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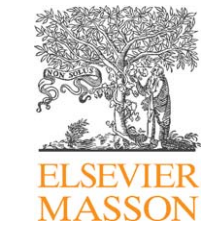

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UPDATE

Infantile haemangioma and β-blockers in otolaryngology☆

N. Leboulanger*, A. Cox, E.-N. Garabedian, F. Denoyelle

Service d'ORL et de chirurgie cervicofaciales pédiatriques, centre de références des malformations ORL rares, hôpital d'enfants Armand-Trousseau, AP—HP, université Paris VI—Pierre-et-Marie-Curie, 26, avenue du Dr-Arnold-Netter, 75012 Paris, France

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Summary Infantile haemangioma (IH) is the most common tumour during early childhood. Although these benign lesions resolve spontaneously, up until recently laryngotracheal sites of IH required invasive management. The dramatic efficacy of β-blockers on IH has radically changed the prognosis. Surgery is now no longer indicated as first-line therapy, but should only be performed for difficult, refractory cases, or in the presence of absolute contraindications to β-blockers. Long-term steroid therapy is also no longer indicated. Propranolol can be used as first-line, single-agent therapy.

Infantile haemangioma (IH), in all sites, is the most common tumour in children. Despite its benign nature and its spontaneously favourable course, IH can sometimes be associated with a severe functional (labial or palpebral sites), cosmetic (thoracic site in young women), and vital prognosis (bleeding, respiratory tract involvement).

Paediatric ENT surgeons are mainly concerned by laryngotracheal haemangiomas. Up until recently, IH of the airways required complex and/or invasive treatments, sometimes associated with temporary tracheotomy.

The dramatic efficacy of propranolol (and β-blockers in general) on infantile haemangiomas, described for the first time in 2008 by a French team, has radically changed the prognosis of these lesions, requiring revision of the previously accepted therapeutic indications [1].

Infantile haemangioma

IH is a benign vascular tumour, rather than a vascular malformation. It has a characteristic histological appearance (typical capillary proliferation) and a specific marker is associated with this tumour: GLUT-1 [2].

IH affects 4 to 10% of infants under the age of one year, and up to 30% of low birthweight preterm infants (less than 1,500 g) [3]. This tumour is more frequent in girls, especially in the context of certain syndromes (PHACES syndrome) [4]. Other risk factors have also been identified: white skin, and antenatal or perinatal hypoxia, especially in the presence of placental abnormalities [5].

The lesion is typically discovered at birth or soon after birth, then rapidly increases in volume during the first year of life, sometimes until the age of 18 months. It then slowly, but constantly decreases in size. The very great majority of lesions have resolved by the age of 7 years, possibly

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* Corresponding author. Tel.: +33 01 44 73 61 09; fax: +33 01 44 73 61 08.
E-mail address: nicolas.leboulanger@trs.aphp.fr (N. Leboulanger).

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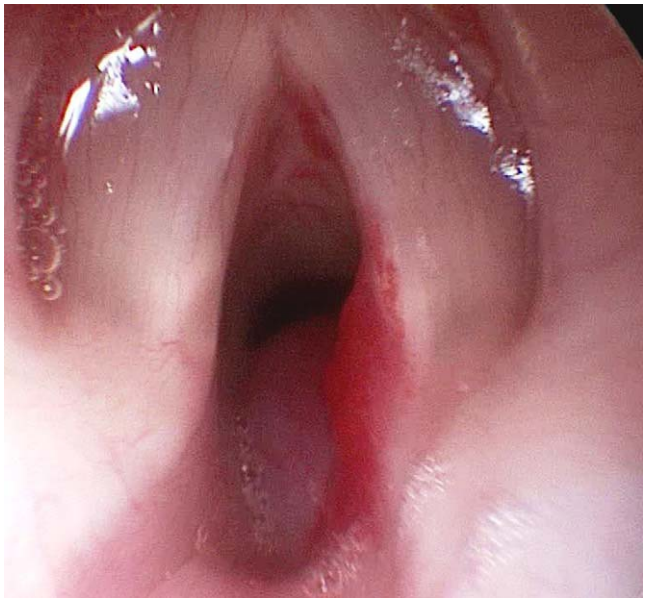

Figure 1 Endoscopic view of the larynx. Glottic (medial edge of the posterior half of the right cord) and posterior subglottic haemangioma.

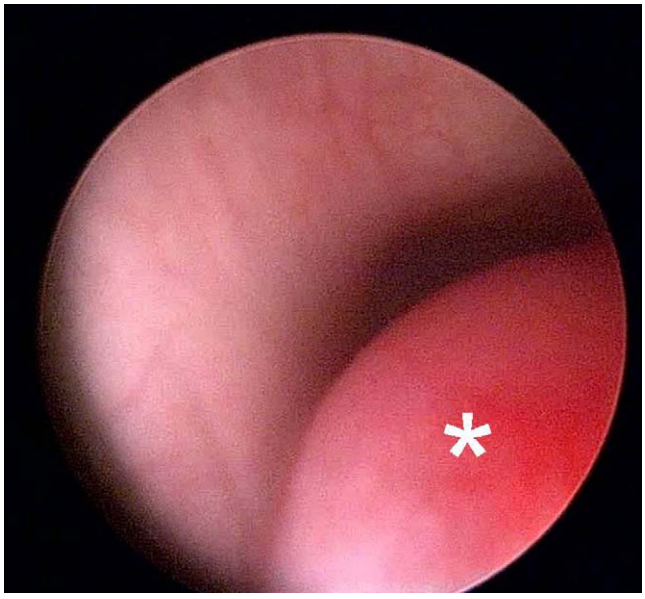

Figure 2 Same patient, rigid 0° 4 mm tracheoscopy: very large right posterior IH (*) causing about 80% obstruction.

leaving only minor cosmetic sequelae: distended skin zones or fibroadipose residues [6]. Prior to the introduction of propranolol, the severe complication rate was estimated to be 10% [7].

IH is the most common tumour of the airway in children. Subglottic lesions are generally responsible for rapid onset of clinical features, as, according to Poiseuille's law, resistance to flow of a liquid in a pipe is equal to the radius raised to the fourth power. This means that if the radius of the airways is decreased by one half, airflow resistance, and therefore the effort required to maintain satisfactory ventilation, increase 16-fold. The subglottic region, physiologically the narrowest segment of the upper airways, is therefore the most likely to be the site of clinical symptoms related to an angiomatous lesion of the airway. The diagnosis is established on complete endoscopy of the airway (Figs. 1 and 2). MRI can be useful to define the extent of very large lesions (Fig. 3).

Prior to the introduction of β-blockers, medical treatment was based on corticosteroids (systemic or topical), vincristine, and interferon, all of which have potentially serious adverse effects. Surgery was performed either via an open approach or by endoscopy (laser). Tracheotomy was required in the most severe cases, despite the higher morbidity and mortality of this procedure in children than in adults [7].

Beta-blockers

Beta-blockers are antagonists of the β-adrenergic effects of catecholamines, with multiple systemic effects (decreased cardiac output, bronchoconstriction, decreased insulin secretion). Most are fat-soluble and have a very good bioavailability. They have been used in therapeutics in children and adults, essentially in cardiology, for more than 50 years [8].

The efficacy of propranolol on cutaneous IH was discovered incidentally in 2008 [1,9] and the first case of successful treatment of laryngotracheal haemangioma was reported the following year [10].

The mechanisms of action of β-blockers on IH have not been fully elucidated. IH is currently thought to be the consequence of pathological neoangiogenesis in reaction to ischaemia of a skin territory during foetal life (systemic ischaemia would explain segmental IH, while localized ischaemia would be responsible for circumscribed IH, predominantly situated on the head [60% of cases] and prominences, representing possible pressure points during the antenatal and perinatal periods). This hypoxic stress

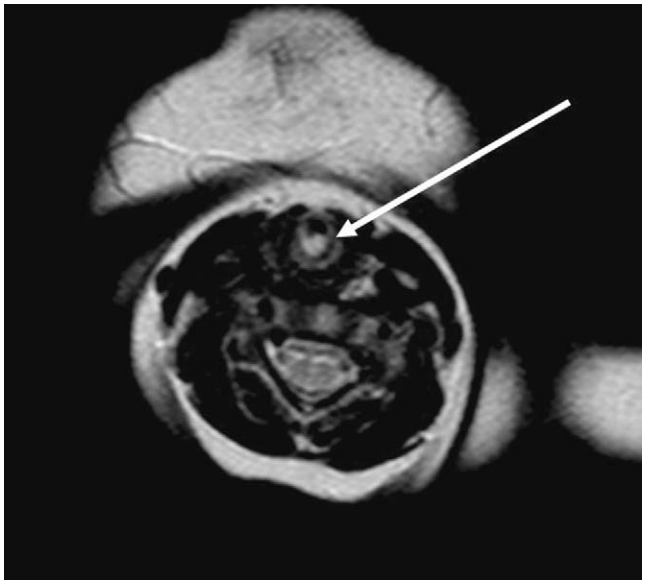

Figure 3 Same patient, cervical MRI, T2-weighted sequence: right posterior tracheal IH with high-intensity signal (arrow).