T1 intensity as well as gadolinium-enhanced images are observed [10]. However, gadolinium injection should be avoided during pregnancy.

To date, no prenatal effective treatment has been reported. Whether there is a role for high doses of placenta-crossing steroids or digitalis therapy during pregnancy still remains controversial. There is also no established consensus on exact timing and coordination of delivery. Extreme prematurity (as in case 1) has been described to reduce treatment chances, highly increasing the mortality rate [11]. A better outcome has been described with moderate prematurity [12]. High output heart failure and fetal hydrops, frequently associated with this life-threatening disease, should lead to pluridisciplinary discussion of birth induction or therapeutic abortion according to the gestational age of the fetus, despite the absence of consensus as in case 1.

In case 2, the prenatal diagnosis was not made. Consequently, therapeutic abortion, birth induction, or parents’ preparedness, was not discussed during pregnancy. However, as our case presented without heart failure or fetal hydrops during pregnancy (normal ultrasound), it is likely that neither therapeutic abortion nor birth induction would have occurred.

In postnatal periods, KHE or TA usually present as solitary, firm red-purplish lesions, involving mostly superficial soft tissues [13]. KMP is characterized by severe thrombocytopenia due to platelet trapping within the tumor. Hypofibrinogenemia and fibrinolysis are secondary. Activated partial thromboplastin time is minimally high and anemia is caused by the sequestration of red blood cells in the tumor [7]. While biopsy is not mandatory, an MRI is preferred for accurate diagnosis [2, 6, 14].

Expert recommendations are a first-line therapy with weekly vincristine for 24 weeks associated with corticosteroids which should be weaned after 3–4 weeks [6]. Platelet transfusion is recommended only in case of active bleeding and/or before immediate surgery. Inconsistent results are reported from antiplatelet and antifibrinolytic therapy [6]. Interferon and radiotherapy cannot be used at a young age, as a first course of treatment [14]. Other treatments such as embolization, sclerotherapy, and surgery have been reported with variable rates of success [6]. In our neonatal case, no such treatment could be performed due to patient’s age, lesion size, and localization. A combination of medications, using high dosage of steroids, vincristine, ticlid, and aspirin was used, and led to

Figure 3. Aspect of the lower limb after 3 months of multimodal treatment of case 2.
rapid improvement. However, vincristine was maintained for 24 months, due to the risk of local recurrences.

Congenital KMP can be encountered in the perinatal period. Prenatal presentation can be life threatening, leading to discussion of termination of pregnancy, particularly in cases of poor hemodynamic condition. However, prenatal counseling should include the possibility of neonatal management with a multimodal treatment that can lead to favorable outcomes.

Consent

Written informed consent was obtained from the patients’ parents for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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Conflict of Interest

None declared.

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