

KASABACH-MERRITT SYNDROME IN A NEWBORN: FROM PRENATAL DIAGNOSIS WITH MRI TO TREATMENT WITH SIROLIMUS

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ABSTRACT

Kasabach-Merritt Syndrome (KMS) is a rare clinical entity, found in 1% of angiomatous lesions, characterized by severe consumption coagulopathy/thrombocytopenia in association with highly aggressive neonatal vascular lesions. We describe a case of prenatally diagnosed vascular neof ormation of the neck, revealed by obstetric ultrasound and then confirmed by fetal Magnetic Resonance, with subsequent onset of KMS at birth. The newborn was treated with Propranolol and Prednisone, without any benefit; Magnetic Resonance (MRI) at day 14 of life confirmed the hypervascularized lesion of about 6x7x6 cm on the right laterocervical site. Sirolimus therapy was then initiated leading to rapid improvement in thrombocytopenia and a volumetric reduction of the vascular lesion on MRI. After 12 months of treatment, MRI scan showed a further reduction in volume of the vascular lesion; also, the KMS-related thrombocytopenia was completely resolved: Sirolimus could represent the first line of treatment of vascular lesions in the neonatal age.

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1. Introduction

Kasabach-Merritt Syndrome (KMS-OMIM 141000) is a rare clinical entity, found in 1% of angiomatous lesions, characterized by severe consumption coagulopathy/thrombocytopenia in association with highly aggressive neonatal vascular lesions such as kaposiform hemangioendothelioma (90% of cases) or tufted angioma (1). Mortality rate ranges between 10-30% (2, 3). We describe a case of prenatally diagnosed vascular neof ormation of the neck, confirmed at birth, with subsequent onset of KMS.

2. Case report

Term baby born by elective cesarean section at 38 weeks' gestational age (GA) was referred on day of life (DOL) 4 for evaluation of a right laterocervical neof ormation, seen by prenatal ultrasound at 31 weeks' GA and then confirmed by fetal MRI at 37 weeks' GA (Figure 1).

At birth, the baby was breathing spontaneously with no distress (Apgar 9); a hard-elastic mass (6 cm diameter) was evident on the right cheek and ipsilateral supraclavicular region. A severe thrombocytopenia (minimum value: 6000/uL) requiring several platelet transfusions occurred, therefore a diagnosis of KMS was made.

Echo-color-Doppler identified, in the adipose planes of the subcutaneous, a solid, hypoechoic inhomogeneous highly vascularized mass.

Propranolol was started (2 mg/kg/day) and then increased, after 10 days, to 3 mg/kg/day. Prednisone (2 mg/kg/day) was associated, due to poor therapeutic response. Because of the diagnosis of KMS with significant thrombocytopenia, no biopsy was performed. On DOL 14, Magnetic Resonance (MRI) showed the hypervascularized lesion of approximately 6x7x6 cm, originating from the subcutaneous tissue of the right cheek, reaching the ipsilateral supraclavicular fossa, extending to the deep muscular planes and in the retropharyngeal site and infiltrating the right tongue, also displacing the pharyngo-laryngeal air lumen (Figure 2).

Due to the inefficacy of both Propanolol and Prednisone, Sirolimus (0.4 mg/m^2) was immediately initiated and progressively adapted according to its serum values. After about 2 months of therapy, a second MRI scan of the neck was performed, revealing dimensional stability of the vascular lesion, with edema reduction and normalization of the normal pharyngo-laryngeal caliber. Also, thrombocytopenia was no longer present. After 1 year, a new MRI scan showed a further volume reduction of the vascular lesion (Figure 3).

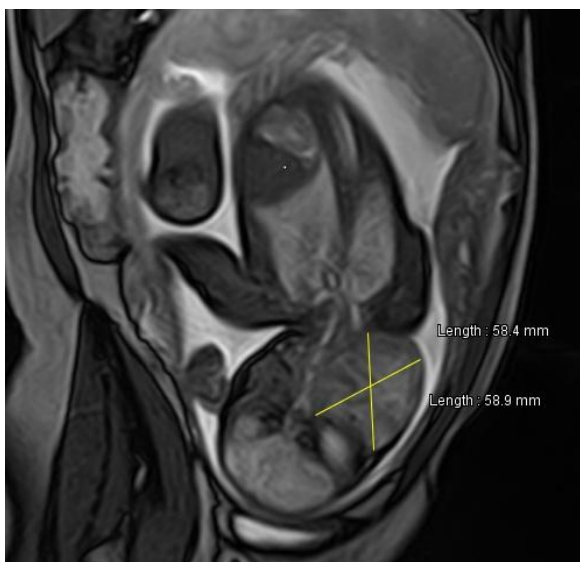


Figure 1. Fetal MR. Coronal T2-weighted image shows a solid neoformation (about 6x6 cm) in the right laterocervical site, hyperintense compared to the plane of the soft tissues.

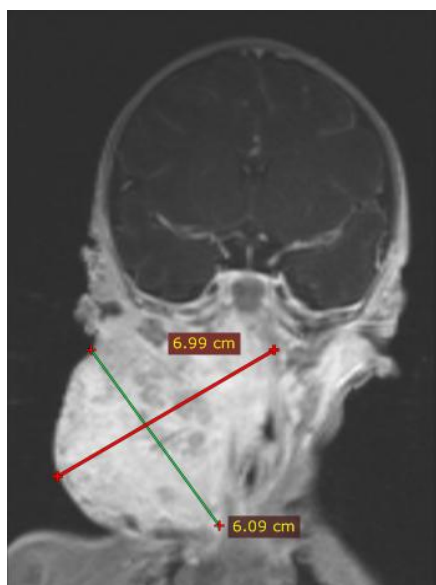


Figure 2. MR coronal T1-weighted TSE image, after contrast medium. After classical therapies, the voluminous vascular type mass (about 7x6 cm) persists in the right laterocervical site and determines compression of the pharyngo-laryngeal air lumen.

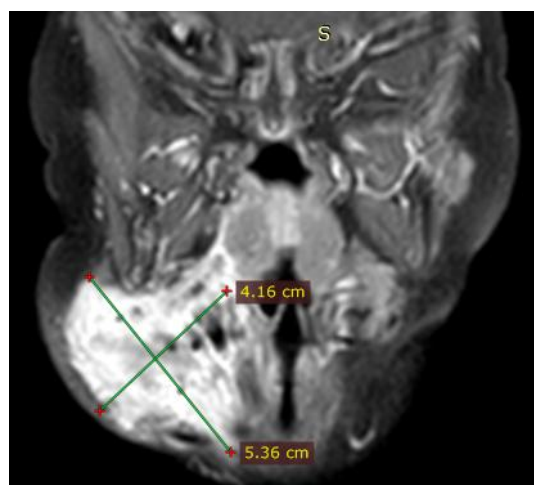


Figure 3. MR coronal T1-weighted TSE image, after contrast medium. After 12 months of Sirolimus therapy, the vascular lesion volumetric reduction (5.5x4 cm vs 7x6 cm) is evident, with multiple contextual necrotic-colliquative areas.

3. Discussion and conclusions

Neonatal vascular lesions develop rapidly during the first months of life, mainly if associated with KMS (2, 3). The severity of this hematological condition does not allow for biopsy and therapeutic management is very difficult.

MRI is the diagnostic method of choice for the characterization of angiomatous lesions, in particular in "alarming hemangiomas": these are large vascular lesions (with a diameter greater than 5 cm) that can compromise life or the functionality of an organ (4). Our clinical case was an "alarming hemangioma" of the head-neck region, that could cause sudden airway obstruction; in our case report, MRI played a role both in the diagnosis in the fetal period and for follow up after 12 months of therapy.

Currently, due to the rarity of the pathology, no definitive guidelines have been established for the pharmacological treatment of KMS, especially during the neonatal period (1): corticosteroids, beta-blockers (in particular Propanolol) and chemotherapeutic agents such as vincristine and cyclophosphamide, in addition to anti-angiogenetic and anti-aggregation factors have been employed, with contradictory results. In recent years, Sirolimus (a mTOR protein kinase inhibitor) has been used for the treatment of neonatal lymphangiomatosis, demonstrating an adequate therapeutic response (5).

Recently, Sirolimus has also been used in the treatment of angiomatous lesions in the pediatric age, in particular for the refractory forms of KMS, despite its use being off-label for this disease (6).

In accordance with the limited literature (case reports and case series), our clinical case shows that after failure of cortisone and beta-blocker therapy, the use of Sirolimus hindered the growth of the vascular neoformation of the neck on MRI and resolved the severe KMS-related thrombocytopenia. After 12 months of treatment, no side effects have been reported. Our case report lends strength to the argument for the efficacy of Sirolimus accompanied by MR iconography from fetal life to 12 months after therapy as the first line treatment of vascular lesions in the neonatal age, which is in accordance with the available literature data.

References

1. Wang P, Zhou W, Tao L, Zhao N, Chen X-W. Clinical analysis of kasabach-merritt syndrome in 17 neonates. *BMC Pediatr.* 2014 Jun; 14(1):146.
2. Arunachalam P, Kumar VRR, Swathi D. Kasabach-Merritt syndrome with large cutaneous vascular tumors. *J Indian Assoc Pediatr Surg.* 2012 Jan-Mar; 17(1):33–36.
3. Hesselmann S, Micke O, Marquardt T, Baas S, Bramswig JH, Harms E, Willich N. Case report: Kasabach-Merritt syndrome: A review of the therapeutic options and a case report of successful treatment with radiotherapy and interferon alpha. *Br J Radiol.* 2002; 75(890):180–184.
4. Dimarelos V, Konstantinou D, Bintoudi A, V. Kyriakou V, Michaelides M, Tsitouridis I. Soft-tissue hemangiomas of head and neck: MR imaging evaluation. E-Poster C-3332 in European Congress of Radiology [Internet] 2010 Mar 5-8. Available from: https://posterng.netkey.at/esr/viewing/index.php?module=viewing_browseposterselastic&task=
5. Laforgia N, Schettini F, De Mattia D, Martinelli D, Ladisa G, Favia V. Lymphatic Malformation in Newborns as the First Sign of Diffuse Lymphangiomatosis: Successful Treatment with Sirolimus. *Neonatology* 2016; 109(1):52-55.
6. Wang Z, Li K, Dong K, Xiao X, Zheng S. Refractory Kasabach-Merritt phenomenon successfully treated with sirolimus, and a mini-review of the published work. *J Dermatol.* 2015 Apr; 42(4): 401-404.