

EFFICACY OF PROPRANOLOL IN DIFFUSE NEONATAL HEMANGIOMATOSIS WITH PREDOMINANT CENTRAL NERVOUS SYSTEM INVOLVEMENT – A CASE REPORT

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Abstract

Diffuse hemangiomas is characterized by the presence of multiple mucosal and visceral hemangiomas. Usually, these are benign, but some of them can be harmful by their hemodynamic impact.

We present a rare case of neonatal diffuse hemangiomas with predominant central nervous system involvement who presented intracerebral hemorrhage, successfully treated with Propranolol.

Propranolol is a recently approved medication for infantile hemangiomas. In our case the treatment was successful and propranolol brought good results in treating malignant hemangiomas of the central nervous system.

Key words: neonatal diffuse hemangiomas, intracerebral hemorrhage, Propranolol

Introduction

Diffuse neonatal hemangiomas is a rare condition, defined by the presence of at least 5 cutaneous hemangiomas, under 5 mm diameter, that can be present at birth or appear in the first weeks of life. The clinical evolution is similar of infantile cutaneous hemangiomas. There are two subtypes: diffuse and benign. The diffuse

hemangiomas is characterized by mucosal and visceral involvement (hepatic, central nervous system, gastrointestinal tract, lungs, eyes, etc.). The benign hemangiomas can have mucosal or visceral involvement, but without hemodynamic impact. Visceral involvement can lead to hemorrhagic complications, consumptive coagulation or congestive heart failure, being associated with high mortality [1]. Propranolol, a nonselective beta-blocker, has recently become the first line systemic therapy for infantile hemangiomas, due to its high efficacy and low risk of secondary reactions [2].

We present a case of neonatal diffuse hemangiomas with predominant central nervous system involvement successfully treated with Propranolol.

Case report

A 12 days old male, presenting with about 30 small cutaneous hemangiomas (Figure 1 and Figure 2), with diameter between 0,3 and 1 cm, bright red in color and a 0,5 cm gingival hemangioma. The lesions appeared soon after birth. The baby is from a twin pregnancy, his brother is perfectly healthy, without any cutaneous lesions.



Figure 1 and Figure 2. Five months infant presenting hemangiomas.

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Transfontanelle ultrasound reveals multiple nodular tumors (>10) with increased echogenicity, spreaded bilaterally in the white matter, with the highest diameter of 8

mm. Similar images can be seen in the cerebellum and the brain stem. All the lesions are well defined, with no interior signal.

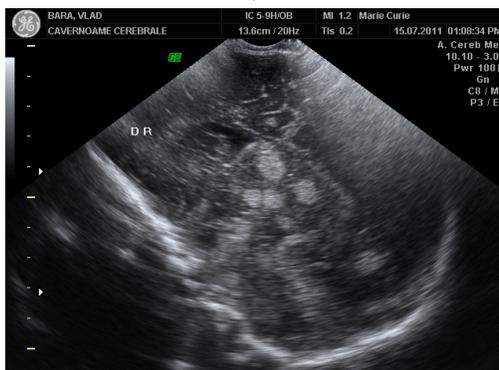


Figure 3. Transfontanelle ultrasound – sagittal section, right paramedian sagittal section – multiple intracerebral nodular tumors.

Abdominal ultrasound didn't reveal any hepatic tumors.

intubation and mechanical ventilation followed by tracheostomy. CT and MRI revealed an intracerebral hemorrhage (Figure 4-7).

At 6 weeks old, the child present with altered general status and altered respiratory function. He required

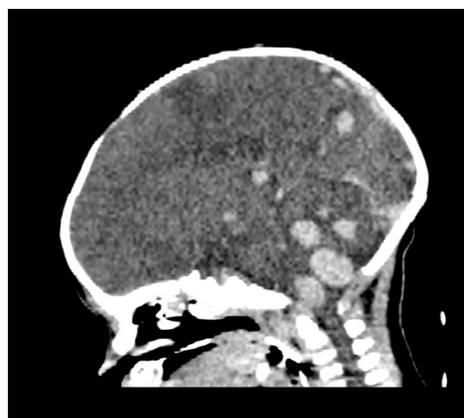
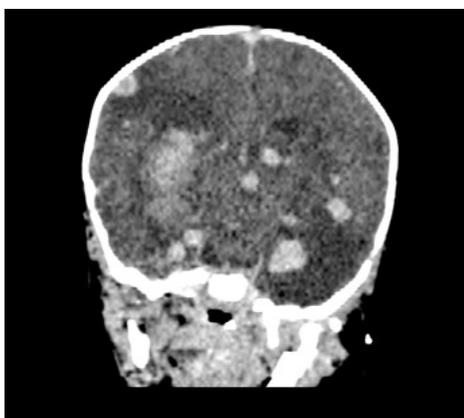


Figure 4 and Figure 5. Cerebral Computer Tomography with contrast shows multiple diffuse intracerebral nodular tumors, with high, persistent, homogenous contrast. Some of them have signs of bleeding and perilezional edema.

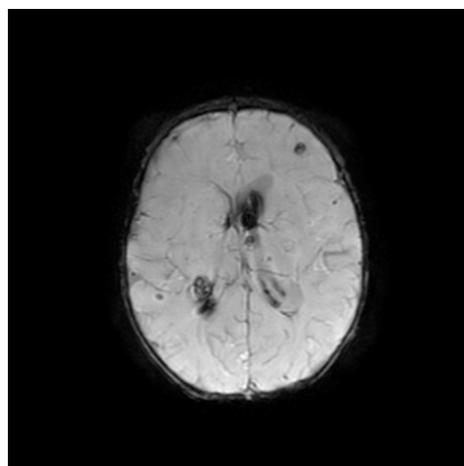
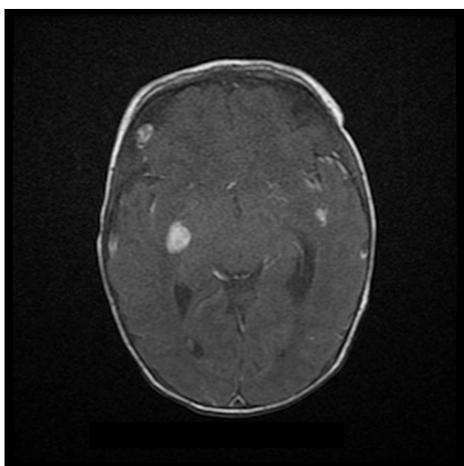


Figure 6 and Figure 7. MRI-multiple diffuse intracerebral nodular tumors, some with bleeding signs.

Laryngeal endoscopy doesn't find any hemangiomas at this level.

Propranolol 2mg/kgC was started.

At 5 months old, the child developed gastrointestinal reflux, followed by pneumonia. Bacterial cultures showed tracheostomy colonization by Pseudomonas and Staphylococcus. Systemic antibiotherapy was started with slow improvement of status. At 6 month old is detubation is possible and at 8 months old the child was discharged from hospital.

Propranolol treatment was continued for two years, with fully recovery of the patient. The intracerebral hemangiomas left nodular cavernous lesions and the cutaneous hemangiomas over 1 cm left residual fibro-adipose tissue (Figure 8-10). One year after completing the treatment, the child has no psychomotor deficit, just a slight growth delay comparing with his twin brother. No adverse effects of treatment were noted.

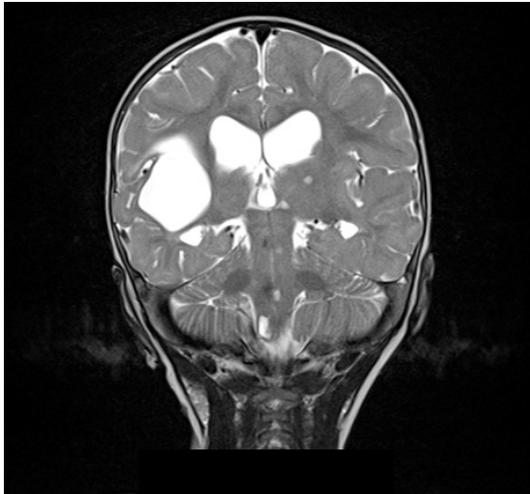


Figure 8 and Figure 9. Cerebral MRI 3 years old- right insular residual cavity. Multiple nodular cavernous lesions.



Figure 10. Cutaneous hemangiomas over 1 cm left residual fibro-adipose tissue.

Discussions

Diffuse neonatal hemangiomatosis with predominant central nervous system involvement is a rare disease, with high mortality due to hemorrhagic complications. Risk factors are unknown, male:female ratio is 2:1 and genetic transmission was not observed [1].

Propranolol is a recently approved medication for infantile hemangiomas. The mechanism of action is not fully understood. It inhibits the adrenergic response by competitive blocking beta-1 miocardic receptors and beta-2 bronchial and vascular smooth muscles receptors. Both receptors were found in cutaneous hemangiomas but the exact mechanism of action has not been identified [3].

Propranolol has also been reported to bring good results in treating hemangiomas where cosmetic surgery was difficult (like facial region) or for reduction of the tumoral mass and easier excision where dissection was difficult [4].

From our knowledge, this is the only case published of diffuse neonatal hemangiomatosis with predominant nervous system involvement treated with Propranolol.

Conclusions

Imagistic evaluation is mandatory in children with multiple cutaneous hemangiomas.

Although the skin and liver are most frequently affected by neonatal diffuse hemangiomatosis, the central nervous system involvement should be evaluated and if tumours are present, treatment should promptly be initiated in order to prevent hemorrhagic complications.

Propranolol is an efficient and safe therapeutic method for neonatal diffuse hemangiomatosis.

References

1. Maruani A., Piram M., Sirinelli D. et al. Visceral and mucosal involvement in neonatal haemangiomatosis. J EADV 2011
2. Lou Y, Peng WJ, Cao Y, et al. The effectiveness of propranolol in treating infantile hemangiomas: A Meta-analysis including 35 studies. Br J Clin Pharmacol. 2013 Sep 3.
3. Chisholm KM, Chang KW, Truong MT et al. beta-Adrenergic receptor expression in vascular tumors. Mod Pathol 2012; 25:1446–51.
4. Nisipasu IC, Plesca D, Nisipasu C, Spataru R. Tratatamentul hemangioamelor de la nivelul zonei orale si periorale. Ro J Stomatol 2014; 9(3): 147-151.

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