Case Report

Infantile Hemangioma in a V2 Distribution: Treatment with Nadolol

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Abstract

Infantile hemangiomas are common benign tumours of infancy affecting up to 10% of children. They are typically not present at birth but undergo a rapid proliferation stage and then plateau in growth before resolving spontaneously. Recently, beta-blockers have been favoured over systemic corticosteroids for treatment of disfiguring or life-threatening infantile hemangiomas. We present a case of an 11-week-old female with a 7 week history of an evolving hemangioma along a facial V2 distribution. Physical exam revealed a well-defined bright red plaque over the right zygoma and lower eyelid. MRI, echocardiograph, and liver ultrasound were normal. Patient was treated with nadolol and had a rapid and substantial regression of the hemangioma. Nadolol is an effective treatment option for disfiguring facial infantile hemangioma. The use of beta-blockers as treatment offers clues into the pathogenesis of infantile hemangioma, which is not yet completely understood

Keywords: Beta-Blockers, hemangioma, pediatric

Introduction

Infantile hemangiomas (IH) are benign tumors in the pediatric population with an incidence of up to 10%.[1] They are usually not present at birth but undergo a rapid proliferation within the first weeks of life.[2] This is followed by the plateau stage and then a slow involution of the lesion such that 60% of 4-year-olds and 76% of 7-year- olds will experience complete regression of their hemangiomas.[1] A subset of IH that could be considered high risk and might require treatment would include multiple IH, ocular involvement, oropharyngeal and airway involvement, large or disfiguring lesions, and ulcerated hemangiomas.

For high risk IH, corticosteroids have traditionally been the mainstay of treatment with variable response and significant side effects including hypertension, increased risk of infection, cushingoid appearance, and growth suppression.[1] Since 2008, propranolol has become a favored first line treatment for IH. Propranolol shows good efficacy, rapid improvement in the lesion and fewer severe adverse events compared to corticosteroids.[3] Nadolol is a beta-blocker that has similar mechanism of action as propanolol, but has less central nervous system penetration and is dosed twice rather than three times per day.

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Case Report

An 11-week-old healthy baby girl presented to the dermatologist with a well-defined red plaque over her right face that had been getting progressively more visible over the last 7 weeks [Figure 1]. The baby's parents had noticed a whitish-red mark over the patient's cheek in the hours after her birth, which they attributed to trauma from vaginal delivery. The lesion developed a bruised appearance over the next 2 weeks, and then grew more noticeably red, well defined and thickened.

Physical exam revealed a well-defined 7 × 3 cm, soft, warm red plaque following a V2 distribution on the right side of the patient's face affecting the right temple, zygoma, malar cheek and lower eyelid, compatible with an IH. Due to concern over the facial V2 distribution, PHACES syndrome, which can be associated with segmental IH, was ruled out. Ophthalmology exam, EKG, abdominal ultrasound, echocardiogram, and MRI of head were all normal. PHACES refers to posterior fossa malformations, hemangiomas, arterial anomalies cardiac defects, eye abnormalities, sternal cleft and supraumbilical raphe syndrome.

The patient was started on nadolol at 0.5 mg per kg, adding

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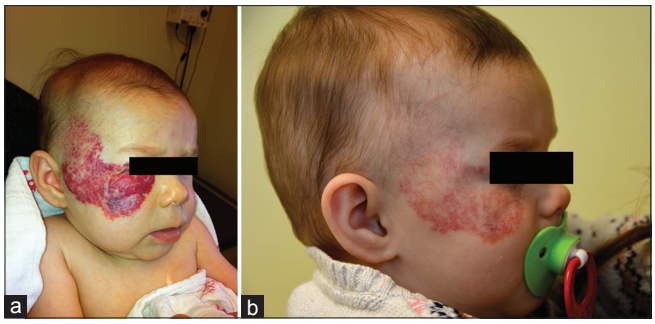

Figure 1: (a) Patient at 11 weeks of age, before receiving nadolol treatment. (b) Patient at 21 weeks of age, after 10 weeks of treatment

0.5 mg per kg each week until the 4th week where a maintenance dose of 2 mg per kg was reached. Pulse, blood pressure and glucose were monitored while the dose was titrated upward. The parents reported no side effects from nadolol. Within 3 weeks there was marked decrease in the redness, vascularity, and elevation of the hemangioma, including over the lower eyelid [Figure 1]. Ongoing improvement in the appearance of the hemangioma on nadolol was noted at age 22 weeks, with a plan to continue therapy until age 1 and then titrate slowly off the medication.

Discussion

Many recent studies have shown propranolol to be highly effective in treating high-risk or disfiguring IH.[4] Potential advantages of nadolol over propranolol include its inability to cross the blood–brain barrier, which may lead to decreased sleep disturbance and irritability, and a longer half-life with dosing twice a day. A small cohort-blinded study showed that nadolol might be somewhat more effective as a treatment for IH than propranolol.[5] Typically, few side effects are reported in patients receiving beta-blockers for IH. Blood pressure, heart rate, and serum glucose should be monitored in infants receiving beta-blockers. Sweating, shakiness, tachycardia, hypotonia, and hunger are early signs of hypoglycemia in infants.[6] Asthma is a contraindication for beta-blocker treatment.[3]

Beta-blockers are theorized to have several potential mechanisms of action on IH. Beta-blockers produce an immediate vasoconstrictive effect due to inhibition of adrenaline-mediated vasodilation.[1] This leads to decreased erythema and softening of the hemangioma within a few treatments. During the proliferative stage of IH, beta-blockers are thought to decrease the expression of vascular endothelial growth factor (VEGF), thereby opposing aberrant angiogenesis.[7] Beta-blockers have been also theorized to decrease inhibition of apoptotic pathways in IH, which may hasten tumor involution.[7]

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