Hemangioma parotídeo tratado con propranolol: a propósito de un caso

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Resumen

Los hemangiomas parotídeos son los tumores salivares más frecuentes en la infancia. Debido al rápido y expansivo crecimiento característico de estas lesiones, pueden aparecer complicaciones significativas como pérdida de función del órgano o desfiguración permanente. En estos casos la intervención terapéutica precoz podría ser decisiva para minimizar efectos indeseables. El propranolol está considerado, actualmente, como el fármaco de primera elección en el tratamiento de los hemangiomas infantiles complicados, en múltiples localizaciones, presentando un adecuado perfil de seguridad así como una excelente eficacia. Se presenta el caso de una lactante de 45 días de vida diagnosticada de hemangioma de parótida derecha y que fue sometida a tratamiento con propranolol; a propósito de este caso se realiza una breve revisión del abordaje de esta patología.

Palabras clave: Hemangioma infantil, parótida, propranolol.

Abstract

Title: Parotid hemangioma treated with propranolol: a case report

Parotid hemangiomas are the most common salivary tumors of childhood. Due to the rapid and expansive growth, typical of these lesions, significant complications such as loss of organ function or permanent disfigurement may be present. In these cases, early therapeutic intervention can be crucial to minimize these undesirable effects. Propranolol is currently considered the drug of choice in the treatment of complicated infantile hemangiomas in various locations, with a good safety profile combined with excellent efficiency. We present the case of an infant girl, 45 days old, diagnosed with hemangioma of the right parotid and treated with propranolol; in this regard, we present a brief review of the management of this disease.

Keywords: Infantile hemangioma, parotid, propranolol.

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Introduction

Salivary gland tumors are rare in children, with the parotid gland being the most affected. Of these, hemangiomas are the most common, accounting for about 50% of parotid tumors in this age group.[1] As hemangiomas of other locations, they have a typical growth pattern: often not evident at birth, they quickly become visible with a first rapid growth phase between 1-2 months, followed by a second peak of growth between 4-6 months. Over the next decade there is a phase of slow involution, with replacement by fibrofatty tissue.[2] The parotid hemangiomas are classified, according to their distribution, in isolated or focal and segmental. The origin of this disease appears to be an imbalance of positive and negative regulators of angiogenesis in association with the expression of vascular endothelial growth factor and basic fibroblast growth factor.[1]

In the presence of a rapidly growing mass in pre-auricular region, the diagnosis of parotid hemangioma should be evoked, which can be confirmed by performing a magnetic resonance imaging (MRI); other examinations are rarely needed. Currently, in addition to the conservative approach (expectant), acceptable in patients with small, slow growing, not complicated lesions, there are various therapeutic modalities.

The authors describe a case of a focal parotid hemangioma in a small infant who underwent medical treatment with propranolol, making a brief review of the literature on this topic.

Case report

Female infant with forty-five days of life, with irrelevant prenatal and neonatal history, referred to consultation because of a progressive swelling on the right preauricular region, with three days of evolution, in association with two erythematous macules on the overlying skin. No associated symptoms were reported. There was no context of disease in the family; the existence of a cat at home was mentioned.

On physical examination, the infant appeared well and had adequate growth. She showed a poor-defined, pre-auricular swelling of soft consistency on the right, apparently painless and without inflammatory signs (figure 1). She also presented two erythematous macules, less than 5 mm, which did not disappear with pressure, on the overlying skin of the swelling. The remaining examination was normal.
Analytical study including blood count, blood smear, inflammatory markers and biochemistry panel revealed no significant changes.

The blood culture showed no bacterial growth and virological exam of nasopharyngeal secretions was negative. Serologies for epidemic mumps virus and *Bartonella henselae* did not suggest acute infections by these agents; polymerase chain reaction (PCR) in blood for detection of cytomegalovirus and Epstein-Barr virus were both negative.

The ultrasound of the parotid region on the 54th day (D54) of life, showed a multilobulated and solid nodule, with 15 per 7 mm in the inferior third of the right parotid gland, but it was not conclusive as to its origin.

In order to better clarify the etiology of this lesion, an MRI was done on D97 of life, which identified, in the right parotid region, a mass (43 x 21 mm in the axial plane and 42 mm in maximum craniocaudal dimension), solid, lobulated, hyperintense on T2 (not as much as subcutaneous fat) and hypointense on T1. This mass was relatively well-defined and not invading the adjacent structures neither the deep lobe of the parotid (figure 2).[5]
Thus, according to the clinical data and imaging findings it was considered the diagnosis of hemangioma of the parotid.

Given the significant growth of the injury, we started treatment with oral propranolol (2 mg/kg/day) on D99 of life after obtaining a normal cardiovascular examination (including electrocardiogram and echocardiogram), by a Pediatric Cardiologist. The treatment was initiated in an inpatient regimen within the first 24 hours, without any side effects.

The infant was discharged home on oral propranolol with periodic adjustments of therapy according to her weight.

Before completing two months of treatment, a significant reduction of the parotid swelling associated with attenuation of the cutaneous hemangiomas was noted, which continued over time –at the age of seven months it was no longer possible to palpate any swelling in the pre-auricular region. Likewise, the echographic control showed a progressive reduction of the lesion which, at 5 months of age, showed a maximum dimension of 3 cm, 2 cm at 9 months, 1.2 cm at 14 months, with complete regression by the age of 17 months.

At that time, we started reducing propranolol, which was suspended within 4 weeks. No adverse side effect was noted during treatment.
In the follow-up of this child until 2 years of age, there was no reappearance of the lesions. The cutaneous hemangiomas also suffered almost complete involution, so the final cosmetic result was extremely good (figure 3).

Discussion

Diseases of salivary glands, although rare in children, can be important causes of morbidity and even mortality in this age group.

Inflammatory and/or infectious diseases (acute or chronic) account for most cases, but tumoral disease (vascular or solid) remain an important etiology to consider.[2]

Infantile hemangiomas are the most common vascular tumors of the salivary glands, and the parotid gland is involved in 80% of the cases.[2]

Children with parotid hemangiomas typically exhibit an asymptomatic facial asymmetry by the appearance of a floating mass, soft or elastic, on the cheek. Concurrently, there may be associated cutaneous vascular macules suggesting the etiology.

The diagnosis is usually based on the clinical history and detailed physical examination. If necessary, imaging methods (especially MRI with characteristic lesional features such as presence of a lobulated, homogeneous, high-flow lesion, with the same signal strength of the muscle at T1 and hyperintense at T2, with or without fat saturation) can confirm the diagnosis.[1,3] A biopsy is rarely necessary, except when the diagnostic is uncertain or there is an atypical evolution.

Most infantile hemangiomas regress spontaneously: of the affected children, 90% present complete involution at 9 years old.[2]

However, in some situations, it will be necessary to intervene therapeutically, especially when there is risk of airway obstruction, periocular or periauricular location, presence of complications (heart failure, ulceration) or in case of a lesion with the potential to cause permanent disfigurement.

Until recently, treatment of hemangiomas of the parotid was a significant challenge not only by the expansive growth of the lesion and its anatomical relationship with the facial nerve (providing greater surgical risk) but also by the resistance to available treatments (with significant side effects).

Propranolol (a non-selective beta-blocker) has been described since 2008[4] as an effective treatment for treating infantile hemangiomas and is currently considered first-line treatment of complicated hemangiomas, particularly of the head and neck.[5,6] Propranolol appears to act by vasoconstriction of endothelial cells, angiogenesis inhibition and induction of apoptosis.[7] The most common side effects of propranolol are bradycardia, hypotension, and hypoglycemia. However, the occurrence of these side effects in children without risk factors (excluded through a detailed personal and family history and complete physical examination [table 1]) is extremely low.[8-11]

Thus, latest international guidelines don't recommend universal pre-treatment cardiac exams or initiation of treatment in an inpatient regimen in children with no risk factors. The latter can be substituted by heart rate and blood pressure monitoring during 2-3 hours on an outpatient basis, at the beginning of therapy and whenever is necessary to significantly increase the drug dose (>0.5 mg/kg/day).[8,9,11] There is no absolute agreement on the dose to be administered but it usually begins at 0.5-1 mg/kg/day with gradually increases to a target dose of 2-3 mg/kg/day, divided into 3 daily doses.[9,11] Duration of treatment is variable, on average up to 12-14 months old.[7,9,11] It is always recommended a 2-4 weeks weaning period to prevent reflex tachycardia associated with abrupt withdrawal of the drug.[7,9,11]

When there is no good therapeutic response, other treatments may be considered as systemic or intralesional corticosteroids, endovascular sclerotherapy with bleomycin or even surgical resection with or without nervous mapping.[1] Treatment with pulsed dye laser of 595nm could act as adjuvant to treat associated skin lesions. However, it does not show enough penetration power to treat deeper lesions as those located in the parotid.[1]

The initial presentation of this case concerning a small infant presenting a lesion with short evolution time in which vascular skin lesions were hardly visible, led to the exclusion of other causes of parotid swelling in particular infectious and neoplastic.

After their exclusion, the use of MRI clarified this situation by identifying a parotid lesion with benign characteristics, compatible with a parotid hemangioma, thus making it unnecessary to perform a lesional biopsy.

Due to the progressive nature of the injury and its location, there was foreseeable risk of loss/change in organ function (salivary parotid gland) and potential risk of disfigurement (facial location) so it has become imperative to intervene therapeutically, being propranolol the chosen drug for the reasons previously stated.
The total duration of treatment was 15 months (starting at 3 and ending at 18 months, including weaning). The decision to extend the treatment was sustained in clinical and echographic evolution of the injury, which demonstrated the full involution of the parotid hemangioma at 17 months. As the segmental hemangiomas, large hemangiomas or those with facial location appear to have a longer growth phase; consequently, an early discontinuation of therapy may result in short-term relapse, requiring re-treatment.[3]

Thus, we consider that serial ultrasound could play a valuable role in the decision to stop pharmacological treatment, as suggested by other authors.[5] In our case, there were no significant side effects attributable to treatment with propranolol, confirming the safety profile of this drug. Finally, we stress the efficacy of propranolol in the treatment of infantile hemangiomas in this particular case of parotid location.[9]

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TABLE 1

Risk factors for treatment with propranolol justifying prior cardiac evaluation	
Electrocardiogram	*Electrocardiogram and echocardiogram*
• Heart rate below normal for age • History of arrhythmia or arrhythmia objectified on examination • Family history of congenital heart disease or arrhythmia, or maternal history of conectivite	• Patients with history, symptoms or signs of heart disease, including suspected high output heart failure • Patients with large segmental hemangiomas of the face or neck and suspected PHACE syndrome

PHACE: Posterior fossa, Hemangioma, Arterial lesions, Cardiac abnormalities, Eye abnormalities. Adapted from Solman et al.[9], Drolet et al.[11]

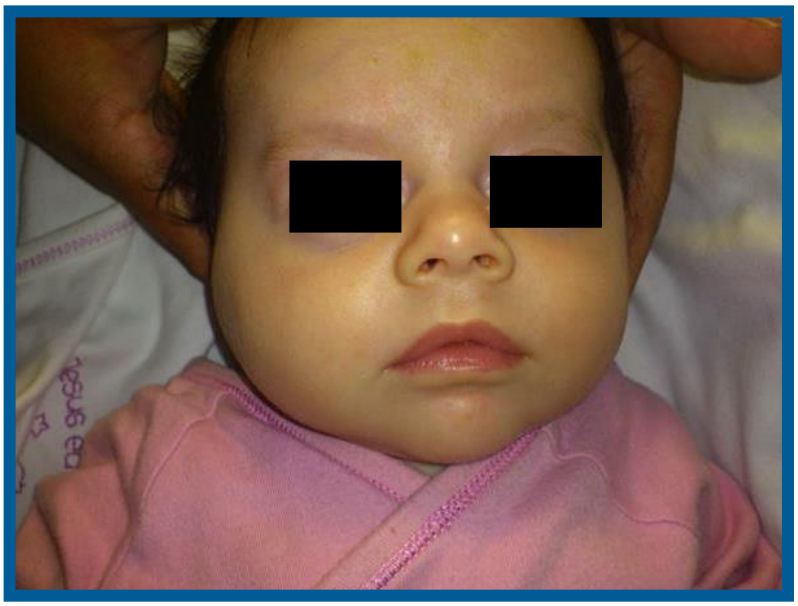

Figure 1. Focal hemangioma before onset of treatment

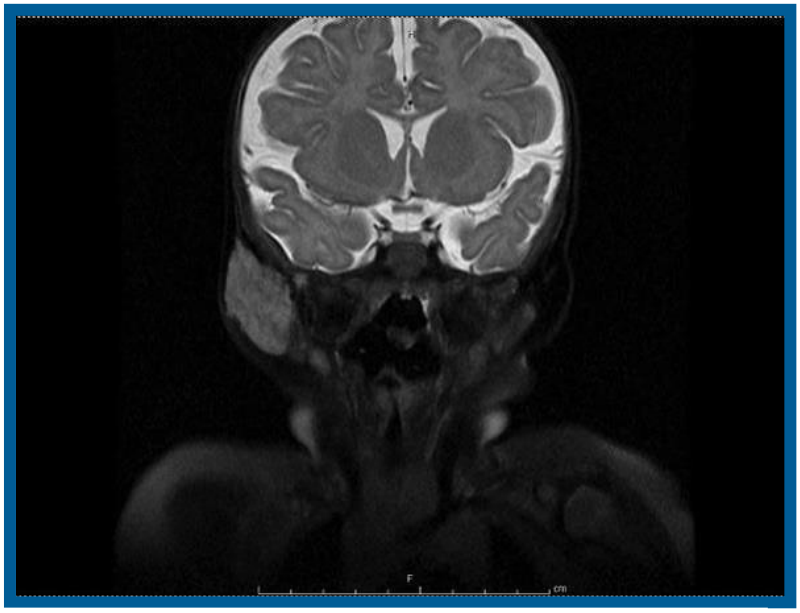

Figure 2. MRI of the parotid - coronal section (T2 with fat suppression), demonstrating focal hemangioma of the right parotid

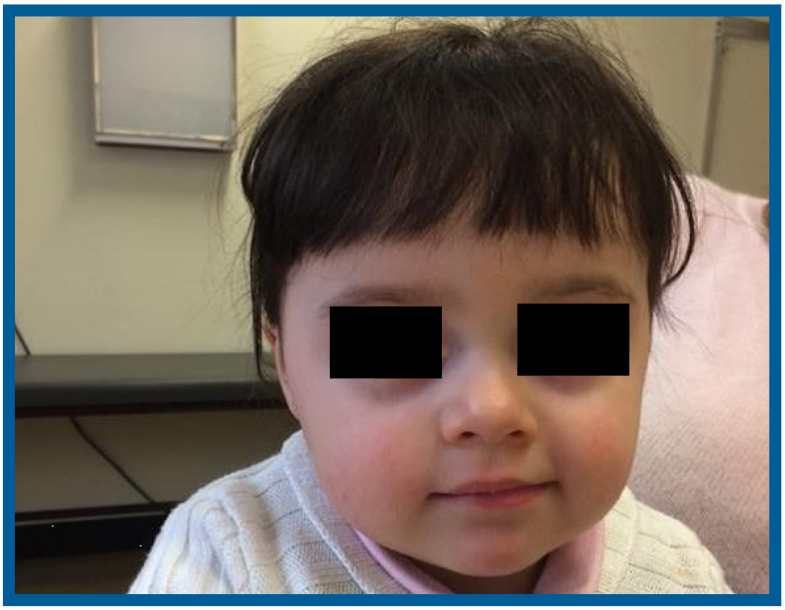

Figure 3. Final clinical/cosmetic result (after treatment)

