

Role of endoscopic CO₂ laser surgery in the treatment of congenital infantile subglottic hemangioma. Experience in the Department of Otolaryngology, "Sick Children Hospital", Toronto, Canada

Il ruolo della chirurgia endoscopica laser CO₂ nel trattamento dell'emangioma sottoglottico congenito infantile. Esperienza del Dipartimento di Otorinolaringoiatria del "Sick Children Hospital" di Toronto, Canada

M. RE, V. FORTE¹, C. BERARDI, V. MALLARDI

Clinic of Otorhinolaryngology, University of Ancona, Italy;

¹Department of Otolaryngology, "Sick Children Hospital", University of Toronto, Canada

Key words

Laryngeal disease • Congenital subglottic hemangioma • Surgical treatment • CO₂ laser

Parole chiave

Malattie della laringe • Emangioma sottoglottico congenito • Terapia chirurgica • Laser CO₂

Summary

Subglottic hemangioma is a rare, histologically benign congenital neoplasm. The natural history is characterized by progressive obstruction of the airways during the proliferative stage, followed by gradual regression of the obstructive symptomatology in the involutational phase. After an asymptomatic neonatal period, the infant presents a characteristic biphasic stridor as the lesion progressively obstructs the subglottic space. In 80-90% of cases, these symptoms appear in the first six months of life. The involutational process generally begins at 12 months of age and continues until the subglottic hemangioma regresses completely. Due to high incidence of mortality in untreated cases, therapy should be undertaken immediately. Aim of therapy is to restore normal respiration, attempting to preserve the child's voice and alter the quality of life both of the infant and the family as little as possible. A retrospective study was carried out on all cases of infantile subglottic hemangioma treated in the Department of Otolaryngology, "Sick Children Hospital", Toronto, between 1980 and 2000. The therapeutic strategy adopted until breathing returned to normal comprised repeated endoscopic CO₂ laser treatment of the lesion and perioperative administration of oral cortisone (1 mg/kg/day dexamethazone, subdivided in 3 doses) for 24-48 hours. CO₂ laser was used each time the patient presented progressive worsening of obstructive respiratory symptoms. The interval between two laser treatments was \geq 6 weeks. Repeated endoscopic laser treatment, combined with other therapeutic modalities, enabled tracheotomy to be avoided in all but 4 (7.2%) cases.

Riassunto

L'emangioma sottoglottico è una neoplasia congenita rara ed istologicamente benigna. La sua storia naturale è caratterizzata da una progressiva ostruzione delle vie respiratorie durante la fase proliferativa, a cui fa seguito, nella successiva fase involutiva, una graduale risoluzione della sintomatologia ostruttiva. Dopo un periodo neonatale asintomatico, come la lesione ostruisce progressivamente lo spazio sottoglottico, il bambino manifesta un caratteristico stridore bifasico. Nell'80-90% dei casi tale sintomatologia si presenta nei primi 6 mesi di vita. Il processo involutivo inizia generalmente a 12 mesi di età e continua finché l'emangioma sottoglottico non regredisce completamente. L'alta incidenza di mortalità nei casi non trattati impone un tempestivo intervento terapeutico. Scopo della terapia è di consentire una normale attività respiratoria cercando di preservare la voce e di alterare il meno possibile la qualità della vita del bambino e della sua famiglia. È stato effettuato uno studio retrospettivo su tutti i casi di emangioma sottoglottico congenito trattati presso il Dipartimento di Otorinolaringoiatria del "Sick Children Hospital" di Toronto, nel periodo 1980-2000. La strategia terapeutica adottata prevede l'utilizzo, fino a normalizzazione dell'attività respiratoria del bambino, di ripetuti trattamenti chirurgici endoscopici con laser CO₂ della lesione e somministrazione peri-operatoria di terapia cortisonica orale (desametasone 1 mg/kg die suddiviso in 3 somministrazioni giornaliere) per 24-48 ore. Il laser CO₂ viene utilizzato ogni qualvolta il paziente presenti sintomatologia ostruttiva respiratoria ad andamento progressivo. L'intervallo tra 2 trattamenti laser successivi non deve essere inferiore a 6 settimane. I trattamenti endoscopici laser in serie, in combinazione con altre modalità terapeutiche, hanno permesso di evitare la tracheotomia in tutti i pazienti con emangioma sottoglottico congenito, tranne che in 4 casi (7.2%).

Introduction

Subglottic hemangioma is a rare, histologically benign congenital neoplasm. The first description of a laryngeal hemangioma of the larynx was by Mc Kanzie in 1864¹, while Phillips and Ruh reported a first case of infantile subglottic hemangioma in 1913².

Histologically, a subglottic hemangioma may be capillary, cavernous or a combination of both; the majority are capillary and present submucosal endothelial hyperplasia.

Subglottic hemangiomas are more frequent in females, with a ratio of 2:1, and some 50% of cases, are associated with cutaneous hemangiomas³.

The natural history of this lesion is characterised by the progressive obstruction of the airway during the proliferative phase, followed by a gradual regression of the obstructive symptomatology during the later involutive phase.

After an asymptomatic neonatal period, the infant begins to manifest a characteristic biphasic stridor as the lesion progressively obstructs the subglottic space. In 80-90% of cases, these symptoms appear during the first 6 months of life³. Besides the biphasic stridor itself, the initial symptoms include coughing and hoarse crying. Other signs may occasionally be associated, such as dysphagia, cyanosis, vomiting and hemoptysis.

In most cases, the involutive process begins at 12 months of age and continues until the subglottic hemangioma has completely regressed. Approximately 50% of the hemangiomas regress entirely by 5 years of age, about 70% regress by 7 years of age, with a slow, progressive regression of the remainder by 10-12 years of age^{4,5}.

What determines the involutive process remains to be clarified: haemodynamic variations, stromal haemorrhages or alterations in the inflammatory reaction processes of the mucosa-submucosa junction have all been hypothesised⁶.

Diagnosis is made endoscopically, via nasal fibroscope or direct microlaryngoscopy under general anaesthesia. The endoscopic evaluation may be negative if the hemangioma is not in an acute phase. The hemangioma is usually situated in the posterolateral subglottic area, involving one side more than the other; in some cases, it may have a circumferential extension. The anterior subglottic area is rarely affected. The appearance of the lesion, during endoscopy, is that of an exophytic submucosal mass, red or roseaceous in colour. It is very important that assessment of the tracheobronchial tree be completed, as many patients can present other angiomatous lesions of the airways.

Due to the high incidence of mortality in untreated cases (30-70%), treatment must be started immedi-

ately^{3,6}. The aim of treatment is to allow normal breathing, whilst attempting to preserve the child's voice and alter the quality of life of both the infant and the family as little as possible.

Various modes of treatment, aimed at keeping the airway patent during the proliferative phase of the lesion, have been described in the literature: 1. tracheotomy alone or associated with other treatment; 2. external radiotherapy; 3. external surgical approach; 4. radioactive gold grain implants; 5. cryotherapy; 6. electrocauterization; 7. sclerosing agents; 8. corticosteroids (systemic or intralesional), alone or – more typically – combined with other treatments; 9. endotracheal intubation and corticosteroid therapy; 10. endoscopic vaporization of the lesion with the CO₂ laser; and 11. interferon alfa-2A (IFN α -2a) therapy. The various therapeutic approaches employed confirm the fact that an ideal treatment of infantile subglottic hemangioma does not yet exist⁷.

Radiotherapy, used until 1973, and radioactive gold grain implants, introduced by Holborow and Mott in 1973⁸ and by Benjamin in 1978⁹ are methods that have now been abandoned entirely, due to the risk of inducing secondary neoplasms.

The external surgical approach, first described by Sharp in 1949¹⁰, runs a high risk of post-operative scarring, which can even determine speech problems and subglottic stenosis.

As far as concerns long-term systemic corticosteroid treatment, the potential side-effects must be taken into consideration, in particular stunted growth, endocrine disorders and the increased risk of infection. In 1990, Meeuwis described the use of intralesional steroids associated with a brief period of intubation¹¹. This method requires prolonged hospitalization associated with continuous monitoring of the small patient in an intensive care unit, thus determining not only high costs, but excessive tension and stress for the family.

Tracheotomy, maintained until the initial involutive process of the subglottic hemangioma, is considered by many to be the best therapeutic approach. A review of the literature has revealed that from 54 to 67% of the children presenting subglottic hemangioma required tracheotomy, either alone or associated with other treatment modalities^{3,6}. Mortalities resulting from accidental decannulation or obstruction of the tracheal cannula have been reported³. Prolonged intubation may impair voice and language development.

In deciding upon the treatment to be carried out, it is important to bear in mind the social situation of the family as well as the accessibility of hospital centres. To avoid the complications related to tracheotomy, the family needs to be properly informed and strict following of the patient is necessary, with repeated laryngoscopic exams, to document the involutive process of the subglottic hemangioma and exclude endotracheal granulation tissue.

Simpson et al., in 1979¹², and Healy et al., in 1980¹³ introduced the use of CO₂ laser in the treatment of infantile subglottic hemangioma. CO₂ laser therapy presents indisputable advantages and enables the iatrogenic effects of prolonged intubation, long-term systemic corticosteroid therapy, and tracheotomy to be avoided^{14 15}. It should be stressed that CO₂ laser ablation does not entirely eliminate the hemangioma, but only the part that develops in the submucosa, and that angiomatous neoplasms that do not respond to repeated laser treatment probably extend to the perichondrium and beyond the trachea.

CO₂ laser therapy presents the risk of subglottic stenosis, a risk which is directly proportional to the extent of the angioma.

Since the hemangioma is characterised by a rapid multiplication of the endothelial cells in the proliferative phase, IFN α has been shown to inhibit angiogenesis both *in vitro* and *in vivo*, blocking endothelial cell motility and proliferation, together with other pathways¹⁶.

IFN α has been employed since 1994¹⁷, in combination with CO₂ laser and tracheotomy, in the management of patients with circumferential subglottic hemangioma in whom conventional treatment has proved unsuccessful. It has also been used in patients with multiple angiomas of the upper airways as an alternative to the use of superselective embolization and chemotherapy, both of which present by significant morbidity¹⁸.

Materials and methods

A retrospective study has been carried out on all cases of congenital subglottic hemangioma treated in the Department of Otolaryngology at Sick Children Hospital, Toronto, between 1980 and 2000.

The treatment strategy followed (Fig. 1) comprises repeated endoscopic CO₂ laser surgery, until the child's breathing returns to normal, with perioperative administration of oral cortisone treatment (Dexamethazone 1 mg/kg daily, subdivided in 3 doses) for 24-48 hours. CO₂ laser is used every time the patient presents progressive obstructive respiratory symptoms. The interval between two laser treatments must not be less than 6 weeks.

If recurrence of biphasic stridor is observed before this period has elapsed, high-dosage long-term oral cortisone treatment is started. After about 2 months, if the breathing situation remains normal, CO₂ laser treatment is repeated.

If this is not the case, the patient receives either an intralesional injection of cortisone (Prednisone) associated with intubation for about 3 days or long-term IFN α -2a. Tracheotomy remains the only therapeutic option open.

In some cases, during laser surgery exeresis for voluminous obstructive subglottic hemangiomas, intraoperative tracheotomy may be performed to support the airway. Following removal of the hemangioma, the tracheotomy site is closed surgically and the patient is intubated for 3-5 days.

Endoscopic CO₂ laser surgery is carried out under general anaesthesia with spontaneous ventilation when possible; the eyes and head are protected by gauzes and damp cloths.

Under microscopic control, the subglottic hemangioma is reduced with CO₂ laser. Care must be taken to avoid circumferential lesions of the mucosa to minimise the risk of subglottic stenosis.

To avoid excessive penetration in depth, the laser is employed in the pulsed emission mode (0.05 sec) and with the intensity varying between 2 and 5 watts. The minimum, discontinuous quantity of energy thus released allows the tissue to cool between impulses, enhancing the effects of vaporisation and reducing the thermal effects of the CO₂ laser. For coagulation purposes, laser intensity is reduced to 1-2 watts.

Patients are monitored, in an intensive care unit, for 24 hours following surgery. Inhalation of humidified oxygen or racemic epinephrine may be used, if necessary.

Results

Between 1980 and 2000, 53 patients were identified and treated for congenital infantile subglottic hemangioma.

Series of endoscopic laser treatments, associated with other treatment modalities, enabled tracheotomy to be avoided in all but 4 of the patients (7.2%). No deaths occurred.

Corticosteroid therapy was employed in all infants. Steroids were used exclusively in the perioperative period (< 5 days) in 40 patients, and continued in the long term (approximately for the first year of life) in 9 patients.

An intralesional injection of steroids followed by 3 days of intubation associated with systemic steroids was successfully employed in 1 infant. Corticosteroid therapy was withdrawn in those patients in whom tracheotomy was necessary due to failure of medical treatment.

IFN, used in 3 patients, was not success in 2, who, therefore, underwent tracheotomy, and successfully in 1 patient, in combination with systemic steroids and laser therapy.

IFN treatment was not employed in the other 2 infants who required tracheotomy.

There were no complications, either intra- or perioperative, nor any significant side-effects related to the long-term use of steroids or IFN.

Two infants required intraoperative tracheotomy to

support the airway during laser treatment. All the children in whom tracheotomy was maintained in the long term were later successfully decannulated. One patient presented a slight subglottic stenosis and it was, therefore, necessary to maintain the tracheotomy until the age of three years. The child was later decannulated without any complications. The treatment protocol we employ and recommend is outlined in Figure 1.

Conclusions

CO₂ laser, combined with other forms of medical treatment, may be safely and effectively employed in the management of infantile subglottic hemangioma. Tracheotomy can be avoided in most cases, thus preserving the child's voice and improving the quality of life both of the infant itself and of its family during the first year of life.

References

- ¹ MacKenzie M. *Essay on growths of the larynx*. Philadelphia, PA: Lindsay and Blakeston 1987.
- ² Phillips J, Ruh HO. *Angioma of the larynx, especially its relationship to chronic laryngitis*. *Am J Dis Child* 1913;5:123-30.
- ³ Shikhani AH, Jones MM, Marsh BR, Holliday MJ. *Infantile subglottic hemangiomas. An update*. *Ann Otol Rhinol Laryngol* 1986;95:336-47.
- ⁴ Simpson JR. *Natural history of cavernous hemangioma*. *Lancet* 1959;2:1057-9.
- ⁵ Ezekowitz RA, Mulliken JB, Folkman J. *Interferon alfa 2a therapy for life-threatening hemangiomas of infancy*. *N Engl J Med* 1992;326:1456-63.
- ⁶ Brodsky L, Yoshpe N, Ruben RJ. *Clinical-pathological correlates of congenital subglottic hemangiomas*. *Ann Otol Rhinol Laryngol* 1983;92(Suppl 105):4-18.
- ⁷ Gregg CM, Wiatrack BJ, Koopmann CF. *Management options for infantile subglottic hemangioma*. *Am J Otolaryngol* 1995;16:409-14.
- ⁸ Holborow CA, Mott TJ. *Subglottic hemangioma in infancy*. *J Laryngol Otol* 1973;87:1013-7.
- ⁹ Benjamin B. *Treatment of infantile subglottic hemangioma with radioactive gold grain*. *Ann Otol Rhinol Laryngol* 1978;87:18-21.
- ¹⁰ Sharp HS. *Hemangioma of the trachea in an infant, successful removal*. *J Laryngol Otol* 1949;94:494-7.
- ¹¹ Meeuwis J, Box CE, Hoeve LJ, VanderVoort E. *Subglottic hemangioma in infants: Treatment with intralesional corticosteroid injection and intubation*. *Int J Pediatr Otorhinolaryngol* 1990;19:145-50.
- ¹² Simpson GT, Healy GB, McGill T, Strong MS. *Benign tumors and lesions of the larynx in children. Surgical excision by CO₂ laser*. *Ann Otol Rhinol Laryngol* 1979;88:479-85.
- ¹³ Healy GB, Fearon B, French R, McGill T. *Treatment of subglottic hemangioma with the carbon dioxide laser*. *Laryngoscope* 1980;90:809-13.
- ¹⁴ Remacle M, Declaye X, Maynet A. *Subglottic hemangioma in the infant: contribution by CO₂ laser*. *J Laryngol Otol* 1989;103:930-4.
- ¹⁵ Sie KC, McGill T, Healy GB. *Subglottic hemangioma: ten years' experience with the carbon dioxide laser*. *Ann Otol Rhinol Laryngol* 1994;103:167-72.
- ¹⁶ Brouty-Boye D, Zetter BR. *Inhibition of cell motility by interferon*. *Science* 1980;208:516-8.
- ¹⁷ Ohlms LA, Jones DT, McGill TJ, Healy GB. *Interferon alfa-2a therapy for airway hemangiomas*. *Ann Otol Rhinol Laryngol* 1994;103:1-8.
- ¹⁸ Hellmann JR, Myer CM, Prenger EC. *Therapeutic alternatives in the treatment of life-threatening vasoformative tumors*. *Am J Otolaryngol* 1992;13:48-53.

■ Received January 22, 2002.

■ Accepted May 12, 2002.

■ Address for correspondence: Dr. M. Re, via Monteverde 8, 63037 San Benedetto del Tronto (AP), Italy. Fax: +39 071 35657. E-mail: remassimo@hotmail.com