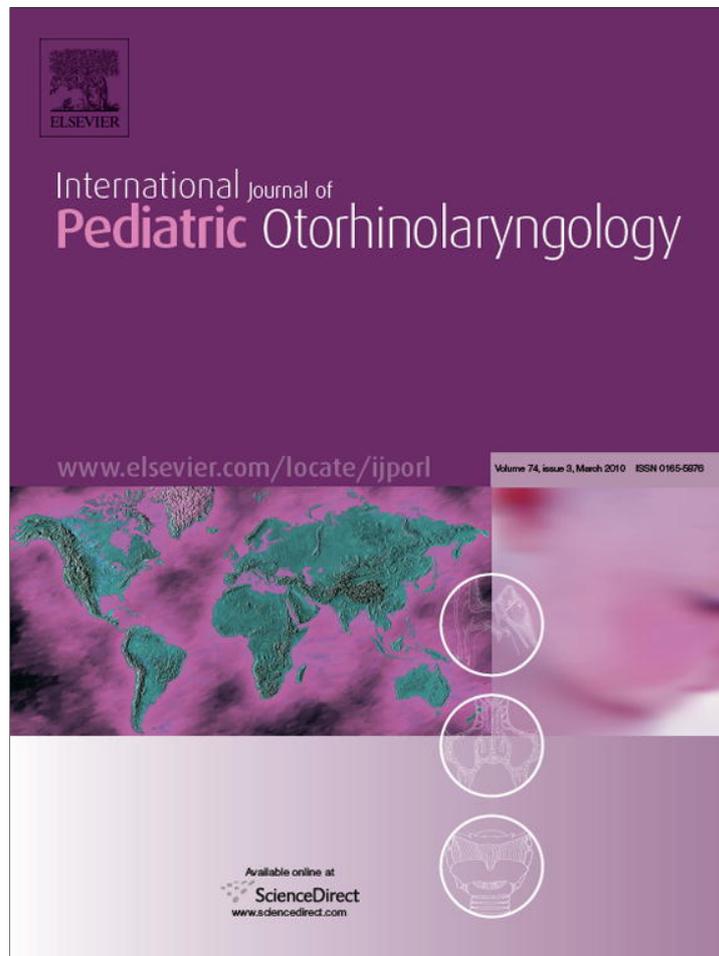


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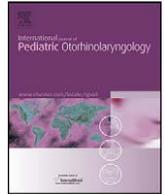
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Case report

Initial experience using propranolol as the sole treatment for infantile airway hemangiomas

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ABSTRACT

The objective of this study is to describe the initial use of propranolol as the sole treatment for focal infantile airway hemangiomas, and to report on available literature describing the use of propranolol for airway lesions. This retrospective case series was carried out at a tertiary pediatric medical center. We obtained the following results: two children demonstrated significant response to oral propranolol therapy and avoided not only invasive surgical procedures, but also long-term administration of oral corticosteroids. This is the first report of treating infantile airway hemangiomas with only propranolol without additional surgical intervention or corticosteroid use. Review of literature reveals initial case series with similar, successful results using propranolol as an adjuvant treatment along with other medications and surgical interventions. We conclude that the initial use of propranolol as the sole treatment for infantile airway hemangioma is promising. Literature review reveals that propranolol as the sole treatment for most head and neck hemangiomas shows significant promise based on early case reports. Further studies are needed to determine the long-term effectiveness, dosing strategies, and side effect profile of propranolol treatment for hemangiomas.

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1. Introduction

Infantile hemangiomas are the most common pediatric tumor occurring in approximately 1–2% of newborns, with a much higher rate in premature infants [1]. The natural course has been well documented with most becoming apparent within the first 2 months of life, undergoing a proliferative phase in the first year of life, and slowly involuting over the early childhood years. Frequently infantile hemangiomas involve the head and neck region and have a significant cosmetic component. More serious lesions involving the airway and orbit necessitate early intervention to avoid airway compromise and vision abnormalities.

Medical treatment of infantile airway hemangiomas has centered upon intralesional and oral steroids with interferon and vincristine being reserved for life threatening lesions [2]. Surgical treatment has included tracheotomy, laser excision, and open airway excision [3]. None of these treatments are without significant side effects. Long-term corticosteroid administration can result in growth suppression and other developmental and metabolic derangements. Furthermore, steroid treatment alone will result in the need for a tracheotomy in over one-third of

patients [2]. Infant tracheotomy has a well documented morbidity rate, laser excisions pose a significant risk for airway scarring, and open airway procedures require experienced surgeons with highly skilled intensivists post operative care [4–6].

Propranolol has recently been introduced as a treatment for infantile hemangiomas [7–11]. Initial case reports have demonstrated rapid response to oral propranolol in both skin and airway hemangiomas after primary medical and surgical treatment were unsuccessful [7–11]. No report though has specifically identified using propranolol as the initial and only treatment for airway hemangioma. In this paper we describe infantile hemangiomas involving the supraglottic and subglottic airway that were all treated solely with propranolol.

2. Report of cases

2.1. Case 1

A 3-month old, otherwise healthy infant female, presented with gradual onset of inspiratory stridor over a 2-week period. There were no feeding difficulties and no apneic or cyanotic episodes. Skin exam did not reveal any lesions and head and neck exam was normal except for a flexible nasopharyngoscopy which revealed a supraglottic mass suspicious for a hemangioma. Imaging to include an MRI of the neck revealed an isolated paraglottic mass consistent with a hemangioma. Ultrasound of the brain and abdomen did not reveal any other lesions.

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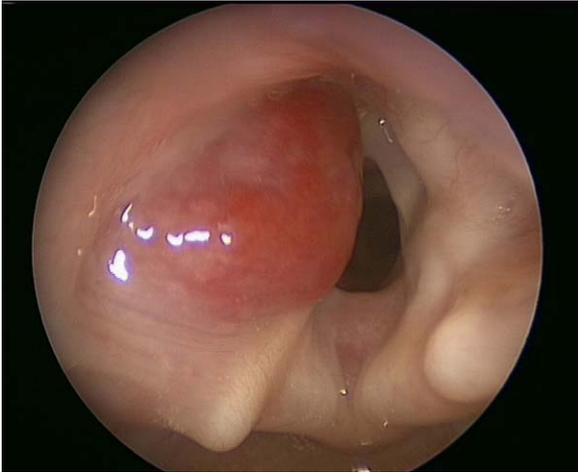


Fig. 1. Transglottic hemangioma as described in Case 1.

The infant was brought to the operating room where a direct laryngoscopy and bronchoscopy was carried out with the findings as shown in Fig. 1. The mass extended inferiorly to the subglottis, but an appropriate sized endotracheal tube could be placed. An intraoperative frozen biopsy was done which was consistent with an infantile hemangioma. Limited CO₂ laser was applied to the lesion to help control bleeding from the biopsy site. The infant was left intubated overnight, extubated the next morning, and started on propranolol which was gradually increased over 24 h to a dose of 2 mg/kg divided twice daily. Six-month follow up revealed the patient to be asymptomatic and repeat laryngoscopy demonstrated the findings in Fig. 2.

2.2. Case 2

A 5-month old, otherwise healthy female infant was referred for inspiratory stridor since birth. The stridor had been stable and there were no feeding difficulties. Head and neck examination was normal except for a nasopharyngoscopy which revealed fullness in the left subglottic region. CT scan of the neck with contrast revealed an isolated lesion consistent with a hemangioma while ultrasound of the head and abdomen were negative. The child underwent a direct laryngoscopy and bronchoscopy with the findings as shown in Fig. 3 where approximately 80% of the



Fig. 3. Right sided subglottic hemangioma as described in Case 2.

subglottic airway was obstructed. Given that the infant was in no acute distress she was started on propranolol the night of surgery and the dose was increased to 2 mg/kg divided twice daily within 48 h. Repeat laryngoscopy and bronchoscopy 1 week later resulted in the findings in Fig. 4 where well over 50% of the airway was patent. She was discharged home and repeat laryngoscopy/bronchoscopy 3 months later revealed a normal airway.

3. Literature review

Propranolol treatment for infantile hemangiomas has only recently been described [7–11]. Initial success was found fortuitously when a nasal hemangioma was noticed to decrease in size after propranolol treatment was started for obstructive cardiomyopathy [7]. Since this time there have been case reports describing successful treatment of infantile hemangiomas with propranolol as an adjuvant medication after other medical and surgical treatments have failed; successful treatment of laryngeal hemangiomas has not been shown with propranolol as a sole treatment agent [9–11]. Remarkable, rapid response with limited medication side effects has resulted in significant interest in using propranolol as a first line agent in infantile hemangioma

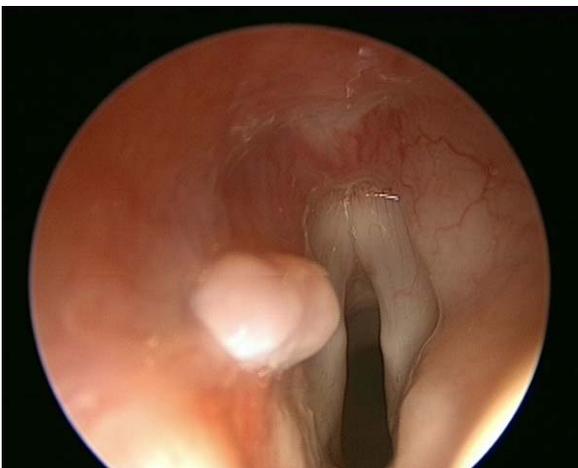


Fig. 2. Appearance of larynx after 6 months of treatment with propranolol as described in Case 1.



Fig. 4. 48 h after treatment with propranolol the size of the airway is markedly increased.

treatment. We have begun to use propranolol as a sole therapy for infantile hemangioma as we have been able to avoid corticosteroids and invasive airway procedures.

It is unknown how propranolol causes hemangioma regression. Theories include vasoconstriction, down regulation of growth factors, or cellular apoptosis [7,11]. The use of propranolol is not without its risks. Hypotension, bradycardia, and hypoglycemia are the more serious side effects, yet these side effects are usually seen in neonates in the first week of life and less commonly seen in otherwise healthy infants [8]. Given its nascent use in the treatment of infantile hemangiomas a standardized, universal protocol has yet to be determined for propranolol. Most reports have suggested obtaining a baseline electrocardiogram and initial hospitalization when first starting the medication [8,11]. Initial dose of 0.5–1 mg/kg is started and if well tolerated increased to a dose of 2–3 mg/kg divided bid to tid over 24–48 h. It is unknown how long the child should remain on propranolol, but currently we believe that the child should remain on propranolol usually for the first year of life until the proliferative phase is usually completed. Both of our patients continue to remain on propranolol as they have yet to reach their first birthday. Once the decision has been made to stop therapy it is likely best to carry out a gradual taper and monitor for any regrowth of the hemangioma.

We have an in depth discussion with the parents prior to starting the child on propranolol. We discuss options such as oral steroids, tracheotomy, endoscopic surgery, and open airway surgery as appropriate. We stress that although not specifically approved for infantile hemangioma treatment, propranolol has a well established safety profile in children. Initial administration of propranolol is done on an inpatient basis after consultation with pediatric cardiology and hematology and obtaining a separate, informed consent from the parents. Our admission protocol consists of a one night stay. An electrocardiogram is obtained prior to giving the first dose of 0.5 mg/kg. Blood pressure and heart rate are checked hourly for the first 4 h after administration. Routine glucose checks are not ordered unless the child has not established a routine feeding pattern. If patients tolerate the initial dose then the next dose is increased to 1.0 mg/kg. Patient is then monitored for 4 h, and if doing fine is discharged home on 2 mg/kg divided twice daily. We tell parents that the medication will likely be continued through their first birthday, and that the dose should be adjusted to changes in the child's weight. We also instruct the parents to check the child's pulse daily and we give them instructions on signs and symptoms of hypoglycemia.

4. Conclusion

There is a growing literature base that demonstrates the effectiveness of propranolol as a treatment for head and neck infantile hemangiomas. Initial success along with a low side effect profile is an exciting breakthrough for the treatment especially of infantile airway hemangiomas where many children suffer the untoward side effects of corticosteroids and the complications inherent in tracheotomy and multiple laser procedures. Airway hemangiomas are relatively rare so long-term prospective data may be difficult to gather, but as propranolol use becomes more widespread for cutaneous lesions, optimal dosing and any long-term side effects may be better elucidated.

Conflict of interest statement

Authors report no financial conflicts of interest relative to this article. There was no external funding associated with this report.

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