Use of Propranolol In Treatment of an Infantile Hemangioma Complicating Cleft Lip Repair

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Introduction
Infantile hemangiomas and cleft lips are relatively common lesions of infancy. Hemangiomas are found in one in twenty-five newborns while cleft lips occur with an incidence of one in 700 Caucasians.1,2 Roughly 60% of the infantile hemangiomas occur in the head and neck region. A 6-month-old African American female presented with right cleft lip complicated by an infantile hemangioma.

Case Report
A 6-month-old African American female presented with right cleft lip complicated by an infantile hemangioma located in the left maxilla lateral to the alar sidewall (Figure 1). The patient was initially evaluated at birth for her cleft lip, and a nasal alar base mold device was placed to aid in the correction of her cleft defect.

Around six weeks of age, the mother noticed what she thought to be a scratch on the left side of the face. This area quickly progressed to a 2x2 cm cherry red hemangioma. The patient was otherwise healthy and a computed tomography study illustrated the extent of the concomitant craniofacial abnormalities that are compromised by hemangiomas.

The patient’s right complete cleft lip was repaired using the Millard advancement rotational flap technique in 2008, the use of propranolol to treat infantile hemangiomas was discovered by Laeute-Lebèze C, et al. We report the use of propranolol to accelerate the involution of a hemangioma complicating the repair of a unilateral cleft lip in a 6-month-old girl.

At 8 months of age the patient returned for cleft lip repair. It was noted at that time that the patient’s cleft lip was repaired using the Millard advancement rotational flap technique (Figure 4). The patient’s post-operative course was uncomplicated except for a two-week period of the day after the procedure due to concerns over wound mobilization and removal of the dressings. The patient returned two weeks after the operation for removal of her sutures. At that time her repair appeared to be healing well and a subjective reduction in the size of her hemangioma was also noted. The patient was continued on her propranolol regimen until 12 months of age.

While all three above cases had their cleft lips successfully repaired, we wished to avoid any unnecessary incision or scarring that might occur with the previous traditional methods to remove hemangiomas. Additionally, significant bleeding from these vascular tumors upon excision was a major concern in the previously reported cases. Therefore, we considered other methods, including consultation of our radiology department for possible embolization of the growth feeding vessels. However, the relatively recent discovery of propranolol’s efficacy in treatment of infantile hemangiomas gave us a medical alternative, and we proceeded with a two-month pre-operative course of propranolol to 2mg/kg/day. Although the recommended duration for propranolol is at least 12 months or until full involution of the hemangioma, we reasoned that the drug would prevent further growth in addition to the hope of some size reduction in the time prior to surgery.

When the patient arrived at the hospital for her cleft lip correction, the hemangioma appeared to have decreased in size and in redness. The medial deviation of the septum and left ala was less noticeable. Unfortunately, no objective or quantitative measurements were taken to evaluate the changes in the tumor, but the reduction was significant enough for us to feel comfortable proceeding with repair of the patient’s cleft lip. The patient’s cleft lip repair was completed without any complications. There was some concern for the cardiac side effects of propranolol in the intraoperative and postoperative period, as the dose we used has been shown to affect the heart rate and blood pressure, but no adverse events occurred.

Conclusions
We report the use of propranolol to treat an infantile hemangioma that was located on the maxilla and complicating the repair of a unilateral cleft lip. The primary complications and risks of this kind of surgery include potential facial deformities and need for repair of cleft lip repair. We believe that propranolol is a safe and effective drug to use on children with these tumors. Propranolol can be safely employed in children at a very young age if proper initiation and monitoring are followed. Furthermore, the use of this new medication can facilitate a more timely and proper correction of cleft lips and other craniofacial abnormalities that previously would have been difficult with the coexisting hemangioma.

References

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Abstract
CASE DESCRIPTION: A 6-month-old female presented with right complete cleft lip and infantile hemangioma of the left maxilla. The immediate repair of the cleft defect was delayed as the hemangioma was causing significant distortion of the ala and the nasal tip. The child was started on oral propranolol according to protocol at our institution. Two months later, the hemangioma had decreased in size and it was deemed safe to proceed with the repair of the patient’s cleft lip. The patient’s cleft was repaired using the Millard advancement rotational flap technique and concurrent cleft miniplasty. She was continued on propranolol until full involution of her hemangioma.

DISCUSSION: This case illustrates the decision making process to delay the surgical repair of a unilateral complete cleft lip until the partial involution of a facial hemangioma being treated with propranolol. Propranolol can be safely employed to facilitate proper correction of cleft lip and other craniofacial abnormalities that are compromised by hemangiomas.

Discussion
Infantile hemangiomas are the most common tumor of infancy with 80% occurring in the head and neck.3 The true incidence is unknown, but the best estimate is thought to be around 4-5%.1 Hemangiomas are clonal proliferation of endothelial cells from the process of vasculogenesis, which is characterized by formation of blood vessels from angioblasts and not from pre-existing vessels as in angiogenesis.4 These tumors progress through a proliferation phase, an involution phase, and often to complete involution. Rapid proliferation typically occurs until around 4 months when the tumor reaches its most rapid growth. This usually is followed by a slower proliferation phase that can last until up to 24 months for large lesions. Only around 10% require intervention of any kind as their natural involution occurs at about 10% per year. Treatment indications include ulceration, bleeding, impairment of breathing, eating, voiding, or stooling, impairment of vision or hearing, high-output cardiac failure, and impending poor cosmetic outcome.3

Many different methods have been attempted in the treatment of hemangiomas in the past. Surgical excision, laser therapy, sclerotherapy, embolization, radiotherapy, interferon, hydrocortisone, and even tattooing have been used in the past,2 but oral and intraregional corticosteroids seemed to be the main medical therapy employed prior to the discovery of propranolol’s utility by Laeute-Lebèze et al in 2008.2,4 An additional study revealed that systemic corticosteroids appear to have similar efficacy at accelerating involution of hemangiomas but come with a more significant side effect therefore favoring propranolol use.2 With the relatively recent advent of propranolol therapy, there still exists some uncertainty and disagreement as to the proper treatment protocol when using propranolol for infantile hemangiomas. A report on a consensus conference was published in Pediatrics in 2013 that provides a detailed description on when to use and how to initiate propranolol in the treatment of infantile hemangiomas.4 A Phase IIIb Investigational New Drug application (ClinicalTrials.gov NCT1066341) has recently been completed and approved by the FDA for use in IH.

The co-occurrence of a cleft lip and infantile hemangioma appears to be an extremely rare combination with only three reported cases in English literature to our knowledge.4 One patient was actually reported twice by separate authors.2,4 One of these case reports suggested an association with Wolf-Hirschhorn syndrome, but there is a unique report and lacks additional support.2 Wolf-Hirschorn syndrome is characterized by a deletion of the short arm of chromosome 4 and leads to craniofacial abnormalities, growth and mental retardation, congenital heart and renal anomalies, and hypoplastic or absent thymus. Afflicted babies are born with their face out of position, and Wolf-Hirschhorn syndrome is very rare, with one report noting that all 11 patients so far have been girls, ages 3 months and 4 years.2,4 All three cases underwent surgical correction of their cleft lip. One took 5 attempts at correcting the lip and took six months to complete.2,4 All three cases were treated with propranolol prior to repair of the cleft lip at 4-6 months of age.2,4 In the group of cases, the management of the hemangioma between attempts 2 and 3 varied. The hemangioma was treated with propranolol in the third instance.2,4 In the second instance, the patient had his cleft lip repair delayed in hopes that the hemangioma would involute, but ultimately it was excised concurrently with the repair.2,4 The third report had an immediate cleft correction with only partial resorption of the tumor over the lip.2,4

We report the use of propranolol to treat an infantile hemangioma that was located on the maxilla and complicating the repair of a unilateral cleft lip. The primary complications and risks of this kind of surgery include potential facial deformities and need for repair of cleft lip repair. We believe that propranolol is a safe and effective drug to use on children with these tumors. Propranolol can be safely employed in children at a very young age if proper initiation and monitoring are followed.2,4 Furthermore, the use of this new medication can facilitate a more timely and proper correction of cleft lips and other craniofacial abnormalities that previously would have been difficult with the coexisting hemangioma.

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Figure 1: Preoperative photo showing the right complete cleft lip with naseal base molding device in place, in combination with a left maxillary infantile hemangioma.

Figure 2: Axial CT scan showing the left maxillary IH.

Figure 3: Coronal CT scan showing the left maxillary IH.

Figure 4: Shown is the Millard advancement-rotational flap technique for repair of the cleft lip. Also shown is the improvement in the size of the IH.

Figure 5: Photo of our patient at 2.5 years of age. The hemangioma has completely resolved, and her right sided cleft lip repair has healed well.