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RESULTS OF THE COMBINATION OF ORAL AND TOPICAL BETA - BLOCKERS IN THE TREATMENT OF GIANT ORBITO - PALPÉBRAL HEMANGIOMA : A CASE REPORT

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ABSTRACT **PURPOSE:** We discuss through a case report the results of using oral and topical beta blockers to treat a voluminous cutaneous and orbital capillary hemangioma. Observation: We report the case of a 2-month-old girl who had a large cutaneous and orbital capillary hemangioma of the left eye causing obstruction of the visual axis. Oral and topical beta-blockers induced hemangioma regression.

DISCUSSION: Capillary hemangioma is the most common vascular tumor in children that usually regresses spontaneously. When complications such as amblyopia, strabismus, corneal exposure, optic nerve compression or malformations of the bony orbit occur; a rigorous management becomes compulsory. Beta-blockers generate abnormal vessels vasoconstriction, inhibition of the production of angiogenic factors and stimulation of endothelial cell apoptosis. They are effective during the involution of the hemangioma, unlike steroids which are active only during the proliferative period, which justifies our therapeutic choice.

CONCLUSION: Oral beta-blockers have been shown to be effective in the treatment of severe and extensive forms of orbito-palpebral hemangiomas, and the results of the combination have shown added value of topical beta-blockers with rarely noted adverse effects.

KEYWORDS : Capillary Hemangioma, Eyelid , Orbit ,amblyopia, Beta-blockers

INTRODUCTION

Infantile hemangiomas are benign vascular tumors of endothelial origin, occurring in 4 to 10% of infants under one year of age. They are usually small at birth and increase rapidly during the first months of the newborn's life, eventually shrinking slowly over time. Although their presence during the crucial period of the development of visual function requires rapid and appropriate care. Thus, the indications for treatment are the threat of visual function through amblyopia and cosmetic damage [1]. Therapeutic options include corticosteroids, pulsed dye laser, topical imiquimod, beta-blockers, and surgery, Oral β-blockers are now considered the mainstay of treatment for periorbital hemangiomas, but are still unaddressed. a consensus on their administration and monitoring. The topical form or more selective beta-blockers may be the solution to minimize side effects [2]. We report the case of a giant orbito-palpebral hemangioma in a newborn and discuss the different therapeutic approaches.

OBSERVATION

A 2-month-old girl was referred to us for management of a rapidly progressive swelling of the upper left eyelid beginning with a 10 mm erythematous macula on the forehead at the age of 15 days. The interrogation found no family or personal history except for a 2nd degree inbreeding. A complete ophthalmological examination was carried out showing a well-limited erythematous cupboard with a nippled surface and elastic consistency of raspberry red color, broad, diffuse, of metameric seat (following the path of the nerve V3) infiltrating the upper eyelid of the left eye and half left of the frontal and temporal region and making a size of 10X7.5 cm on the long axis, and two small plates at the level of the left cheek which partially fade at the vitro pressure. This tumor resulted in total eyelid obstruction (Figure 1) making the rest of the eye exam inaccessible. The Adelphe eye examination is unremarkable and the rest of the somatic examination is without abnormality.

An angio-scanner for lack of means was performed in emergency and revealed a left fronto-palpebral vascular formation with extra conical endo-orbital extension homolateral left orbital. (Figure 2). The diagnosis of capillary orbito-palpebral hemangioma was accepted. A cardiovascular assessment was performed and the patient was hospitalized in dermatology and was put on beta-blocker "propr anolol" at a rate of 1 mg / kg / day for 14 days under monitoring in intensive care for 48 hours then at a dose of 2 m / kg / day under strict monitoring then an introduction of timolol eye drops 0.5% a cutaneous application 10 drops x 2 / d on hemangioma. We controlled locally, the appearance of the tumor, its size, its coloring, the opening of the palpebral cleft and generally, we looked for side effects related to treatment. The evolution was marked by clinical improvement from the first week of treatment. Indeed, at 10 months of treatment, we obtained a reduction in the tumor volume, a lightening of its coloration and an opening of the palpebral slit (Figure 3) and the ophthalmological examination did not reveal any anomaly with in parallel a decrease from hemangioma to cerebro-orbital Angio-MRI (Figure 4). beta-blockers at a dose of 2 mg / kg / day and eye drops 0.5% were maintained until the age of one year. We have not seen any side effects from beta blockers.

DISCUSSION :

Capillary hemangiomas are the most common vascular tumors in children, particularly women and of low birth weight. The etiopathogenesis of this proliferation remains unknown, but hormonal, immunological, genetic factors and vascular dysgenesis are often blamed [3]. Histologically, capillary hemangiomas result from the organization of immature endothelial and pericytary cells in the form of vascular channels in the presence of pro angiogenic factors such as the basic fibroblast growth factor (b FGF) and the vascular endothelial growth factor (VEGF). They are in continuity with the orbital vessels

and present their same hemodynamic regime. Hemangiomas can be associated with secondary glaucoma, choroidal hemangioma in Sturg Weber syndrome, arterial, cardiac, ocular abnormalities, and tortuosities of the brain vessels in PHACE syndrome or other hemangiomas (20%) with the risk of bleeding, ulceration, airway obstruction and congestive heart failure.

In the absence of functional consequences, surveillance is the rule given the tendency to resolve in the majority of cases. Sometimes, the visual prognosis is put into play requiring urgent care as in the case of our patient. Indeed, in the palpebral or orbital locations, amblyopia can occur in 60% of cases [4], it is linked to the pressure exerted by the hemangioma on the oculomotor muscles and the eyeball causing anisometropia or significant astigmatism or even optic neuropathy [4]. Exophthalmos, corneal exposure, or bone damage have also been reported [5].

The aim of treatment is therefore to stop the proliferation of the hemangioma and to accelerate its involution in order to prevent amblyopia.

Several therapeutic means have been used with success such as cryotherapy, radiotherapy, pulsed laser, Interferon alpha, embolization of the nourishing vessels by a sclerosing product, immunosu ppr essants. But their side effects limit their indications.

For our part, we opted for a general propranolol and a topical treatment because since its first appearance among the therapeutic means of capillary hemangiomas (especially in severe forms) in 2008, it has not stopped giving spectacular results and has become first-line treatment for this condition. The exact mechanism by which propranolol shrinks childhood hemangioma is unknown.

Various explanations have been proposed, including: vasoconstriction, decreased expression of vascular endothelial growth factors and fibroblast growth factors,apoptosis of capillary endothelial cells, bloc king of kinase receptors coupled to the G protein Leu41, metallo pr oteinase with reduced matrix 9 and effect on the differentiation of mesenchymal stem cells. [19]

In several studies, oral propranolol has shown remarkable regression in patients with capillary hemangiomas of the eyelids up to 5 years of age [16] [17].

Holmes et al. [18] studied 31 consecutive patients with rapid prolife rative hemangioma with visual impairment or cosmetic disfigurement who have been treated with propranolol as a first-line treatment. A rapid halt in the proliferation of hemangiomas was observed in 100% of patients and a significant decrease in 87% of patients.

In our case, there was a very rapid proliferation of the lesion during the first two months of life. We therefore indicated this treatment at a dose of 1 mg / kg / day for 14 days and then at a dose of 2 mg / kg / day without noting a recurrence [4]. It is a treatment well tolerated in children, systemic adverse effects were noted in 7% [10] such as bradycardia, bronchospasm, hypotension and hypoglycemia [11] [12] [13] requires a pre-therapeutic evaluation as well as periodic pediatric monitoring. This treatment has long been preferred for orbital hemangiomas which respond poorly to local treatments [7]. It has also been shown to be effective in corticosteroid-resistant forms with no rebound effect. In our case, despite the large volume of the lesion, this treatment allowed a spectacular regression from the first week.

The proposed dose is 2 mg / kg in 2 divided doses requiring a prior cardiovascular examination and hospitalization at least 24 hours at the start of treatment. The age of initiation of treatment can be very early and the improvement is noted for most of the authors of the first days. The success is not only anatomical but also functional with an improvement in anisometropia, astigmatism and strabismus offering better chances for the treatment of amblyopia. Resumption of tumor growth can be observed when treatment is interrupted during the proliferative period, so propanolol must be maintained until the end of this period or until the age of 1 year [12].

Timolol maleate 0.5%, currently represents an interesting alternative to the general treatment given its favorable action not only on superficial lesions but also those which are relatively deep [3] [19] [20]. Its absorption by transcutaneous route can be explained by the immaturity of the skin barrier before the age of 1 year, and by the presence of maleate increasing absorption. Its action concerns both early lesions in children and mature forms in adults [18] [19] [20].

Xue et al [20] use Timolol maleate 0.8% at a dose of 6 drops per day which would be equivalent to a dose of 2 mg / kg / d of propranolol with digital massage at the level of the lesion. Adverse effects due to the systemic passage of this eye drops are rare, of the order of 1% [19] We therefore preferred to keep the combination of propranolol at a dose of 2 mg / kg and timolol 0.5% an application of 10 g 2X / d topically for our patient.

Intra-lesional injections of propanolol were recently used successfully in a study which compared intra-lesional injections of corticosteroids to those of propanolol with no significant difference between the effectiveness of the two types of injections [15].

CONCLUSION

Capillary hemangiomas are benign lesions, regression is the rule. The risk of amblyopia often requires urgent and rapid treatment. Oral beta-blockers allow rapid and favorable development for large and deep lesions and require close monitoring. The Timolol maleate recently introduced into the therapeutic arsenal has proven to be effective in the treatment of palpebral hemangiomas and even small orbital ones.

CONFLICTS OF INTEREST

Authors do not declare any conflict of interest

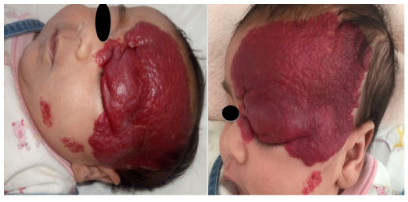

Figure 1. Initial appearance of the left upper palpebral heman gioma of raspberry red color, bulky obstructing the visual axis.

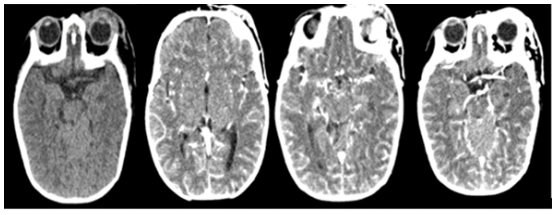

Figure 2. Cerebral CT scan without injection (a) Cerebral angio gram (b, c) aspect of the orbital hemangioma and the frontot e mporal region: Left fronto-palpebral vascular formation with extra conical extension endo orbital homolateral with vascular appearance related with a hemangioma

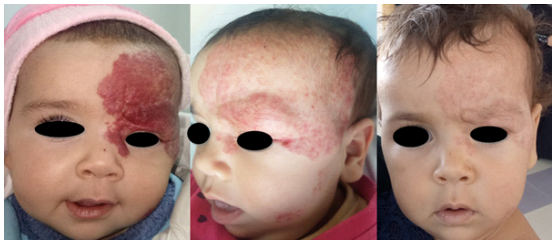

Figure 3. Evolution of the capillary hemangioma under beta-blocker. (a, b): appearance at 5 months and 8 months of treatment, (c, d): appearance after 10 months of treatment (N.B: the patient was lost to follow-up for 5 months she was under dosed).

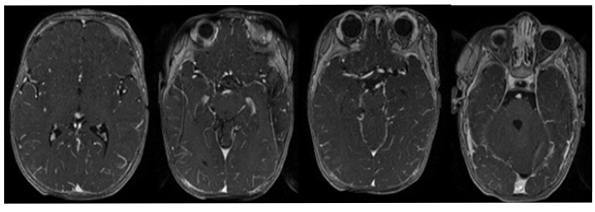

Figure 4: Brain magnetic resonance imaging (MRI) with injection showing a decrease in the size of the left palpebro-orbital angioma

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