International Journal of Pediatric Otorhinolaryngology 92 (2017) 126–129

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology

journal homepage: http://www.ijporlonline.com/

Case Report

Minimally invasive endoscopic treatment for pediatric combined high grade stenosis as a laryngeal manifestation of epidermolysis bullosa

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ARTICLE INFO

Article history:
Received 24 August 2016
Received in revised form
16 November 2016
Accepted 19 November 2016
Available online 23 November 2016

Keywords:
Epidermolysis bullosa
CO_2 laser
Commissure stenosis
Minimally invasive laryngo-microsurgery
Arytenoid abduction lateropexy
Pediatric airway stenosis

ABSTRACT

Epidermolysis bullosa refers to a clinically and genetically heterogeneous group of inherited mucocutaneous diseases. Laryngotracheal lesions are momentous regarding the risk of sudden airway obstruction. The traditional treatment is tracheostomy. This case report highlights the advantages of minimally invasive interventions. A successful combined endoscopic management of a life-threatening respiratory crisis is presented in a 4-year-old child. Combined commissure stenosis with supraglottic spread was treated by CO_2 laser dissection and bilateral endoscopic arytenoid abduction lateropexy, supplemented with mitomycin C application. Due to expectable less scarring, the combination of these modern methods may be an efficient solution in these vulnerable respiratory tracts.

1. Introduction

Epidermolysis bullosa (EB) is a group of inherited disorders characterized by mucocutaneous fragility due to genetic defects in structural proteins of the skin. Besides blister formations and erosions on the skin and mucous membranes, extracutaneous manifestations such as oro-pharyngeal, laryngeal, ocular, gastrointestinal, genitourethral stenosis, scarring, anemia, contractures, malignancy, cardiovascular symptoms and psychological problems can complicate the patients' lives. Symptoms can range from mild to lethal, from minimal mucosal and visceral involvement to the most severe recessive form with several cutaneous and extracutaneous lesions influencing lifetime and quality of life [1].

The natural history of inherited EB varies significantly across subtypes. Nowadays, more than 1000 mutations on at least 14 structural genes have been documented in the literature of EB [2]. Four major types and at least 30 subtypes are differentiated according to the related structural protein and level of the blisters: simplex (EBS; epidermolytic), junctional (JEB; lucidolytic), dystrophic EB (DEB; dermolytic), and Kindler syndrome (mixed levels of blistering) [1–3]. Primary diagnosis relies on specific clinical features and pathological analysis. Today the immunofluorescence mapping is considered as gold standard in the diagnosis. The structural proteins of the basal membrane zone are detected with specific antibodies, this technique shows the level of the defect and the amount of protein expression [2,3].

The onset of EB is usually at birth, or shortly after, thus mild cases can remain undetected [1]. Respiratory tract involvement, especially laryngeal lesions mostly occur in JEB [4]. Signs and symptoms can vary from mild to severe, life-threatening: weak or hoarse cry, inspiratory stridor, edema, blistering of mucosa, thickening and scarring of the vocal cords, cicatrical lesions or severe upper airway stenosis.

According to the literature tracheostomy should be considered early in any child with EB and laryngotracheal involvement to avoid life-threatening airway obstruction and further iatrogenic injuries [4,5]. Endoscopic management is thought to play secondary role due to the vulnerability of the tissues.

In this case report, we present a history of a child with JEB suffered from severe, extended laryngeal stenosis. The well-designed, combined minimally invasive endoscopic procedures provided satisfactory result without tracheostomy.

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http://dx.doi.org/10.1016/j.ijporl.2016.11.020
0165-5876/

2. Case report

A 4-year-old girl was admitted to our clinic with life-threatening inspiratory stridor. JEB was diagnosed since no breathing difficulties were detected at birth and only blister formations were present on her face. Before her admission she had dyspnea for a year. The severe inspiratory dyspnea necessitated an urgent surgical intervention.

In supraglottic jet ventilation (AcutronicAms® 1000 device with the following parameters: inhalation time: 40–50%; frequency: 50–60/min; volume: 3–400ml; respiratory minute volume: 1,8–2,4l; pressure: 50 mbar (Acutronic Medical System AG, Hirzel Switzerland) and total intravenous narcosis (25 mg/kg propofol (1%), 10 μg/kg fentanyl, 1 mg/kg mivacurium) direct laryngoscopy was performed. For safety reasons 8 mg/kg methylprednisolone (Solu-medrol®) and 15 mg/kg meropenem (Meropenem®) were administered at the introduction of anesthesia. The larynx was approached through a Weerda laryngoscope. A combined severe multilevel laryngeal stenosis was observed: anterior and posterior commissure stenosis with supraglottic spread into the interarytenoid region. Thus, a pinhead-sized airway was only detectable (Fig. 1).

To avoid tracheostomy minimally invasive transoral laser resection was performed as a definitive solution. Firstly, the anterior and posterior commissure and the supraglottic interary area adhesions were dissolved by ultra dream pulse (UDP) mode CO_2laser (Dhaesin U-40; peak power: 252 W; relaxation time: 500 μs; duration time: 5 ms) until proper mobility of the arytenoid cartilages could be achieved.

A Bogdasarian-Olson [6] type 2 posterior (the scars spread into the interarytenoid space) and a Cohen [7] type 2 anterior glottic stenosis (web involving 35–50% of the glottis) were confirmed (Fig. 2a and b).

In our experiences, in accordance with international observations without any further interventions severe restenosis may occur in the near future because of the large row facing wound surfaces in the larynx. Earlier we suggested a surgical method designed for other isolated posterior glottic stenosis: a bilateral endoscopic arytenoid abduction lateropexy (EAAL) by endolaryngeal thread guide instrument (ETGI) was performed to keep the facing areas apart from each other [8,9], (Fig. 2c). After this fast and straight forward maneuver a maximal physiological abducted position was created by suture-lateralization of the arytenoid cartilages [10].

Originally, we planned to place a temporary silicon stent into the anterior commissure, but the large angle of the anterior commissure– considering the high vulnerability of the mucosa –let us to abandon this intervention. After the uneventful awakening procedure adequate airway and breathing were observed and the child was delivered to the ICU for observation. Reintubation or ventilation was not necessary. In the postoperative period antibiotics (3 × 15 mg/kg meropenem: Meropenem®) and steroids (2 × 3 mg/kg methylprednisolone: Solu-medrol®) were administrated intravenously for 5 days.

One week later, control direct laryngoscopy showed a wide adequate airway, and mitomycin c (MMC) (1 mg/ml for 5 min), an antiproliferative agent was applied on the wound surfaces. 3-months-postoperative direct laryngoscopy confirmed no sign of restenosis. After removing the bilateral lateralizing sutures through a short skin incision, regained mobility of both cricoarytenoid joints was detected (Fig. 3).

Follow up examinations were performed every third month in the first year. At the end of the third postoperative year the child is free from any symptoms.

Postoperatively voice and life quality was evaluated by voice analysis, Voice Handicap Index (VHI) and Quality of Life questionnaire (QoL) [11]. The objective voice analysis and the VHI showed a continuous improvement of her voice to normal level in Jitter, Schimmer (Fig. 4) and harmonic to noise ratio (HNR) (Fig. 5). However, the mean phonation time was very short. It might be explained by the patients' age-related cooperation difficulties. By the evaluation of her mother, VHI has become excellent after a year.

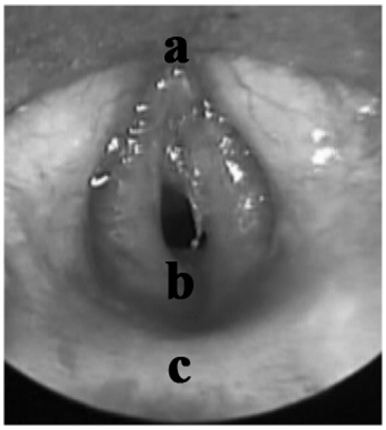

Fig. 1. Preoperative picture: combined anterior (a) and posterior glottic stenosis (b) with supraglottic spread into the interarytenoid region (c).

3. Discussion

The nature of EB makes the management of these children difficult and demanding. Each manipulation may cause de novo lesions on the laryngeal mucosa, which can exasperate the already poor respiratory status [4]. Secondly, the anatomical situation, the small airways in early childhood, the great demand of open surgery, the possible impairment of swallowing and speech development and the resulting technical issues play remarkable role in pediatric airway surgery. High skills and experiences of the surgeon are indispensable for avoiding inducing further lesions.

In 1978 Ramadass and Thangavelu [12] were the first to report laryngeal involvement in EB and the first to suggest tracheostomy as a definitive treatment. Since then, several cases, publications have confirmed that laryngotracheal lesions may play an important role for EB patients, especially in JEB [12–16].

A retrospective study published by Fine et al. [13] used 3280 cases of the National Registry of Bullous Epidermolysis of the USA to define the frequency of upper airway complications and assess the cumulative risk of laryngeal stenosis in EB patients. The most common laryngeal complication was chronic hoarseness occurring in 7% of EBS. It occurred most frequently in JEB types, 33% in non-Herlitz JEB (JEB-nH) and 50% in JEB-Herlitz (JEB-H). JEB-H subtype is the most severe and usually fatal form, associated with the absence of laminin-332 (laminin-5) expression. JEB-nH has better prognosis, it results from reduced expression of this glycoprotein [2,14].

Lifetable analysis predicted the cumulative risk of severe upper airway stenosis or obstruction, which has provided an outcome of 13% and 40% at the age of 1 and 6, in JEB-H respectively and 8.3% at the age of 1 and 12.75% after the age of 9 in JEB-nH [13].

Monitoring in the first years of life is inevitable for identifying the early laryngotracheal symptoms. Fine et al. estimated, that approximately 10% and 23% of JEB-H and JEB-nH patients had died probably from airway obstruction (excluding pneumonia, sepsis, failure to thrive and renal failure). They concluded that each EB child with laryngeal symptoms should be electively

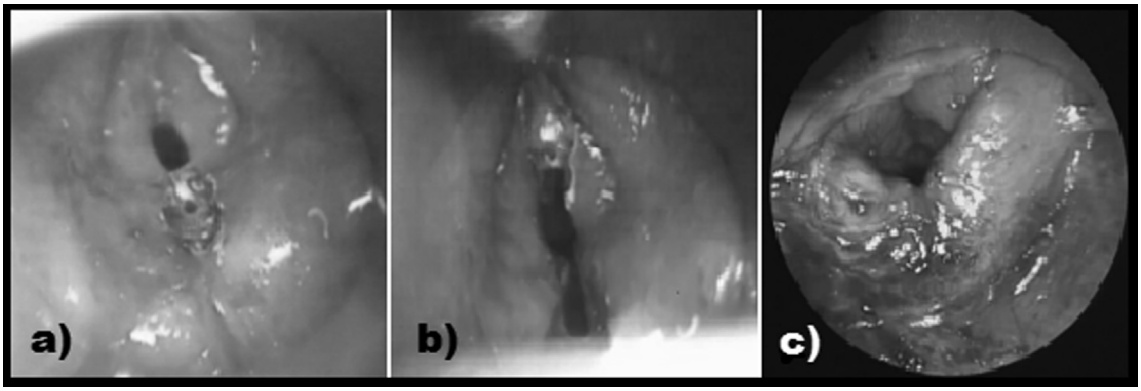

Fig. 2. Intraoperative pictures: laser dissection of posterior (a) and anterior (b) commissure; bilateral endoscopic arytenoid lateropexy (c).

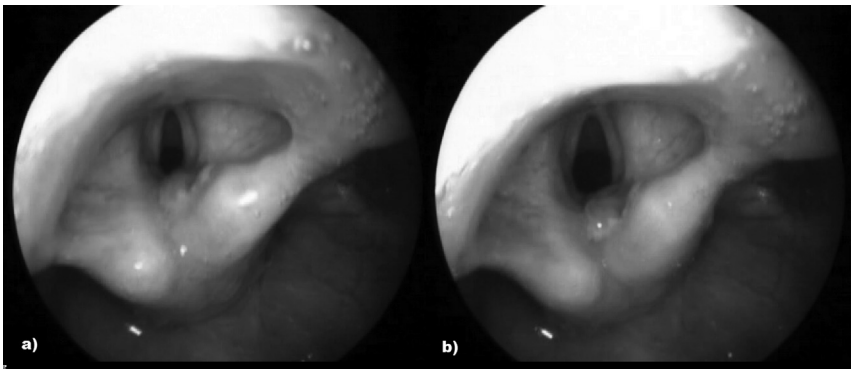

Fig. 3. 3-months postoperative picture after the removal of the lateralizing sutures from external incision: the regained mobility of the cricoarytenoid joints can be seen during sleeping right after the procedure (a) normal (b) open position.

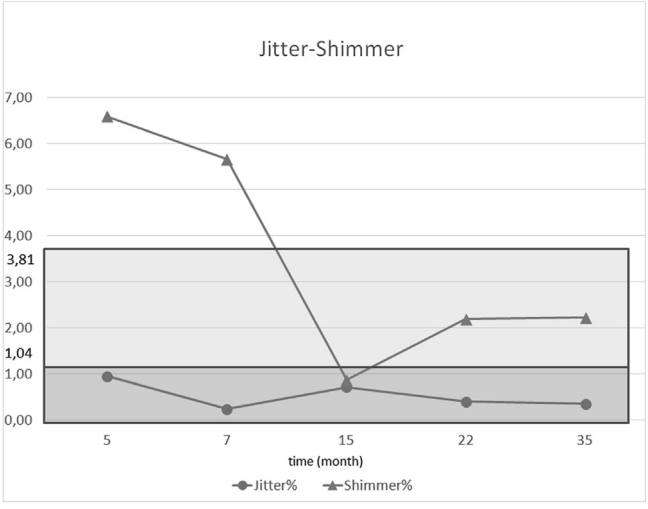

Fig. 4. Results of voice analysis I.: Jitter, Schimmer.

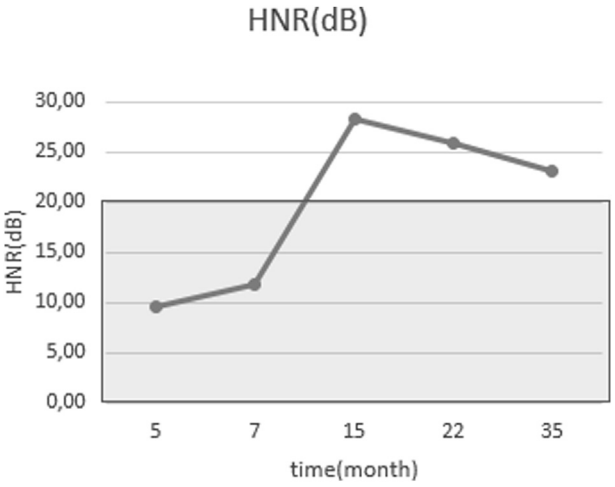

Fig. 5. Results of voice analysis II.: HNR.

tracheostomised to prevent sudden airway obstruction [13].

Despite solving respiratory status, tracheostomy requires further reconsiderations regarding its influence on swallowing and speech development, social and emotional life [17–20]. Due to the extremely vulnerable tissue, the long-lasting cannula wearing may induce erosions, blistering, de novo stenosis and accumulation of fibrin or mucous [4].

According to the literature tracheostomy might be the solution for difficult, extended cases. Mellerio [15], Hore [14], Babic [4] et al. reported altogether 8 cases with airway involvement, in which tracheostomy was not the first chosen therapy, conservative steroid or adrenalin nebulizer was applied, but in six out of eight cases tracheostomy could not be avoided. Minimally invasive transoral procedures played only secondary role: Hore [14] et al. used laser dissection and topical MMC application as additional treatment to facilitate decannulation after tracheostomy, which was successful in two cases.

Considering the nature of EB and the abovementioned disadvantages of tracheostomy, we performed a definitive minimally invasive combined endoscopic surgery for a life-threatening upper airway stenosis without tracheostomy: CO_2 scar dissection followed by bilateral EAAL and delayed MMC application.

For the dissection of the combined commissure stenosis modern CO_2 laser was used in UDP mode. This recently developed new mode accompanied with micro-spot technique has been introduced to reduce thermal tissue damage and minimize the necrotic zone. Setting of relaxation time decreases thermal spread by allowing the surrounding heated tissues to cool down [21]. The possibility of using high peak power and achieve less tissue damage by impulsive mode may simplify its use in pediatric airway surgery, especially in more vulnerable cases like EB patients.

In our prior article – following the international recommendations - we suggested a combined silicone tube-sheet stent insertion into the anterior commissure until wound healing [22]. However it was confirmed in our recent cadaver morphometric study [23], that a sufficiently large angle could be achieved in the anterior commissure by EAAL, especially after bilateral intervention. Considering the anatomy of the pediatric larynx, even larger angles might be reached in children, than in adults. The angle was large enough to maintain an optimal distance between the vocal folds [24], which necessitated no stent insertion. Bilateral arytenoid abduction provided an optimally wide airway functioning as a temporary hidden stent by keeping the free mucosal surfaces apart, preventing restenosis in the posterior commissure. The lateralizing sutures were placed under the skin, they caused no skin irritation.

Stent emplacement (accompanied with temporary tracheostomy) could have been a useful method to avoid restenosis, but in these vulnerable tissues, it might aggravate the situation by further mucosal damage.

The topically applied MMC is functioning as an antiproliferative agent by inhibiting RNA and protein synthesis. Regarding the management of vocal fold scarring, it has been shown to lead to reduced anterior glottis web formation, decreased total collagen deposition, improved cricoarytenoid joint mobility, and decreased granulation tissue development [22,25,26]. Although the exact use, dosage and timing of MMC are controversial in the literature, an optimal balance should be found to control scar formation, but allow the necessary repair of tissue. Delayed application of MMC seems to be effective. One would expect a better result, if MMC is applied during the cell proliferation phase at the end of the first postoperative week, when fibroblasts are present in the tissue and active in collagen secretion [26].

4. Conclusion

The management of pediatric upper airway stenosis is still a great challenge especially for children with EB. The young age of the patients, the small size of the larynx, the nature of the disease and the possibility of sudden airway obstruction increase the complexity of the problem. Direct surgical interventions have been proposed only for milder cases, tracheostomy is suggested for severe ones. Our case proved that introducing a new concept of treatment strategy: modern laser surgery, endoscopic arytenoid abduction lateropexy and mitomycin c might provide excellent result even in difficult cases.

References

[1] C.M. Salavastru, E. Sprecher, M. Panduru, J. Bauer, C.S. Solovan, V. Patrascu, H.S. Morariu, A. Tudorache, T. Lotti, I. Tagliente, A. Ciasulli, M.R. Marchili, G. Sabatino, E. Burciu, R. Cosgarea, K. Fritz, G.S. Tiplica, Recommended strategies for epidermolysis bullosa management in Romania, Maedica J. Clin. Med. 8 (2013) 200–205.
[2] L.R. Intong, D.F. Murrell, Inherited epidermolysis bullosa: new diagnostic criteria and classification, Clin. Dermatol. 30 (2012) 70–77.
[3] D.R. Berk, L. Jazayeri, M.P. Marinkovich, U.N. Sundram, A.L. Bruckner, Diagnosing epidermolysis bullosa type and subtype in infancy using immunofluorescence microscopy: the Stanford experience, J. Pediatr. Dermatol. 30 (2013) 226–233.
[4] I. Babić, M. Karaman-Ilić, N. Pustisek, S. Susić, I. Skarić, A. Kljenak, D. Cikojević, Respiratory tract involvement in a child with epidermolysis bullosa simplex with plectin deficiency: a case report, Int. J. Pediatr. Otorhinolaryngol. 74 (2010) 302–305.
[5] C. Gonzalez, R. Roth, Laryngotracheal involvement in epidermolysis bullosa, Int. J. Pediatr. Otorhinolaryngol. 17 (1989) 305–311.
[6] R.S. Bogdasarian, N.R. Olson, Posterior glottis laryngeal stenosis, Otolaryngol. Head Neck Surg. 88 (1980) 765–772.
[7] S.R. Cohen, Congenital glottic webs in children, Ann. Otol. Rhinol. Laryngol. 94 (Suppl. 121) (1985) 1–16.
[8] L. Rovó, K. Venczel, A. Torkos, V. Majoros, B. Sztanó, J. Jóri, Endoscopic arytenoids lateropexy for isolated posterior glottic stenosis, Laryngoscope 118 (2008) 1550–1555.
[9] L. Rovó, S. Madani, B. Sztanó, V. Majoros, G. Smehák, L. Szakács, J. Jóri, A new thread guide instrument for endoscopic arytenoid lateropexy, Laryngoscope 120 (2010) 2002–2007.
[10] B. Sztanó, L. Szakács, S. Madani, F. Tóth, Z. Bere, P.F. Castellanos, L. Rovó, Comparison of endoscopic techniques designed for posterior glottic stenosis–a cadaver morphometric study, Laryngoscope 124 (2014) 705–710.
[11] Y. Jaquet, F. Lang, R. Pilloud, M. Savary, P. Monnier, Partial cricotracheal resection for pediatric subglottic stenosis: long-term outcome in 57 patients, J. Thorac. Cardiovasc. Surg. 130 (2005) 726–732.
[12] T. Ramadass, T.A. Thangavelu, Epidermolysis bullosa and its E.N.T. manifestations. Two case reports, J. Laryngol. Otol. 92 (1978) 441–446.
[13] J.D. Fine, L.B. Johnson, M. Weiner, C. Suchindran, Tracheolaryngeal complications of inherited epidermolysis bullosa: cumulative experience of the national epidermolysis bullosa registry, Laryngoscope 117 (2007) 1652–1660.
[14] I. Hore, Y. Bajaj, J. Denyer, A.E. Martinez, J.E. Mellerio, T. Bibas, D. Albert, The management of general and disease specific ENT problems in children with Epidermolysis Bullosa–a retrospective case note review, Int. J. Pediatr. Otorhinolaryngol. 71 (2007) 385–391.
[15] J.E. Mellerio, F.J. Smith, J.R. McMillan, W.H. McLean, J.A. McGrath, G.A. Morrison, P. Tierney, D.M. Albert, G. Wiche, I.M. Leigh, J.F. Geddes, E.B. Lane, J. Uitto, R.A. Eady, Recessive epidermolysis bullosa simplex associated with plectin mutations: infantile respiratory complications in two unrelated cases, Br. J. Dermatol. 137 (1997) 898–906.
[16] J.D. Fine, E.A. Bauer, J. McGuire, A. Moshell, in: Epidermolysis Bullosa: Clinical, Epidemiologic and Laboratory Advances and the Findings of the National Epidermolysis Bullosa Registry, The Johns Hopkins University Press, Baltimore, 1999, pp. 206–224.
[17] B.M. Simon, S.M. Fowler, S.D. Handler, Communication development in young children with long-term tracheostomies: preliminary report, Int. J. Pediatr. Otorhinolaryngol. 6 (1983) 37–50.
[18] D. Jiang, G.A. Morrison, The influence of long-term tracheostomy on speech and language development in children, Int. J. Pediatr. Otorhinolaryngol. 67 (S1) (2003) S217–S220.
[19] V. Norman, B. Louw, A. Kritzinger, Incidence and description of dysphagia in infants and toddlers with tracheostomies: a retrospective review, Int. J. Pediatr. Otorhinolaryngol. 71 (2007) 1087–1092.
[20] M. Parris, Family adaptation to a child's feeding and swallowing disorder: a social work perspective, Semin. Speech Lang. 18 (1997) 71–78.
[21] Y. Yan, A.E. Olszewski, M.R. Hoffman, P. Zhuang, C.N. Ford, S.H. Dailey, J.J. Jiang, Use of lasers in laryngeal surgery, J. Voice 24 (2010) 102–109.
[22] B. Sztanó, A. Torkos, L. Rovó, The combined endoscopic management of congenital laryngeal web, Int. J. Pediatr. Otorhinolaryngol. 74 (2010) 212–215.
[23] L. Szakács, B. Sztanó, V. Matievics, Z. Bere, A. Bach, P.F. Castellanos, L. Rovó, A comparison between transoral glottis-widening techniques for bilateral vocal fold immobility, Laryngoscope 125 (2015) 2522–2529.
[24] G.S. Sandhu, S.A.R. Nouraei, L. Rovo, J.P. Marie, A.H. Mueller, P.F. Castellanos, Bilateral impaired vocal cord mobility, in: G.S. Sandhu, S.A.R. Nouraei (Eds.), Laryngeal and Tracheobronchial Stenosis, Plural Publishing Inc., San Diego, 2015, pp. 195–226.
[25] J.L. Roh, Prevention of posterior glottic stenosis by mitomycin C, Ann. Otol. Rhinol. Laryngol. 114 (2005) 558–562.
[26] N.Y. Li, F. Chen, F.G. Dikkers, S.L. Thibeault, Dose-dependent effect of mitomycin C on human vocal fold fibroblasts, Head Neck 36 (2014) 401–410.