The Laryngoscope

Case Report

Laryngotracheal Transplantation: Technical Modifications and Functional Outcomes

D. Gregory Farwell, MD, FACS; Martin A. Birchall, MD, PhD; Paolo Macchiarini, MD, PhD; Quang C. Luu, MD; Angelo M. de Mattos, MD, MPH; Brian J. Gallay, MD, PhD; Richard V. Perez, MD; Matthew P. Grow, MD; Rajen Ramsamooj, MD; Moses D. Salgado, MD; Hilary A. Brodie, MD, PhD; Peter C. Belafsky, MD, PhD, MPH

Objectives/Hypothesis: Laryngeal transplantation offers the potential for patients without a larynx to recover their voice, which is critical in our communication age. We report clinical and functional outcomes from a laryngotracheal transplant. Widespread adoption of this technique has been slowed due to the ethical concerns of life-long immunosuppression after a nonvital organ transplant. Our patient was already on immunosuppressive medication from prior kidney–pancreas transplantation, and therefore was not exposed to added long-term risk. We describe the unique technical advances, clinical course, and rehabilitation of this patient and the implications for future laryngeal transplantation.

Study Design: Case report.

Methods: A laryngotracheal transplantation was performed in a 51-year-old prior kidney–pancreas transplant recipient presenting with complete laryngotracheal stenosis. Surgical modifications were made in the previously described technique related to retrieval, vascular supply, and reinnervation. This resulted in a robustly vascularized organ with well-perfused long-segment tracheal transplant and early return of motor reinnervation.

Results: A multidisciplinary approach resulted in a successful transplant without evidence of rejection to date. Postoperatively, the patient continues to rely on a tracheotomy but has had the return of an oral and nasal airway, vocalization, smell, and taste, all experienced for the first time in 11 years.

Conclusions: We have demonstrated that our methods may result in a successful laryngotracheal transplant. We describe the preparation, surgical technique, rehabilitation, and interventions employed in achieving optimal outcomes. This report contributes valuable information on this rarely performed composite transplant.

Key Words: Larynx, trachea, transplant, larynx transplant, laryngotracheal transplant, airway reconstruction, larynx stenosis, tracheal stenosis, composite tissue allotransplantation.

***Laryngoscope*, 123:2502–2508, 2013**

INTRODUCTION

Loss of laryngeal function affects quality of life, with significant influence on communication, respiration, and deglutition.[1,2] The majority of patients with laryngotracheal stenosis can be managed with advanced endoscopic and open reconstructive techniques. Complex stenosis, however, may defy surgeons' best efforts.

Laryngeal transplantation has been proposed as an option for patients with laryngeal dysfunction not amenable to alternative treatment.[3,4] Challenges in microvascular reconstruction and reinnervation, as well as ethical considerations for the transplantation of a nonvital organ, have limited the general acceptance of this procedure. In 1998, Strome et al. performed the first successful total laryngeal transplant, and despite evidence of chronic rejection, this patient retained his graft with good voice production 13 years postoperatively.[5,6] Although some reports suggest a series of laryngeal transplants have been performed in Colombia, published results are lacking, meaning that no technical advance has been reported in well over a decade.[7] The purpose of this article is to describe surgical refinements and clinical and functional outcomes in a laryngotracheal transplant recipient.

From the Department of Otolaryngology–Head and Neck Surgery, University of California, Davis, Sacramento, California, U.S.A. (D.G.F., Q.C.L., M.D.S., H.A.B., P.C.B.); Ear Institute, Royal National Throat Nose and Ear Hospital, University College London, London, United Kingdom (M.A.B.); Department of Clinical Science, Intervention, and Technology, Karolinska Institute, Stockholm, Sweden (P.M.); and Department of Medicine, Section of Transplant Nephrology (A.M.D.M., B.J.G.), Department of General Surgery (R.V.P.), Department of Anesthesiology (M.P.G.), and Department of Pathology (R.R.), University of California, Davis, Sacramento, California, U.S.A.

Editor»s Note: This Manuscript was accepted for publication January 22, 2013.

The authors have no funding, financial relationships, or conflicts of interest to disclose.

Send correspondence to D. Gregory Farwell, MD, FACS, Professor, Director of Head and Neck Oncology and Microvascular Surgery, Department of Otolaryngology–Head and Neck Surgery, University of California, Davis, 2521 Stockton Blvd, Suite 7200, Sacramento, CA 95817. E-mail: gregory.farwell@ucdmc.ucdavis.edu

DOI: 10.1002/lary.24053

MATERIALS AND METHODS

The Recipient

A 51-year-old female presented with an 11-year history of traumatic, tracheotomy-tube–dependent, benign, and complete laryngotracheal stenosis resulting from multiple self-extubations during a protracted intubation and hospitalization for renal failure. Her stenosis extended from the apex of the laryngeal ventricle to the second tracheal ring (Fig. 1). In 2006, she underwent a successful kidney–pancreas transplant for diabetes-induced renal failure. She has been maintained on long-term immunosuppression with tacrolimus and leflunomide. She failed endoscopic restoration of laryngeal patency and was determined by a multidisciplinary team of national and international experts not to be amenable to nontransplant alternatives for the restoration of laryngeal function.

Over a preparatory period of 2 years, she underwent psychological assessment, counseling, and informed consent. Clearance to perform the surgery was obtained from the patient's transplant nephrologist. A research protocol and informed consent were approved by the University of California, Davis Institutional Review Board Privileging Committee and the Golden State Transplant Service Ethical Review Board.

Donor Organ Retrieval

Technical preparation included cadaveric training and live animal laryngotracheal transplantation in an established porcine model.[8,9] Two weeks after starting to screen for an acceptable donor, a well-matched, otherwise healthy 38-year-old female donor was identified who had suffered anoxic arrest and had only been intubated for 3 days. An infectious disease panel was positive for cytomegalovirus. The donor ABO blood group was compatible with that of the recipient, and human leukocyte antigen (HLA) alleles mismatched to the recipient were 2A, 1B, 1Cw, 1DR, and 1DQ. The B55 allele was shared by the kidney–pancreas and laryngeal donors, but the patient expressed no anti-B55 antibody, and her panel reactive antibody was 4%, indicating a low level of sensitization against HLA antigens. Given the success of other composite tissue transplants with similar immunosuppression regimens, our priority was to avoid donor HLA antigens against which the recipient expressed antibody, but no attempt at matching minor loci was made. The extent of HLA matching was not considered as important as anatomical and functional attributes of the donor organ given the success of induction and maintenance immunosuppression regimens used in this patient to prevent acute rejection in her kidney transplant regardless of antigen mismatch.

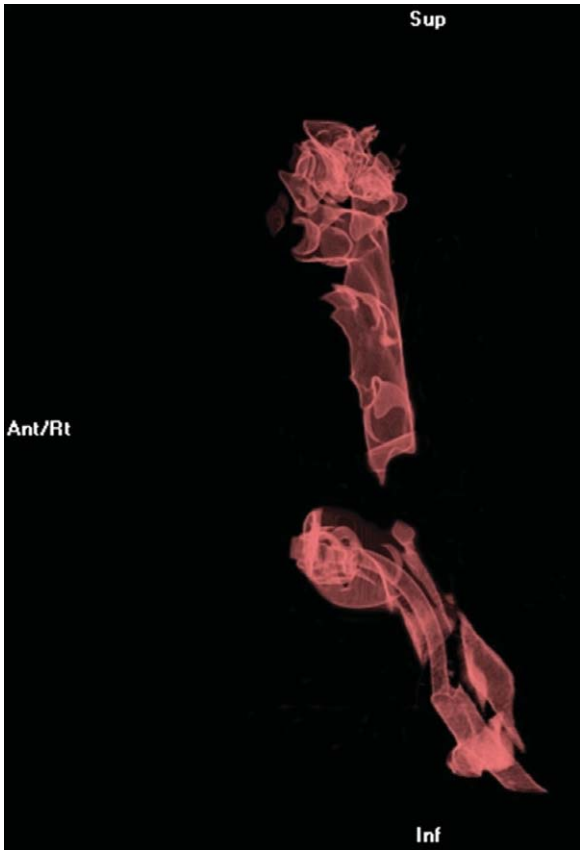

Fig. 1. Computed tomography three-dimensional reconstruction of recipient's airway demonstrating complete glottic, subglottic, and proximal tracheal stenosis. Ant = anterior; Inf = inferior; Rt = right; Sup = superior.

Laryngoscopy of the donor revealed no evidence of laryngotracheal injury. The larynx was procured with the thyroid and parathyroid glands, and all nourishing great vessels, including the supra-aortic trunks (Fig. 2A). Isolation of the internal jugular vein, common and external carotid arteries, and bilateral superior laryngeal nerves at their bifurcations from the vagus nerves was performed from lateral to medial to capture the vascular supply to the larynx and trachea. The strap muscles were removed, and a median sternotomy was performed. The postscalenic subclavian arteries, lateral to the thyrocervical trunk, were isolated bilaterally, as were both brachiocephalic veins and the distal superior vena cava. The proximal recurrent laryngeal nerves were divided in the chest. Liver and kidney procurement proceeded synchronously. When all organs were effectively isolated, the ascending and descending aorta were cross-clamped simultaneously. The larynx was isolated by clamping the postscalenic subclavian and postbifurcation carotid vessels and perfused with 3 L of University of Wisconsin perfusate (DuPont Pharma, Wilmington, DE) delivered through an aortic cannula placed in the ascending compartment. The graft was flushed clear of blood until the thyroid and larynx became pale. Distal cuts of the trachea and esophagus were made with mechanical staplers to avoid bacterial contamination.

Further organ and vessel preparation was executed on sterile ice bathed in iced University of Wisconsin solution. A dominant right-sided arterial and venous vascular supply was observed. The graft was prepared by splitting the esophagus longitudinally along its posterior edge and removing all esophageal mucosa. The superior vena cava was sectioned at its brachiocephalic confluence to permit a macroanastamosis. The left adductor branch of the recurrent laryngeal nerve was isolated and transected at its bifurcation with the abductor branch.

Recipient Evaluation, Preparation, and Implantation

The patient underwent preoperative laryngeal electromyography (EMG), high-resolution pharyngeal and esophageal manometry (HRM), ambulatory pH and impedance testing, and a comprehensive video fluoroscopic swallow study from lips to stomach. Laryngeal EMG revealed normal recruitment of the thyroarytenoid muscles bilaterally, with attempted phonation indicating retained motor nerve function. Pharyngeal and esophageal HRM, ambulatory pH, impedance testing, and video fluoroscopy were normal. The patient underwent placement of a percutaneous gastrojejunal feeding tube 3 months prior to transplantation. Due to its long duration of action and our prior clinical experience in profoundly dysphagic patients, botulinum

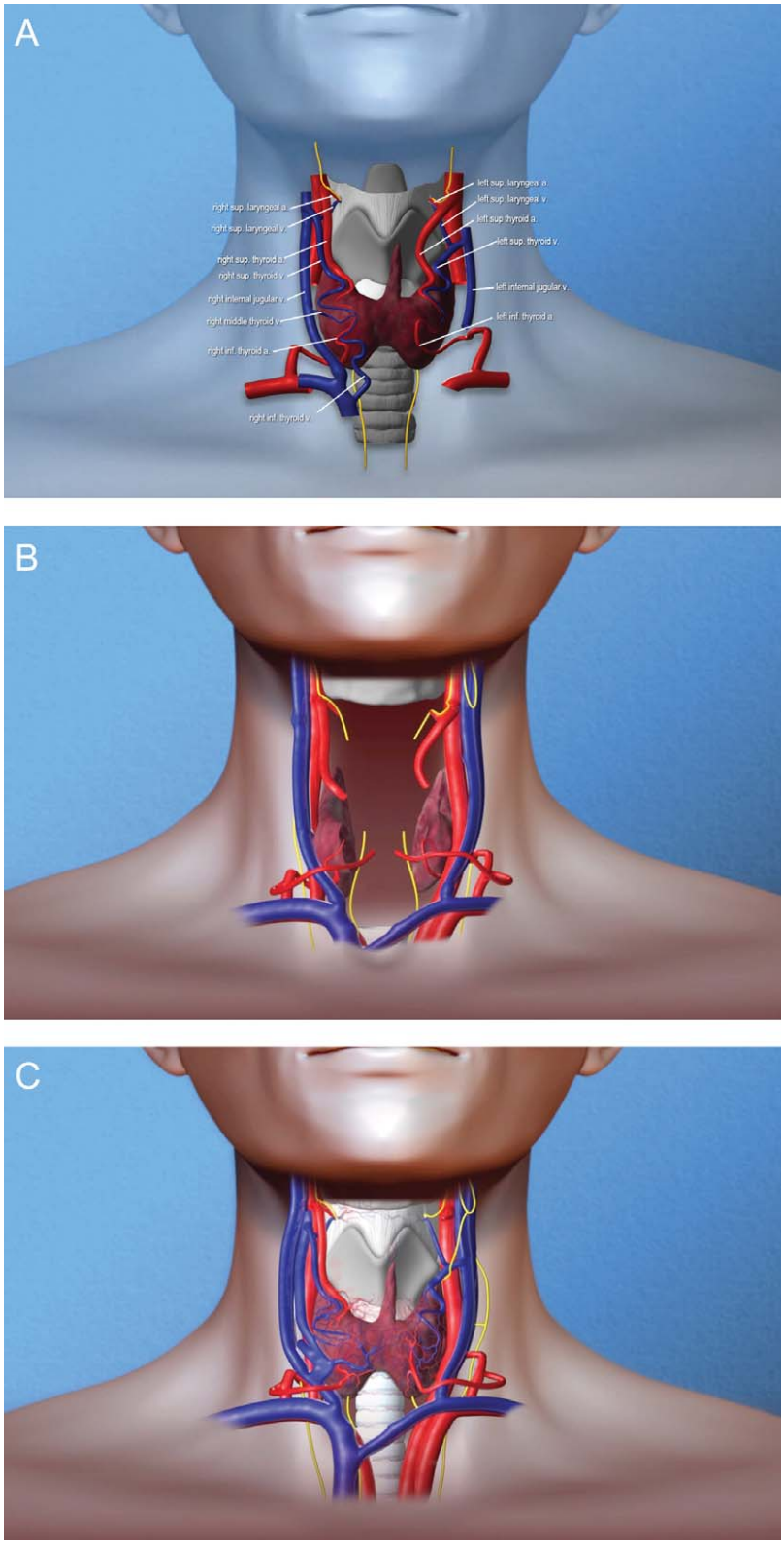

Fig. 2. (A) Organ procurement. Transplanted larynx and trachea are procured with blood supply and bilateral recurrent and superior laryngeal nerves isolated. (B) Recipient preparation. Narrow field laryngectomy is performed with isolation and skeletonization of recipient arteries, veins, and nerves. (C) Transplantation. Transplantation with microvascular anastamoses and microneurorrhaphies is performed. a. = artery; inf. = inferior; sup. = superior; v. = vein.

toxin A (Allergan, Irvine, CA) 20 U was injected under ultrasound guidance into each submandibular gland and 30 U into each parotid gland 2 weeks prior to transplantation.

The recipient had been extensively counseled and was prepared for a laryngectomy and tracheoesophageal puncture as a fallback procedure in the event of a failed transplant. For that reason, simultaneously with retrieval, the recipient was prepared for transplantation via a narrow field laryngectomy leaving adequate distal trachea for a tracheostomy if the transplant failed (Fig. 2B). The right superior thyroid artery, bilateral transverse cervical arteries, and bilateral internal jugular veins were prepared for microvascular anastomoses. The left superior

thyroid artery was approximately 1 mm and judged too small for anastamosis. The thyroid was split and reflected inferiorly on the inferior thyroid artery. Both superior laryngeal nerves, recurrent laryngeal nerves, and the left phrenic nerve and ansa cervicalis were isolated.

Initial vascular anastomoses with donor vessels were right superior thyroid artery to recipient right superior thyroid artery and an end-to-side venous anastomosis from the right brachiocephalic vein to the recipient inferior right jugular vein (Fig. 2C). The organ was reperfused, including revascularization of the distal trachea, with a total ischemia time of 300 minutes. A second right arterial anastomosis was made between the recipient transverse cervical artery and the donor inferior thyroid artery, and epineural microneurorrhaphies were performed between donor and recipient bilateral superior and right recurrent laryngeal nerves. In an effort to minimize the risk of aspiration, redundant pharyngeal mucosa was trimmed and pharyngeal reconstruction was performed. Laryngeal suspension was accomplished between the donor thyroid cartilage and the recipient's hyoid bone with three 2-0 polypropylene sutures. The adductor branch of the donor left recurrent laryngeal nerve was sutured to the left recipient ansa cervicalis nerve trunk to maintain bulk and tone of adductor muscles on the left side. Despite having good flow via the right vascular pedicle, the left donor superior thyroid vein was anastomosed in an end-to-side fashion to the left recipient jugular vein and the left recipient transverse cervical artery was anastomosed to the left donor inferior thyroid artery. A final microneurorrhaphy was performed from the left donor recurrent laryngeal nerve in an end-to-side epineural fashion to the left recipient phrenic nerve in an attempt to provide inspiratory drive to the left posterior cricoarytenoid muscle. A cricopharyngeus muscle myotomy was then performed. After removal of the diseased larynx, trachea, and prior tracheotomy site, eight rings of trachea were transplanted to provide a tension-free anastamosis. The tracheal repairs were performed using a parachute technique on the posterior wall and interrupted sutures laterally, such that it incorporated the tracheotomy anteriorly. Because the transplanted tissue was edematous, the neck was packed and delayed primary closure was performed without tension on the first postoperative day.

Immunosuppression

Prior to the laryngeal transplant, the recipient had been maintained on tacrolimus and leflunomide for her kidney–pancreas transplant. Leflunomide had been chosen due to her BK polyoma virus infection and to prevent overt BK virus nephropathy. She had been tapered off prednisone after her kidney–pancreas transplant and was not on maintenance steroid therapy.

For her laryngotracheal transplant, she received induction immunosuppression with rabbit antithymocyte globulin 75 mg intravenously (IV) on postoperative days (PODs) 0 and 2, 50 mg IV POD 3, up to a cumulative dose of 5 mg/kg bodyweight. She received methylprednisolone 250 mg IV POD 0 and 500 mg POD 2 to 4, and mycophenolate 500 mg twice daily (bid) POD 1 to 6 and 750 mg bid until POD 14. Tacrolimus was restarted on POD 4 (dose was adjusted to keep a 12-hour trough level between 8 and 10 ng/mL). Mycophenolate was discontinued at POD 15 and leflunomide 20 mg daily was restarted due to recurrence of BK viremia. Her tacrolimus trough levels were maintained at approximately 10 ng/mL for the first 3 months post-transplant and then tapered over the next 3 months to a target range of 5 to 7 ng/mL. Our transplant center's experience with steroid-free maintenance immunosuppression following antithymocyte globulin induction in kidney transplant has been successful without increased risk of acute rejection. For that reason, and the successful management of her kidney–pancreas transplant without steroid therapy, maintenance corticosteroids were not utilized in her case.

RESULTS

Immunosuppression and Immune Response

The patient has not manifested clinical or pathologic signs of acute or chronic rejection to date. Biopsies were taken 6 hours post-transplant and on PODs 1, 14, 30, and 137. All showed normal-appearing laryngeal mucosa, with none of the features suggestive of acute rejection of laryngeal allografts (Fig. 3).[6,10–13] No donor-specific anti-HLA antibodies were detected by solid-phase assay at 6 months post-transplant.

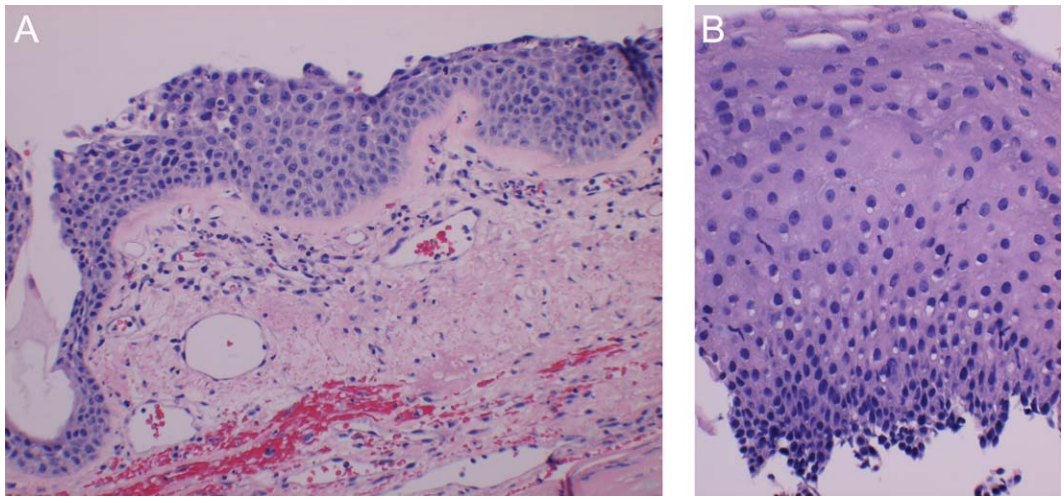

Fig. 3. Hematoxylin and eosin staining of supraglottic biopsy of transplanted larynx on postoperative day (POD) 1 and POD 137. (A) Normal-appearing mucosa and submucosa on POD 1 without evidence of acute rejection. (B) Similar normal appearance of mucosa on superficial biopsy of supraglottis on POD 137.

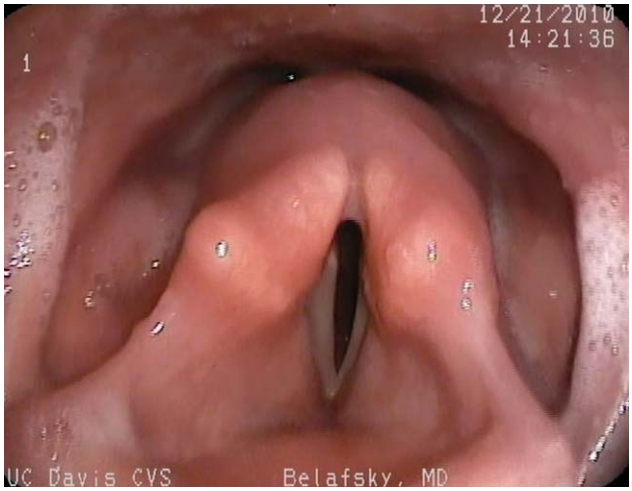

Fig. 4. Video laryngoscopic image of larynx at 9 weeks after transplant.

Airway

The larynx and trachea were inspected daily on PODs 1 to 8, 10, 14, and 20. On POD 10, the patient's tracheotomy cuff was deflated without signs of aspiration. The patient had persistent and variable supraglottic edema, worse in the aryepiglottic folds and epiglottis, that resolved by approximately 8 weeks (Fig. 4). Endoscopic assessment of vocal fold mobility at 18 months revealed evidence of synkinetic activity with limited abduction of the left vocal fold and no mobility of the right vocal fold. The trachea and subglottic larynx remain widely patent (Fig. 5), but the glottic airway is limited and precludes decannulation.

Voice

On POD 14, the patient was able to speak. Three months after surgery, laryngopharyngeal sensory testing revealed a normal laryngeal adductor response bilaterally (thresholds < 4 mmHg). Limited, primarily paradoxical vocal fold movement was noted. Ten units of botulinum toxin A was injected into each false vocal fold 5 months postoperatively in an attempt to encourage reinnervation of the adductors. This resulted in dramatic lateralization of the vocal folds and deterioration in voice quality and volume, indicating reinnervation. However, this intervention reduced her ability to tolerate oral intake, and so it was not repeated. Two months later, the tone returned, and to date the vocal folds remain minimally mobile in a median position.

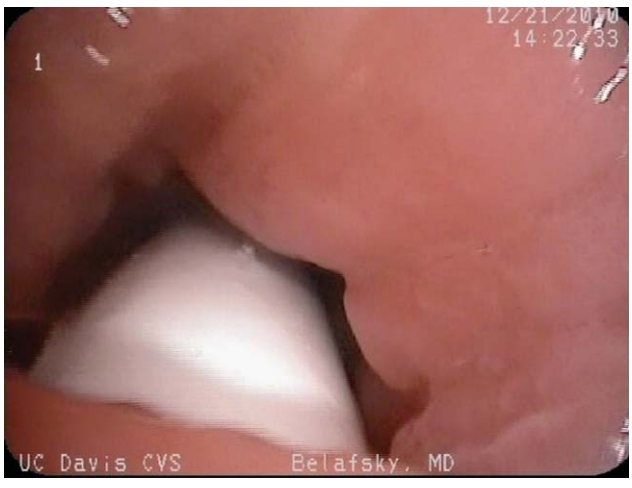

Fig. 5. Video laryngoscopic image of subglottis and trachea at 9 weeks after transplant.

Acoustic voice analysis was performed at 18 months utilizing the Computerized Speech Lab Model 4500 (KayPENTAX, Montvale, NJ). Measures of fundamental frequency, maximum phonation time, noise-to-harmonic ration, and vocal frequency and intensity range were obtained in a sound-proof environment.

Acoustic measures. Acoustic recordings from standardized speech tasks were measured and demonstrated an average sustained phonation of /a/ = 177.8 Hz and /i/ = 176 Hz. Average sentence fundamental frequency (F0) averaged 151.8 Hz, and conversational speaking was at 172.6 Hz. These values fall slightly below normal for adult females. In addition, the average noise-to-harmonic ratio (an estimate of noisiness within the voice) averaged 19.6 dB, which falls within normal limits and suggests that the stronger portion of the voice signal is the voiced portion. The maximum phonation time (MPT), a surrogate measure of glottal competence, was obtained on three successive trials during sustained vowel production. The median MPT was 17 seconds, which falls within normal limits for healthy females.

Vocal range profile. During the modified vocal range profile task, the patient demonstrated a F0 range between 164.8 Hz (E3) and 369.9 Hz (F#4), giving a vocal range of 205.1 Hz (14 ST). These values are considered to be within normal limits. Her intensity ranged between 60 and 88 dB SPL, or 28 dB SPL. This is a normal range of intensity for adult females.

Swallowing

Recovery of swallowing function was prolonged. Endoscopic evidence of pharyngeal motor integrity and epiglottic inversion returned at 4 months. For management of pooled saliva, a repeat salivary gland botulinum toxin A injection was performed 2 months postoperatively. At 5 months, a mild stenosis at the site of pharyngeal anastamoses was identified and dilated in the clinic with a 20-mm controlled radial expansion balloon (Boston Scientific, Natick, MA) to 20 mm. She was cleared for clear liquids after this procedure. She underwent daily dysphagia therapy postoperatively and was transitioned to a three times daily home therapy program guided by a mobile dysphagia application delivered on an iPod touch (iSwallow; Apple Computer, Cupertino, CA). She was cleared to eat a pureed diet at 7 months, and a repeat dilatation of the stenosis was performed 9 months postoperatively. She was placed on a regular diet 11 months postoperatively, and her gastrojejunal tube was removed at 13 months. At 18 months, she denied any symptoms

of dysphagia and had had no bronchitis or aspiration pneumonia.

Perioperative Infection Considerations and Decision Making

She was empirically started on ganciclovir due to the donor testing immunoglobulin (Ig) M and IgG positive for cytomegalovirus. Perioperatively, she was placed on broad spectrum antibiotics both for contamination from the exposed aerodigestive tract and for intraoperative assessment of the graft demonstrating bacterial infection of the tracheal mucosa. Due to her multiple vascular access procedures related to her renal failure and prior dialysis, she had markedly diminished intravenous access and required a long-term femoral line. She developed transient lung and central line infections that were successfully managed with intravenous antibiotics. She developed two episodes of mucosal candidiasis necessitating fluconazole treatment. There was one episode of tacrolimus toxicity and dehydration from diarrhea that required a brief readmission 2 months postoperatively.

DISCUSSION

This report demonstrates the successful transplantation of a larynx with a long segment of trachea. Several refinements and advances are described in this report.

First, we demonstrate successful revascularization and transplantation of a long segment of trachea. The retrieval technique as originally described by Strome was augmented by the retention of the esophageal muscles attached to the posterior wall of the trachea and by an additional inferiorly based blood supply via the inferior thyroid arteries.[5] The muscular esophagus was not incorporated into the pharyngeal repair but served to increase the amount of vascularized tissue on the posterior aspect of the membranous trachea. Although Strome's transplant was also successful, we feel the addition of the inferior blood supply via the bilateral inferior thyroid artery anastamoses contributed significant blood supply to the inferior portion of the long-segment tracheal graft and provided a redundant blood supply should there be a vascular occlusion of one of the other anastamoses. Although we cannot definitively state the necessity of this additional blood supply, anatomic studies have established the vascular contribution of the inferior thyroid artery to this portion of the trachea. We feel that this step creates a technical precedent for the future application of a fully vascularized tracheal transplant.[14,15]

Second, we describe an attempt at selective innervation. Based on the technique described by Marie, our attempt to selectively reinnervate the left vocal fold with adductor supply from the ansa cervicalis microneurorrhaphy and abductor supply from the phrenic microneurorrhaphy is the first reported attempt in a laryngeal transplant.[16,17] However, due to concerns about the possible diaphragmatic paralysis, we elected to perform an end-to-side anastomosis between the recurrent laryngeal nerve (dissected to supply only the abducting posterior cricoarytenoid) and the phrenic nerve on the left side only. Despite attempting a selective reinnervation, the resulting synkinesis and near median position of the vocal folds seen in our patient clearly demonstrate the persistent challenges of selective reinnervation of the larynx. In the future, techniques using accessory phrenic nerve or single roots of the phrenic and cable grafts directly into the posterior cricoarytenoid may be preferred. Our patient will be followed closely for signs of improvement in her airway, but for the foreseeable future, she is prepared to keep her tracheotomy. Should she have significant improvement in her airway, consideration would be made for decannulation. However, given the edema manifest in the Cleveland patient with rejection episodes, great care will be taken in this decision.

Finally, we have demonstrated the recovery of our patient and provided a timeline to complement Strome's report on functional rehabilitation in laryngeal transplantation. The early evidence of sensory innervation at 2 months and synkinetic motor innervation at 3 months postoperatively is similar to the documented recovery of the prior transplant.[18] This rapid reinnervation challenges traditional concepts and timelines of neural regeneration. This early return of sensory reinnervation likely assisted her in avoiding aspiration pneumonia. For future transplants, management of the pharynx will have to be carefully considered. Our efforts to minimize the risk of aspiration from excess pharynx and pooling of secretions may have contributed to her pharyngeal stenosis and delayed swallowing recovery. The challenges of her swallowing are perhaps unique to her longstanding diabetes and associated neuropathy, but must form part of preoperative counseling for future potential laryngeal transplant recipients.

There has been no clinical or serological sign of rejection thus far. Despite studies of laryngeal immunology in animal models of laryngeal and tracheal transplantation, little is known regarding how acute or chronic rejection presents histologically.[10,11,19] Strome describes episodes of laryngeal edema and voice deterioration as symptomatic of acute rejection in his patient.[6] More research is required. Close observation and serial histologic analysis of this and future transplanted patients will help define histologic signs of rejection. In addition, current immunogenetic techniques are able to prospectively monitor the development and determine the strength of anti-HLA antibodies directed against the donor, thus allowing early recognition of alloresponse.[20,21] In this way, it may become possible to objectively titrate immunosuppression for patients where the larynx is the only transplanted organ.

The larynx, like all composite and other allotransplants, requires life-long immunosuppression to avoid rejection. Immunosuppression is associated with a multitude of significant side effects and risks, including opportunistic infection and neoplasm.[22–24] Reasonable arguments can be made regarding the ethical concerns and merits of this procedure. The majority of potential recipients are cancer survivors who have had their

larynx removed. The risk of an immunosuppression-induced neoplasm in a cancer survivor cannot be minimized.[25] Authors have looked at the risks laryngectomy patients would be willing to accept for a functional laryngeal replacement, and in many cases, they would choose the transplant if it is made available.[26,27] Interestingly, our patient was an advanced stage uterine cancer survivor, and the decision had been previously made to transplant her kidney and pancreas and accept the risk of prolonged immunosuppression. Other ethical issues such as the cost and potential risk to her existing transplanted organs were addressed and approved by our institution ethics and investigational review board.

The improvement in our patient's quality of life affirms the importance of voice in the communication age. Although multiple techniques are available for re-establishing speech in patients following laryngectomy and in those with a nonfunctional larynx for reasons such as trauma, traditional reconstructive techniques often result in suboptimal voice.[28] Additionally, in the laryngectomy patient, they do not afford the normal passage of air from the nose and mouth into the respiratory tract. As such, many of the senses that make life enjoyable such as smell and taste are compromised. Laryngeal transplantation offers the possibility of re-establishing the normal anatomical configuration of the upper aerodigestive tract and its functions.

Our procedure has strengthened the argument that laryngeal transplantation represents a treatment option for patients who merit and desire complete laryngeal replacement. The complexities of immunosuppression, although not factors in the decision to operate on our patient, persist for future potential transplant recipients. Advances in our understanding of the human response to laryngeal allografting may lead to minimization of these ethical concerns. We agree with Strome and others that laryngeal transplantation should be reserved for a select patient population with severe traumatic injury and benign laryngeal neoplasms necessitating laryngectomy, and potentially in due course long-term survivors of advanced laryngeal cancer.[6]

CONCLUSION

In this report, we describe our experience with a laryngotracheal transplant. This description of the novel surgical modifications and our patient's recovery add significant information to the world's literature on this rare composite tissue transplant. Although it is likely that laryngeal transplantation will remain an uncommon procedure in the near future, advancements in transplant medicine offer the promise of reduced morbidity and perhaps greater numbers of candidates. With our report, physicians will be better able to counsel patients as to the expected recovery and long-term outcomes available with this procedure.

Acknowledgments

The authors thank Sharon Schauer, Lisa Yee-Isbell, Ann Sievers, Charlotte Wacker, Shannon Whitney, Rebecca Anson, Somerr Verdun, and the fellows, residents, nurses and speech pathologists who provided exceptional care to our patient.

BIBLIOGRAPHY

1. Meyer TK, Kuhn JC, Campbell BH, Marbella AM, Myers KB, Layde PM. Speech intelligibility and quality of life in head and neck survivors. *Laryngoscope* 2004;114:1977–1981.
2. Babin E, Blanchard D, Hitier M. Management of total laryngectomy patients over time: from the consultation announcing the diagnosis to long term follow-up. *Eur Arch Otorhinolaryngol* 2011;268:1407–1419.
3. Work WP, Boles R. Larynx: replantation in the dog. *Arch Otolaryngol* 1965;82:401–402.
4. Kluyskens P, Ringoir S. Follow-up of a human larynx transplantation. *Laryngoscope* 1970;80:1244–1250.
5. Strome M, Stein J, Esclamado R, et al. Laryngeal transplantation and 40-month follow-up. *N Eng J Med* 2001;344:1676–1679.
6. Knott PD, Hicks D, Braun W, Strome M. A 12-year perspective on the world's first total laryngeal transplant. *Transplantation* 2011;91:804–805.
7. Duque E, Duque J, Nieve M, et al. Management of larynx and trachea donors. *Transplant Proc* 2007;39:2076–2078.
8. Macchiarini P, Lenot B, de Montpreville V, et al. Heterotopic pig model for direct revascularization and venous drainage of tracheal allografts. Paris-Sud University Lung Transplantation Group. *J Thorac Cardiovasc Surg* 1994;108:1066–1075.
9. Birchall MA, Kingham PJ, Murison SM, et al. Laryngeal transplantation in minipigs: vascular, myologic and functional outcomes. *Eur Arch Otorhinolaryngol* 2011;268:405–414.
10. Macchiarini P, Mazmanian GM, de Montpreville V, et al. Experimental tracheal and tracheoesophageal allotransplantation. Paris-Sud University Lung Transplantation Group. *J Thorac Cardiovasc Surg* 1995;110(4 pt 1):1037–1046.
11. Birchall MA, Ayling SM, Harley R, et al. Laryngeal transplantation in minipigs: early immunological outcomes. *Clin Exp Immunol* 2012;167:556–564.
12. Strome M, Wu J, Strome S, Brodsky G. A comparison of preservation techniques in a vascularized rat laryngeal transplant model. *Laryngoscope* 1994;104:666–668.
13. Lott DG, Shipchandler TZ, Dan O, Lorenz RR, Strome M. A new mouse laryngeal transplantation rejection grading system. *Laryngoscope* 2010;120:39–43.
14. Salmeron J, Gannon PJ, Shaari CM, Urken ML. Tracheal transplantation: superior and inferior thyroid artery perfusion territory. *Laryngoscope* 1998;108:849–853.
15. Salassa JR, Pearson BW, Payne WS. Gross and microscopical blood supply of the trachea. *Ann Thorac Surg* 1977;24:100–107.
16. Marie JP. Human Bilateral Laryngeal Reinnervation: Implications for Transplantation. Phoenix, AZ: American Laryngeal Association; 2009.
17. Marie JP, Dehesdin D, Ducastelle T, Senant J. Selective reinnervation of the abductor and adductor muscles of the canine larynx after recurrent nerve paralysis. *Ann Otol Rhinol Laryngol* 1989;98:530–536.
18. Lorenz RR, Hicks DM, Shields RW Jr, Fritz MA, Strome M. Laryngeal nerve function after total laryngeal transplantation. *Otolaryngol Head Neck Surg* 2004;131:1016–1018.
19. Lorenz RR, Don O, Fritz MA, Nelson M, Strome M. Rat laryngeal transplant model: technical advancements and a redefined rejection grading system. *Ann Otol Rhinol Laryngol* 2002;111:1120–1127.
20. Everly MJ. Using HLA antibody detection, monitoring, and treatment to improve long-term allograft survival. *Clin Transpl* 2010:317–322.
21. Cai J, Terasaki PI. Post-transplantation antibody monitoring and HLA antibody epitope identification. *Curr Opin Immunol* 2008;20:602–606.
22. Sheiner PA, Magliocca JF, Bodian CA, et al. Long-term medical complications in patients surviving > or = 5 years after liver transplant. *Transplantation* 2000;15;69:781–789.
23. Ciccarelli O, Kaczmarek B, Roggen F, et al. Long-term medical complications and quality of life in adult recipients surviving 10 years or more after liver transplantation. *Acta Gastroenterol Belg* 2005;68:323–330.
24. Fishman JA. Infection in solid-organ transplant recipients. *N Engl J Med* 2007;357:2601–2614.
25. Pollard JD, Hanasono MM, Mikulec AA, Le QT, Terris DJ. Head and neck cancer in cardiothoracic transplant recipients. *Laryngoscope* 2000;110:1257–1261.
26. Buiret G, Rabilloud M, Combe C, Paliot H, Disant F, Ceruse P. Larynx transplantation: Laryngectomees' opinion poll. *Transplantation* 2007;84:1584–1589.
27. Potter CP, Birchall MA. Laryngectomees' views on laryngeal transplantation. *Transpl Int* 1998;11:433–438.
28. Clements KS, Rassekh CH, Seikaly H Johanson JA, Calhoun KH. Communication after laryngectomy. An assessment of patient satisfaction. *Arch Otolaryngol Head Neck Surg* 1997;123:493–496.