Oral propranolol as a new treatment for facial infantile hemangioma: case report

Propranolol oral: novo tratamento para hemangioma facial em bebês: relato de caso

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ABSTRACT

Hemangiomas are the most common benign tumors of infancy. Despite their self-limited course, infantile capillary hemangiomas can impair vital or sensory functions as vision and cause cosmetic deformity. The usual treatments include oral/intralesional steroids, alpha interferon, cytotoxins, pulsed dye laser and cosmetic surgery resection. These treatments are not free of multiple complications and toxic side effects. This report describes the case of a 3-month-old female baby with progressively increasing hemangioma of the left upper eyelid impinging over the visual field. The hemangioma promptly responded to low-dose oral propranolol. A clinical response was noticed few days after the beginning of the treatment, with regression to 1/4 of its original size in 45 days of treatment, and to less than 1/10 after 8 months, free of any major side effects.

Keywords: Hemangioma; Hemangioma, capillary/therapy; Propranolol/therapeutic use; Case reports; Infant, newborn

RESUMO

Hemangiomas são os tumores benignos mais comuns durante o primeiro ano de vida. Apesar do seu curso autolimitado, os hemangiomas capilares podem prejudicar funções vitais ou sensoriais como a visão e causar alteração estética. O tratamento usual inclui esteróides orais ou intralesionais, interferon alfa, citotoxinas, laser e ressecção cirúrgica. Entretanto estes tratamentos não estão livres de complicações e efeitos adversos. Este relato descreve o caso de um bebê feminino de 3 meses com um hemangioma rapidamente progressivo na pálpebra superior esquerda, causando obstrução no eixo visual. O hemangioma respondeu rapidamente a uma baixa dose oral de propranolol. A resposta clínica foi notada poucos dias após o início do tratamento, com regressão a 1/4 do seu tamanho original após 45 dias de tratamento, e a menos de 1/10 após 8 meses, sem ter apresentado nenhum efeito adverso.

Descritores: *Hemangioma; Hemangioma capilar/terapia; Propranolol/uso terapêutico; Relato de casos; Recém-nascido*

INTRODUCTION

Hemangiomas are the most common benign tumors of infancy. They are more common in white Caucasians, females (3:1) and premature babies (22%). Capillary hemangioma generally is presented as a spot or well-defined purple lesion. The diagnosis of these tumors is based on physical examination. Its incidence is 1 to 3% in newborns. Infantile capillary hemangiomas are composed of a complex mixture of clonal endothelial cells associated with pericytes, dendritic cells, and mast cells[1-3].

During the first year of life there is a proliferative phase, with increasing size of the lesion. After this period there is a slow spontaneous involution phase. Regulators of hemangioma growth and involution are poorly understood. During the growth phase, two major proangiogenic factors are involved: basic fibroblast growth factor (bFGF) and vascular endothelial growth factor (VEGF); histologic studies have shown that both endothelial and interstitial cells are actively dividing in this phase. During the involution phase, apoptosis has been shown[3].

In up to 70% of the cases the tumor disappears completely until 7 years of age. Unfortunately, some hemangiomas may become large in size impinging on vital structures such as eyes, mouth, nose or larynx, and require certain therapeutic interventions to prevent major morbidities. Amblyopia is the most common complication of hemangioma of the eyelid. If not treated promptly, it may lead to irreversible visual loss in young children[1,4,5].

Until today, oral or intralesional corticosteroids were the first line of treatment for severe infantile capillary hemangiomas. Other options include alpha interferon, vincristine, intralesional injection of sclerosing solutions, radiotherapy, as well as pulsed dye laser and cosmetic surgery resection[1,3,6-8].

We present a new and safe option for the treatment of severe facial capillary hemangiomas in infancy with a nonselective beta-blocker, low-dose oral propranolol.

CASE REPORT

A 3-month-old girl was examined for a progressively increasing hemangioma of the left upper eyelid. The lesion was a purplish tumor, impinging over the visual field and she could not open her left eye (Figure 1). She was born prematurely at 32 weeks and weighed 1800 g. The ophthalmologic evaluation was normal. Treatment with propranolol, at an oral dose of 2 mg per kilogram of body weight per day was initiated. The heart rate and blood pressure were closely monitored by the pediatrician and the baby never required hospitalization for any side effects.

One month and 15 days later, the child was able to open her eye spontaneously and the mass in the upper eyelid was considerably reduced in size. We were able to measure the visual acuity (with Teller acuity cards) and it was worse in the left eye. Occlusion therapy was started, 4 hs daily. After 3 months of amblyopia treatment,

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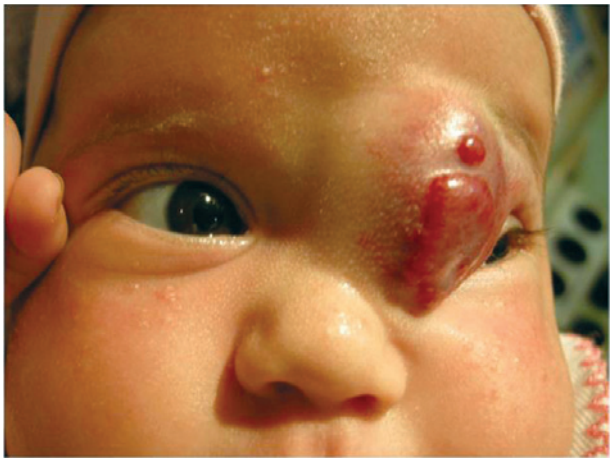

Figure 1. Hemangioma - before treatment.

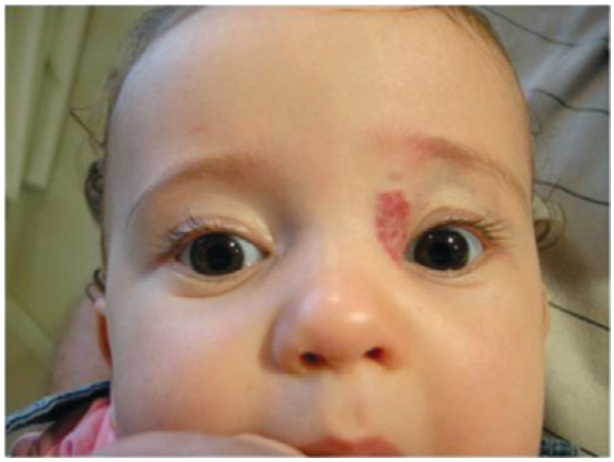

Figure 2. Hemangioma - 8 months after the beginning of the treatment.

the visual acuity was the same in both eyes and occlusion therapy was discontinued. After 5 months of treatment with oral propranolol (baby at the age of 8 months) the involution of the tumor slowed down and the dosage was slowly increased to 4 mg/kg. After 8 months of treatment, the lesion was smaller than 1/10 of its original size (Figure 2). The oral dosage of 4 mg/kg was maintained until the baby was one year old. Discontinuation of therapy through tapering of propranolol over a 3 month period was then performed.

DISCUSSION

With the objective of getting better results and treating lesions with difficult surgical access, new therapeutic modalities have been developed. Until now, the best results were observed with steroids and interferon-alpha with a high percentage of side effects[3].

The efficacy of propranolol in decreasing the size of hemangiomas was discovered by chance and published for the first time by some authors in 2008[3]. They published a case of a child with a nasal capillary hemangioma. Despite corticosteroid treatment, the lesion was stabilized but obstructive hypertrophic myocardiopathy developed, so the patient was treated with propranolol. The hemangioma changed from intense red to purple, and it softened. The corticosteroids were tapered, but the hemangioma continued to improve. When the corticosteroids were discontinued, no regrowth of the hemangioma was noted.

After this first report, other cases have been published[4,5], the greatest series with 30 and 32 patients[4-9].

Potential explanations for the therapeutic effect of propranolol - a nonselective beta-blocker - on infantile capillary hemangiomas include vasoconstriction, which is immediately visible as a change in color, associated with a palpable softening of the hemangioma; decreased expression of VEGF and bFGF genes through the downregulation of the RAF-mitogen-activated protein kinase pathway (which explains the progressive improvement of the hemangioma); and the triggering of apoptosis of capillary endothelial cells[10].

Side effects of beta-blockers are well known. Propranolol can cause transient hypoglycemia, bradycardia, and hypotension and may predispose patients to hypoglycemia. Bronchospasm is usually seen as an exacerbation in patients with underlying reactive airways. These risks can be managed. Frequent pediatric follow-ups during therapy are important.

We did not follow any specific protocol for treatment, because at the time we treated this first baby there were no protocols. Some authors suggest a detailed protocol at their study[9].

In this present case, oral propranolol was very successful in rapidly decreasing the size of the tumor and avoiding severe amblyopia, during the most important period of the visual development, with no side effects.

We add this Brazilian case to the few published by other colleagues and agree that propranolol is highly promising as an alternative pharmacologic agent, and may emerge as the preferred treatment for facial infantile hemangiomas.

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