

CASO CLÍNICO



Propranolol treatment for hemangioma of infancy *

Hemangioma infantil tratado com propranolol

Flavia Kakiuti Bonini¹
Elemir Macedo Souza²

Fernanda Silva Bellodi¹

Resumo: Infante hemangioma or hamangioma of infancy is the most common tumor in children, with great variability of presentation. Most cases resolve spontaneously and treatment is usually indicated for specific cases where injury has a high rate of morbidity or disfigurement after regression. The treatment is based on the use of systemic corticosteroids, which can also be used topically or by intralesional injections. Propranolol has been used recently as a new therapeutic option for the treatment of hemangiomas, with satisfactory, permanent results and fewer adverse effects than corticosteroids. This is a report of the case where a child presenting extensive periorbital and frontoparietal hemangioma was treated with propranolol.

Keywords: Adrenal cortex hormones; Hemangioma; Orbit; Propranolol

Abstract: O hemangioma infantil é o tumor mais comum da infância, com grande variabilidade de apresentação clínica. A maioria das lesões regride espontaneamente e o tratamento está indicado para casos específicos que possam gerar ulceração, disfunção ou desfiguração. O tratamento baseia-se, principalmente, no uso de corticosteroides, seja por via sistêmica, tópica ou intralesional. Recentemente, o propranolol foi descrito como nova opção terapêutica para os hemangiomas, com resultados satisfatórios, permanentes e menos efeitos indesejáveis que os corticosteroides. É relatado o caso de uma criança com hemangioma periorbital e frontoparietal extenso, tratado com propranolol.

Palavras-chave: Corticosteroides; Hemangioma; Órbita; Propranolol

INTRODUCTION

Infantile hemangioma or hemangioma of infancy is the most common benign soft parts tumor in childhood, affecting 1 to 2% of neonates and 10 to 12% of children up to the first year of life. It is more frequent in the female sex and in prematures. The risk of hemangiomas is greater in children whose mothers were subjected to chorionic villus sampling during pregnancy.^{1,2}

Most commonly hemangiomas go through a growth period (proliferative phase), a stability phase (plateau) and a spontaneous regression phase (involution). It is estimated that complete involution of infantile hemangiomas occurs at a rate of 10% a year, so that 30% would involute up to 3 years of age, 50% up to 5 years of age, 70% up to 7 years of age and over 90% between 9 and 10 years of age.²

The pathogenesis of infantile hemangioma is unknown. It is speculated that invasive angioblasts, differentiated by a type of placental cells, or embolized placental cells may originate the vascular tumor.³

Special clinical presentations are rare. Among them, the most relevant are hemangiomatosis (presence of multiple cutaneous hemangiomas, with or without visceral involvement), PHACE syndrome (malformations of the Posterior cerebral fossa, large Hemangioma on the face, Arterial anomalies, cardiac anomalies, aorta Coarctation and Eye abnormalities), spine dysraphism (hemangiomas in the spine region) and Kasabach-Merritt phenomenon (vascular neoplasia associated with thrombocytopenic coagulopathy).¹

The diagnosis is clinical, supported by disease

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¹ Residente de dermatologia da Universidade Estadual de Campinas (UNICAMP) – Campinas (SP), Brasil.

² Doutor em Dermatologia - Professor associado livre docente da Universidade Estadual de Campinas (UNICAMP) – Campinas (SP), Brasil.

history. Doppler ultrasonography, magnetic resonance, computerized tomography and angiography may be used to evaluate the extension of involvement, differential diagnosis and follow-up of response to treatment. Differential diagnosis takes into account port-wine stains or salmon patches, vascular malformations and other infant skin tumors, such as congenital hemangioma, lobular capillary hemangioma and kaposiform hemangioendothelioma.¹

Involvement of the orbit or the eyelid region may determine ocular alterations such as astigmatism, amblyopia and ptosis.^{4,5}

An expectant conduct is recommended in most cases, since there are high rates of spontaneous involution. The lesions affecting the periorbital area, mid-face region, airways, cutaneous folds, anogenital areas and regions at risk for ulceration, dysfunction or disfigurement require treatment.^{6,7} An attempt is also made to prevent or reverse complications that threaten organ life or function.⁸ Lesion size and location, age of the patient, hemangioma growth phase and psychosocial implications to the patient and parents should be considered.

CASE REPORT

A 1-year and 2 months old female child has had a left hemifacial hemangioma that progressively increased in size since she was 3 weeks old (Figure 1). At the initial evaluation, the hemangioma predominantly affected the left frontoparietal and periorbital regions, with partial occlusion of the ipsilateral eye. Smaller lesions could be observed on the front and tip of nose, lip philtrum and back of neck. The child had not been subjected to any prior treatment. The ophthalmological evaluation ruled out structural and functional impairment of left eye and there was merely a recommendation to follow-up (Figure 2).

The patient was hospitalized to begin treatment with propranolol, under monitoring of vital signs.



FIGURE 1: Pretreatment – evaluation at outpatient clinic

Before starting drug administration, abdomen ultrasound, echocardiography, electrocardiogram and computerized cranial angiotomography were carried out, with normal results.

Propranolol administration was started with 0.5mg/kg/day, divided into 3 daily doses. As the child did not present the undesired side effects of the drug, dosage was increased to 1mg/kg/day on the second day and 2mg/kg/day on the third day. She was released from hospital on the fifth day after drug administration was begun, maintaining the 2mg/kg/day dosage (Figure 3).

She was evaluated at the outpatient clinic on the 9th, 18th and 32nd days after the beginning of treatment. During the very first days, the lesion became more deeply wine-colored, with less evident relief and greater ocular opening. The medication was maintained, as well as periodical evaluations of the child at the outpatient clinic (Figure 4).

DISCUSSION

Systemic corticoids, long considered as the therapy of choice for hemangioma of infancy, have hard to control insidious adverse effects, besides variable response.⁹ The use of alpha-interferon is described in the literature with good results, although with the inconvenience of being a prolonged intravenous treatment that has significant adverse effects.¹⁰

Interventionist treatments, such as corticosteroid injections, laser, embolization and surgery may involve risk to the orbital region, like damage to the optic nerve and extraocular muscles.⁴

Propranolol is a new alternative treatment for specific cases of infantile hemangioma.^{4,11,12} It has been used for several decades in the treatment of hypertension, cardiac failure and arrhythmias. It is a nonselective betablocker that antagonizes beta1 and beta2 receptors, causing bradycardia, hypotension and hypoglycemia.^{9,12} Its mechanism of action in heman-



FIGURE 2: Pretreatment – 1st day of hospitalization



FIGURE 3: 9th day of treatment



FIGURE 4: 18th day of treatment

gioma is not well understood. It is speculated that propranolol acts by diminishing the expression of the vascular endothelial growth factor (VEGF) and of the basic fibroblast growth factor (bFGF), triggering endothelial cell apoptosis.¹² Its use not only hinders tumor growth but promotes decrease of lesion volume in a more regular manner than corticoids.⁹ Since there are no randomized and controlled studies defining the ideal drug dosage for children, its safety and effectiveness still have not been established by FDA for use in hemangiomas.¹²

When there is coexistence of cerebral vascular anomalies and insufficient collateral blood supply, propranolol may lead to cerebral infarction due to hypotension. Large lesions or hemangiomatosis may be the cause of high-output cardiac failure, which is worsened by the drug. Ultrasonography of the abdomen, ecocardiography and cranial angiotomography should be used to prevent these complications.⁷ Heart rate, blood pressure, capillary glycemia and electrocardiogram should be evaluated before and

during treatment. The dosage of 2 mg/kg/day should be gradually introduced, starting with 0.17 mg/kg every 8 hours and gradually increasing up to a 0.67 mg/kg/dose, equivalent to 2mg/kg/day. A lower dosage is recommended for children younger than 3 months of age, due to the increased risk of hypoglycemia.⁷

Clinical presentation and natural history of hemangiomas are variable. An expectant conduct is acceptable in the less serious cases; however, intervention is needed when there is significant esthetic or functional compromise. Propranolol has recently been described as a new therapeutic option and an alternative to previously used treatments. Experience has shown good outcomes, in the few cases described, regarding lesion evolution, with few adverse effects connected with the medication. The case described presented progression similar to that observed in other services. Complementary studies are necessary to understand the true role of propranolol in the physiopathology and treatment of hemangiomas of infancy (Figure 5). □



FIGURA 5: Comparative progression chart: A. Pretreatment. B. Third day of treatment. C. Ninth day of treatment. D. Thirty-second day of treatment

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MAILING ADDRESS / ENDEREÇO PARA CORRESPONDÊNCIA:
Flavia Kakiuti Bonini
Rua Dr. Miranda de Azevedo, 1085 - Apto 161.
05027-000 Perdizes – São Paulo – SP, Brazil
E-mail: flabonini@gmail.com

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