CASE SERIES AND REPORTS

Laryngotracheal reconstruction in glottic-subglottic stenosis associated with DiGeorge syndrome in a four and a half-month-old infant

Ricostruzione laringotracheale in stenosi subglottica associata a sindrome di DiGeorge in un neonato di 4 mesi e mezzo

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SUMMARY

Neonatal subglottic stenosis still remains a substantial challenge for paediatric ENT surgeons. Herein, we present a case of a single stage laryngotracheal reconstruction for a glottic-subglottic stenosis in an 18-week-old, 7.2 kg infant with DiGeorge syndrome. Our surgical approach was compared with those reported in the literature. Paediatric airway surgery should be tailored to individual patients according to age, weight, comorbidities and family collaboration, with the ultimate objective to minimise the invasiveness of the procedure.

KEY WORDS: Laryngotracheal reconstruction • Neonatal glottic-subglottic stenosis

RIASSUNTO

La stenosi subglottica neonatale rimane ancora una grande sfida per i chirurghi di ORL pediatrica. In questo lavoro presentiamo un caso di ricostruzione laringo-tracheale di una stenosi glottica-subglottica in un neonato di 18 settimane di età con sindrome di DiGeorge di 7,2 kg di peso corporeo. Il nostro approccio chirurgico è stato confrontato con la letteratura. La chirurgia delle vie aeree pediatrica dovrebbe essere adattata al singolo paziente in base all'età, al peso, alla comorbilità ed alla collaborazione familiare, con l'obiettivo ultimo di ridurre al minimo l'invasività della procedura.

PAROLE CHIAVE: *Ricostruzione laringo-tracheale • Stenosi neonatale glottica-subglottica*

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Introduction

Neonatal subglottic stenosis still remains a substantial challenge despite the significant surgical improvements that have been made in the last 40 years, especially in the effort to carry out less invasive procedures.

According to the literature, the estimated rate of paediatric subglottic stenosis ranges from 1 to 8%, and has remained relatively stable in the past 2 decades [1 2]. The first cause of acquired stenosis is still long-term intubation in need of mechanical ventilator assistance, especially among premature infants. Congenital malformations, caused by failure of laryngotracheal opening mechanisms during embryological life, are relatively rare, accounting for 5% of patients with subglottic stenosis [3]. It is clear that, frequently, these congenital malformations are the manifestation of a genetic aberration, such as 22q11.2 deletion syndrome [4 5].

A recent 12-year review of tracheotomies, performed in a neonatal care unit at a tertiary care institution, reported that subglottic stenosis was the most common indication in neonates (one third of all cases) [6].

Nowadays it is well known that tracheostomy, besides portending a mortality risk of about 1%, may cause long term sequelae in children such as impairment in speech development, social integration and overall development [1]. This concept is even more important for small infants in whom early vocalisation is critical to overall development. Moreover, it has a strong impact in the context of a congenital syndrome determining other impairments affecting normal speech and voice development besides overall growth.

Open or endoscopic surgical procedures used to correct subglottic stenosis are a safe alternative to tracheotomy and allow avoiding the negative consequences of tracheostomy in neonates and infants.

Herein, we present the case of a 4.5-month-old boy affected by glottic-subglottic stenosis in the context of DiGeorge syndrome who underwent single stage laryngotracheal reconstruction and compared our surgical approach with those reported in the literature.

Case report

The patient was referred to our paediatric otorhinolaryngology clinic at 4.5 months of age with a diagnosis of DiGeorge Syndrome. On admission he presented with severe dysphonia and recurrent croup crisis. The baby was delivered full term and his mother's pregnancy was not complicated. His father was affected by Gilbert Syndrome and chronic obstructive pulmonary disease, and his mother by Hashimoto thyroiditis and Von Willebrand disease. There was also a predisposition to autoimmune diseases in the extended family.

DiGeorge syndrome was suspected at birth because of the patient's facial dysmorphism and the severe cat-cry dysphonia that appeared to clear from his first wail. He had no history of severe difficulty in breathing at birth or intubation.

Moreover, a detailed neonatal assessment revealed patency of foramen ovale and a minimum ventricular septal defect, slight axial hypotonia, hypoparathyroidism without clinical manifestations, thrombocytopenia without coagulation defects and a few episodes of velopharyngeal insufficiency without cleft palate. Therefore, chromosome examination was performed, with a definitive diagnosis of 22q11 microdeletion by FISH (fluorescence in situ hybridisation) with diagnosis of DiGeorge syndrome.

A second assessment at 3 months of age found significant posterior plagiocephaly and bilateral nasolacrimal duct stenosis. Furthermore, the patient's growth curve was adequate and he had never had dysphagia.

After several croup crisis and many therapies with steroids and adrenalin, the baby was taken to the emergency department where he was admitted to our clinic.

We planned endoscopic examination to assess mobility of the vocal cords, craniocaudal extension of the stenosis and to evaluate the size of the airway residual lumen. Thus, we ruled out the presence of masses, fistulas, malacia and extrinsic compression. Moreover, endoscopy was performed to evaluate the condition of the "activity" of the mucosa to exclude the presence of an inflammatory status caused by viral infection or gastro-oesophageal reflux disease (GERD) or eosinophilic oesophagitis.

We performed transnasal fibre optic laryngo-tracheo-bronchoscopy with a 3.5 mm diameter flexible endoscope, under digital recording, during spontaneous breathing at first and during general anaesthesia through a catheter mouth by face mask secondly. Moreover, we performed a rigid videoendoscopy with a 4 mm 0° telescope, prior to glottic exposure by a Storz laryngoscope, during general anaesthesia plus topical anaesthesia, above and under the glottic plane, under digital recording.

The baby underwent computed tomography (CT) scan with a CT LightSpeed Pro 32 scanner (General Electric Healthcare, Milwaukee, WI, USA) after intravenous administration of contrast medium in wakefulness supervised by an anaesthesiologist. Technical parameters of acquisition were optimised for the patient size and clinical needs (Th 0.625 mm, kV 120, mAs mod., rotation time 500 msec, pitch 1); a scan range of 9 cm was covered in less than 3 sec. Source images were transferred to a computer workstation (Advantage Windows 4.5; GEMS, Milwaukee, WI, USA) to obtain multiplanar and three-dimensional reconstruction of the airway also using a virtual endoscopic technique. Consequently, after a careful re-evaluation of the clinical and pre-operative condition, we planned a combined endoscopic and open surgery.

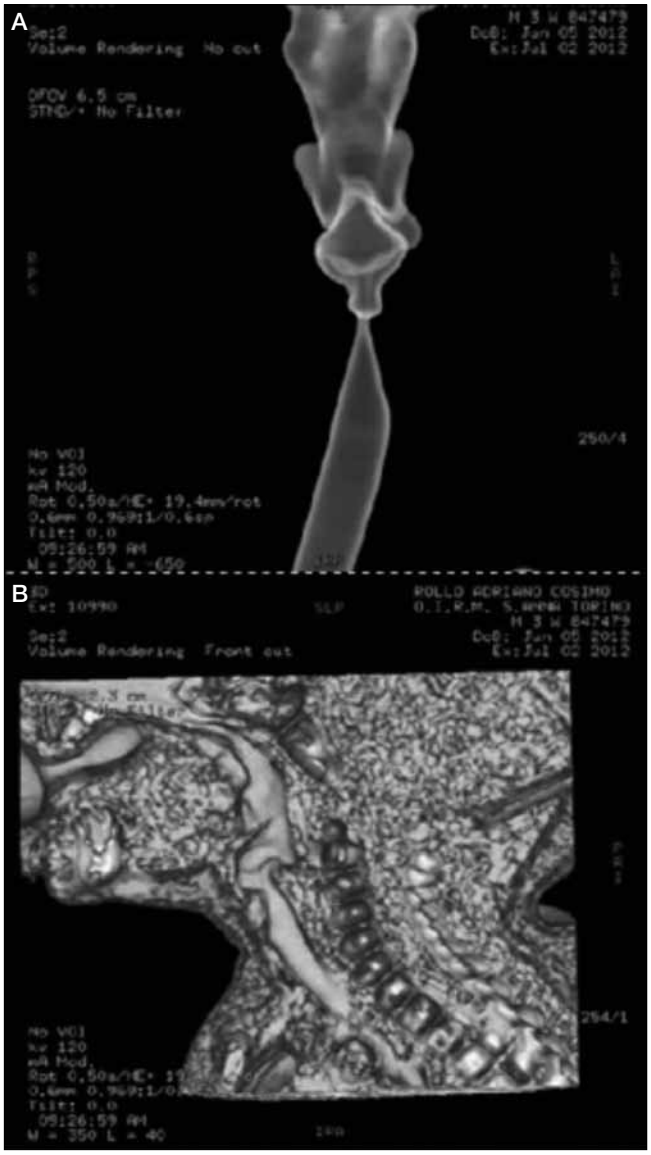

Fig. 1. CT study (A, B).

Endoscopy showed a glottic-subglottic stenosis. The glottic involvement consisted of an anterior fibrous web (III degree Choen) that significantly reduced vocal cord motility. The stenosis was extended to the subglottic area with an anterior fibro-cartilaginous lamina of 0.5 mm craniocaudal length. The cricoid cartilage was normally shaped.

Airway residual lumen size was assessed to be 4.5 mm by a calibration with a 2.5 mm Mallinckrodt endotracheal tube. In accordance with Myer-Cotton classification, we defined grade III sub-glottic stenosis. We did not find other morphological anomalies of the trachea and bronchi.
The CT study revealed a glottic-subglottic stenosis 5 mm in length with an extreme luminal narrowing (transverse diameter < 2 mm).
The infant's weight was 7.2 kg. At first, we performed a diode laser transection of the mucosa portion of the web, monitored by a 4 mm 0° telescope. We then performed a double stage laryngotracheal reconstruction with anterior costochondral cartilage grafting. The costochondral cartilage was harvested from rib 8 at the bony-cartilaginous junction of the sternum, just to achieve the best, slightly concave, surface of the graft. As a result, after cervical exposure of the larynx and trachea, the thyroid isthmus was divided and retracted laterally, preserving the cricothyroid muscles.
The ensuing laryngotracheal fissure included the thyroid cartilage, cricothyroid membrane, anterior cricoid arch and the first tracheal ring. An endoscopic control was performed to evaluate the outcome of the surgical correction. Because of the very small dimensions of the graft (only 2 cm, due to the age of the infant), the typical boat-shaped graft carving was impossible. Thus, a notch in the longitudinal side of the graft was routed with a cold lancet blade and brushed up with a drill used for ear surgery, bilaterally. The graft was positioned and fixed with nine prolene 4.0 stitches with the perichondral side of the graft facing the lumen.
A Portex N. 4 endotracheal tube was positioned by the naso-tracheal path to stent the graft.
After the procedure, the patient was admitted to the Intensive Care Unit. During the post-operative period no complications were recorded and the tube was removed 9 days after surgery.
The first videoendoscopic control, 14 days after surgery, revealed a 6.5 mm glottic-subglottic diameter and only minimal fibrous tissue in the anterior area. Three additional endoscopic evaluations were performed every 8 days. Only one balloon dilation was necessary (balloon dimension: 7-2.4 mm; pressure up to 10 atm). Pulsoximetry measure and functional respiratory tests performed in the post-operative period were negative. At the time of writing the child is at home and on daily proton pump inhibitor therapy. He is free from dysphagia and shows regular growth.

Fig. 2. Cervical exposure of the larynx and trachea.

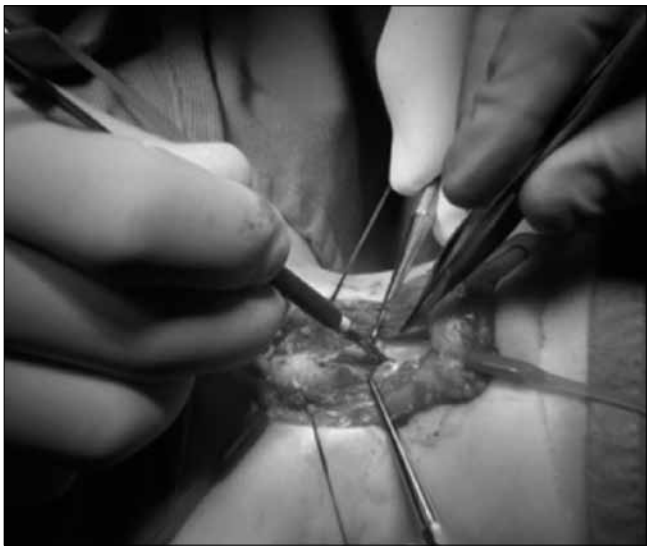

Fig. 3. Laryngotracheal fissure and the stenosis.

Discussion

During embryological life the respiratory tract is first obliterated by actively proliferating epithelial tissue that closes at 8 weeks of gestation starting with vacuolisation and autolytic dissolution. At this point in time, definitive opening of the airway begins. Congenital malformation of the larynx and trachea are caused by failure of that mechanism during embryological life. In some cases of congenital glottic and subglottic stenosis it is possible to define a genetic cause such as in the context of DiGeorge syndrome [7].
DiGeorge syndrome is a chromosomal disorder associated with 22q11 deletion, the most frequent interstitial deletion in humans (incidence of 1/4000 live births). Deletion of 22q11 is inherited only in 6-28% of cases. In most cases, the mutation is somatic [5]. Allelic loss results in altered development of the pharyngeal pouch determining various pathologies of the head and neck [8]. Di George syndrome commonly comprises certain heart defects, facial dysmorphy (small mouth, broad nose root, small ears), al-

tered development of the thymus and parathyroid glands with neonatal hypocalcaemia and psychomotor development delay. Over the years many other clinical features and phenotypes have been reported including laryngeal and tracheal disease [9].

According to the literature the exact frequency of laryngotracheal malformation in the context of 22q11 deletion is not well defined (in particular subglottic stenosis), although it is clear that laryngotracheal status needs to be assessed whenever 22 q11 deletion is suspected [5 7].

In our case, diagnosis of DiGeorge syndrome was suspected at birth because of the typical facial dysmorphism and severe dysphonia.

The rising number of acquired subglottic stenoses, due to the improvement of neonatal disease management in intensive care unit and long-term intubations, has led to the development of alternative techniques to avoid the high rate of morbidity and mortality associated with tracheotomy and the negative impact of tracheotomy on a child's life [1].

In 1953, John Conley published a summary of the known surgical methods for the treatment of stenosis at that time and for the first time used the term *reconstruction*. In fact, the real innovation was in 1956 when A. Rethi, who had had some experience with laryngeal stenosis in patients who suffered from injuries during World War I, described his techniques for laryngotracheal expansion by vertical median anterior and posterior division of the cricoid cartilage without touching the scar tissues, which was significantly different from previously described methods. His report did not include children.

It was not until 1958 that Holinger and Johnston published their case series on laryngotracheal reconstruction (LTR) in children and recommended complete removal of the scar and damaged tissues and a multi stage procedure that included skin graft and stent placement with tracheotomy tube. Next, Fearon and Cotton in 1972 well defined and encoded cricoid splitting and expansion of the subglottis by autologous cartilage graft. In 1988, Prescott presented the first description of single-stage LTR with laryngotracheal tube stenting of the reconstructed airway. These original basic concepts remain valid in the face of the many surgical improvements that have been brought about and allow performing many expansion procedures endoscopically [8 10].

According to the literature, during the past 30 years LTR has been the standard surgical method to treat subglottic stenosis in children. Endoscopic methods are limited to mild stenosis and to assist open surgery in case of glottis involvement; these approaches are contraindicated in case of congenital cartilaginous malformations. Actually, in cases with more severe stenosis (grade 3 and 4) the preferred surgical method is PCTR [11].

In the present case, upon admission to our paediatric otorhinolaryngology department, we performed a meticulous assessment to choose the correct surgical method for the particular condition.

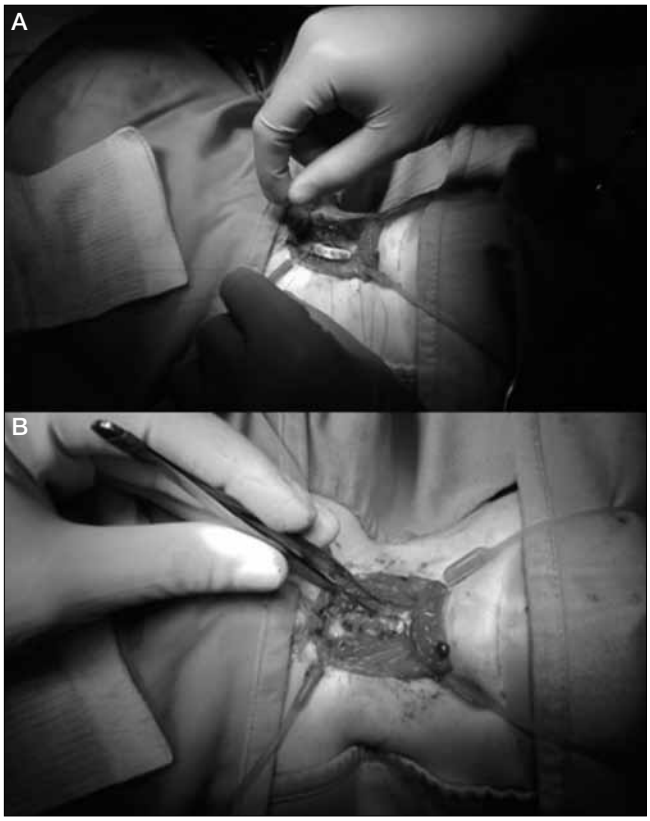

Fig. 4. A-B: Positioning and fixation of the graft.

First, general clinical assessment was done. Next, during the endoscopic evaluation, we were careful to ensure that the larynx and the trachea were not in an "activity" status, i.e. significant inflammation due to infection or acid or basic GERD because that could have minimised surgical efforts. Daily proton pump inhibitor therapy was established before scheduling the operation as suggested by the literature [12 13]. After a consensus with intensive care unit paediatricians, cardiologists, endocrinologists and gastroenterologists, we decided to perform single-stage LTR.

Our choice was supported by the high consensus found in the literature and by the experience of our senior surgeons.

Indeed, many studies have confirmed that LTR is a safe and highly successful procedure for the management of congenital malformation, i.e. glottis-subglottic stenosis in infants and neonates because it allows a high rate of successful extubation and low complication rates [1].

The choice of a single-stage procedure is supported by the literature: firstly, it has been demonstrated to be a safe alternative to tracheostomy even in neonates [1 2 11], secondly, according to the literature, it allows a high grade of decannulation, decreases the risk of granulation and scar tissue re-stenosis and removes potential sources of infectious complications [11 12].

Our choice is also supported by a recent study showing similar outcomes between single and double stage LTR and the importance of an individualised approach to every case [12].

The infant herein was affected by a laryngotracheal malformation in the context of a genetic syndrome with other impairments. Fortunately, he demonstrated good general clinical conditions. Furthermore, the collaboration between surgeons, the anaesthesiologist and chest and speech language therapist allowed to choose the single stage performance and to maximise decannulation. Costal cartilage graft was chosen because of in our paediatric ENT unit we have never had complications with this technique, thus confirming previous reports [14].

Finally, it is worthwhile underscoring that our patient was also very young, only 4.5 months old and weighing 7.2 kg. Thanks to multidisciplinary collaboration among our laryngotracheal team – surgeons, anaesthesiologist, physiotherapist and nurses – we embrace the concept that performing single stage LTR early in life [1] could avoid negative consequences of a tracheostomy, i.e. impairment in voice and speech development, inferior complexity and social integration [7].

In conclusion, careful preoperative evaluation can influence the surgical outcome in the treatment of congenital laryngotracheal malformations. Therefore, we confirm the necessity to assess disease-specific airway condition with general clinical conditions to optimise the patient's status before surgery to minimise post-operative complications, according to the literature [13].

Paediatric airway surgery is a "tailored surgery", which means "tailored on" every single patient considering age, weight, comorbidities and family collaboration. In our case, all these considerations allowed performing the less invasive surgical treatment in a very young and underweight infant. This kind of surgical choice is possible only with good cooperation among all members of a multidisciplinary team [11].

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