■ CASE REPORTS

Cardiac Arrest after Neuromuscular Blockade Reversal in a Heart Transplant Infant

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ARRHYTHMIAS and conduction abnormalities in heart transplant recipients can be signs of acute and chronic rejection, as well as of coronary artery disease.[1,2] Here, we report a 13-month-old, 7.5-kg heart transplant recipient with recent onset of tachypnea, decreased peripheral perfusion, and nonsustained ventricular tachycardia who developed cardiac arrest following administration of neostigmine and glycopyrrolate after undergoing an uneventful endomyocardial biopsy during general endotracheal anesthesia to exclude rejection.

Case Report

The patient was born with anomalous origin of the left coronary artery from the pulmonary artery and underwent a modified Takeuchi procedure (intrapulmonary artery baffle with autologous pericardial patch) at age 2 months. She subsequently developed ischemic cardiomyopathy secondary to occlusion of the left coronary artery repair, necessitating orthotopic heart transplantation at age 1 yr. The transplanted heart exhibited normal left ventricular systolic function, mild left ventricular hypertrophy, and mild restrictive physiology as evaluated by serial echocardiograms. Cardiac biopsies were negative for rejection; however, myocellular edema was present initially, consistent with postpreservation ischemia–reperfusion injury of the allograft.

A week before the events that are the subject of this report and while appearing well, the patient underwent uneventful placement of a right subclavian Broviac catheter during general endotracheal anesthesia. This anesthetic consisted of 50% N_2O, 50% O_2, fentanyl (3 μg/kg), ketamine (3 mg/kg), cisatracurium (0.5 mg/kg), and isoflurane (up to 0.5% end-tidal concentrations). She was in sinus rhythm, and her heart rate varied between 110 and 140 beats/min. Residual neuromuscular blockade was reversed with neostigmine (0.08 mg/kg) and glycopyrrolate (0.016 mg/kg) infused into a rapidly running peripheral intravenous catheter over 1 min; during this interval, the heart rate increased from 110 to 160 beats/min. The trachea was extubated without any complications.

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Approximately 1 week later, she developed nonsustained ventricular tachycardia. An endomyocardial biopsy was therefore scheduled to assess for rejection. An echocardiogram performed the day before the biopsy showed qualitatively good biventricular function. Serum electrolytes, calcium, and magnesium concentrations were all within their respective normal ranges. However, before the procedure, the patient was noted to be tachypneic, with evidence of decreased peripheral perfusion. Her vital signs were as follows: heart rate, 135 beats/min; respiratory rate, 38 breaths/min; and blood pressure, 90/60 mmHg. After placing standard noninvasive monitors, anesthesia was induced with etomidate (0.2 mg/kg), fentanyl (2 μg/kg), and cisatracurium (0.2 mg/kg) and maintained with isoflurane (up to 0.5% end-tidal concentration). The average blood pressure was 90/50 mmHg. She was in sinus rhythm with a heart rate between 100 and 120 beats/min. Transvenous endomyocardial biopsies were obtained without complications. The capillary wedge pressure was 15 mmHg. She was weaned from anesthesia, and neuromuscular blockade was reversed with neostigmine (0.07 mg/kg) and glycopyrrolate (0.014 mg/kg) infused into a rapidly running peripheral intravenous catheter over 1 min. These were mixed together and administered in the same syringe. Subsequent event debriefing and case reviews yielded no evidence of drug administration errors, including incorrect doses or incorrect drugs. Her heart rhythm progressed from sinus bradycardia to asystole within 2–3 min, accompanied by circulatory collapse, which was unresponsive to cardiopulmonary resuscitation (which included external chest compressions, repeated epinephrine boluses, calcium gluconate, and attempts at direct current cardioversion) and transvenous ventricular pacing. Ice was placed around the head to induce hypothermia, and fentanyl (25 μg/kg), pancuronium (0.2 mg/kg), and midazolam (0.2 mg/kg) were administered. Cardiopulmonary resuscitation was continued while the patient was placed on extracorporeal membrane oxygenation in the cardiac catheterization laboratory.[3] Time from onset of cardiac arrest to full flow extracorporeal membrane oxygenation was 30 min; a percutaneous 6-French long sheath was positioned across the atrial septum to decompress the left ventricle. After achieving full extracorporeal membrane oxygenation flow and with improved coronary perfusion, ventricular function recovered. The patient was transferred to the cardiac intensive care unit with a blood pressure of 100/70 mmHg and a heart rate of 45–65 beats/min.

A presumptive diagnosis of humoral rejection was made; thus steroids and intravenous gammaglobulin were administered and plasmapheresis was performed. In the cardiac intensive care unit, the patient's heart rate was 120 beats/min, and the rhythm was sinus. The arterial blood pressure was 150/84 mmHg. The patient was started on milrinone (1 μg · kg^{-1} · min^{-1}) and sodium nitroprusside (5 μg · kg^{-1} · min^{-1}). She was sedated with fentanyl and midazolam. The initial serum lactate level was 5.8 mM and decreased to 1.4 over the next 7 h. The biopsy showed grade 0 cellular rejection (*i.e.*, no cellular rejection; table 1) and changes consistent with humoral rejection, including coronary capillary endothelial swelling and disruption, focal areas of microvascular occlusion by thrombus and leukocytes, and interstitial edema. Serial cardiac ultrasounds demonstrated improvement in ventricular function. Milrinone and sodium nitroprusside were weaned off, and extracorporeal membrane oxygenation was discontinued 3.5 days afterward. No gross neurologic injury was documented, and the trachea was extubated 8 days

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Table 1. Modified International Society for Heart Lung Transplantation Grading for Heart Transplant Biopsies

Grade 0	No rejection
Grade 1, mild	Interstitial and/or perivascular infiltrate with up to one focus of myocyte damage
Grade 2, moderate	Two or more foci of infiltrate with associated myocyte damage
Grade 3, severe	Diffuse infiltrate with multifocal myocyte damage $\pm$ edema $\pm$ hemorrhage $\pm$ vasculitis

Modified from Stewart *et al.*[8]; with permission.

after the arrest. The patient was discharged to the cardiac ward in satisfactory condition 2 weeks later.

The patient returned for cardiac biopsy 1 month after these events and appeared well. Cardiac ultrasound showed normal left ventricular systolic function. The biopsy was performed *via* the right femoral vein because of jugular venous obstruction. This procedure was performed without complications during intravenous sedation with ketamine (1 mg/kg) and morphine (0.1 mg/kg) and caudal anesthesia (1 ml/kg of 0.25% plain bupivacaine). The capillary wedge pressure was 8 mmHg. Histologic evidence of rejection was not present.

Discussion

In this infant, ventricular tachycardia, clinical deterioration, and elevated cardiac filling pressures (roughly twice her previous and subsequent values) suggested the possibility of rejection; features of humoral rejection were present on endomyocardial biopsy. The development of asystole after the administration of neostigmine and glycopyrrolate in this patient was an unexpected event because the allograft had been in place for only 1 month, which likely excludes the possibility of parasympathetic reinnervation. It is difficult to discern whether this event was related to the ongoing rejection process, the use of neostigmine, or the combination.

Clinical signs and symptoms of rejection are variable, nonspecific (*e.g.*, tachycardia, malaise, fever), and frequently subtle. As demonstrated at autopsy, the conduction system, as well as the sinus and atrioventricular nodes, can be targets for rejection in heart transplant recipients. Sinus node dysfunction can be a sign of acute or chronic rejection in this population. Sinus arrest has occurred in heart transplant patients in the setting of rejection necessitating artificial pacemaker therapy.[4] Other rhythm abnormalities, such as atrial flutter and fibrillation, conduction block, and ventricular rhythm disturbances, can also occur.

It has been shown that neostigmine reduces the heart rate in adult heart transplant recipients without evidence of rejection and that the magnitude of reduction is less when compared with patients with native hearts. In heart transplant patients, slowing of the heart rate after neostigmine was more pronounced after 6 months post transplantation than in the first 6 months, indicating some degree of parasympathetic reinnervation in the

donor heart.[5] However, when the heart transplant patients were given atropine, the heart rate increase in response to atropine was similar and slower than in the patients with native hearts, suggesting limited parasympathetic reinnervation of the transplanted heart. Sinus arrest and asystole have been noted after reversal of neuromuscular blockade with neostigmine and glycopyrrolate in adult heart transplant recipients, with no clinical evidence of rejection years after transplantation.[6,7] We postulate that our patient's conduction system was involved during the rejection episode. She had developed nonsustained ventricular tachycardia before the myocardial biopsy. The heart rhythm and function recovered after plasmapheresis, steroids, and immunosuppressive therapy.

Currently, at least two broad types of rejection episodes are recognized after transplantation: cellular and humoral. The former is characterized by several features that include primarily activated lymphocytic infiltration with a resultant local inflammatory process and the development of myocyte necrosis (table 1). Current immunosuppression regimens for the most part are targeted to the T-cell signaling pathways underlying cellular rejection. However, cellular rejection may account for a significantly lower number of rejection episodes accompanied by cardiac functional deterioration than previously thought.

Humoral rejection is caused by a T-cell response mediated by alloantibodies that are mainly directed against human leukocyte antigen class I and II molecules. A major risk factor is likely to be increased antigen exposure and allosensitization from events such as previous surgeries, use of homograft material to repair congenital heart defects, multiple blood product exposures, and previous pregnancy[8]; all but the last of these factors were present in this patient. The result is an inflammatory process that is primarily mediated by alloantibodies and activated complement; it is characterized by capillary endothelial swelling and damage, intravascular coagulation and macrophage accumulation, interstitial edema and hemorrhage, pericapillary neutrophil infiltration, and finally focal ischemia. More advanced immunohistologic and immunofluorescence studies can reveal immunoglobulin (IgA, IgM, and/or IgG) and complement (C4d, C3d, or C1q) deposition on capillaries and CD68 staining of intracapillary macrophages. There is accumulating evidence that humoral rejection is a significant cause of "biopsy-negative" rejection episodes that are potentially significant causes of acute or subacute contractile dysfunction and graft failure, as well as overall mortality.[8-10] Simultaneous histologic evidence for both cellular and humoral rejection can be found in some patients.

Contrary to the adult heart transplant experience with longer-standing allografts developing bradycardia and asystole after neostigmine in the absence of rejection,

our patient's young allograft developed asystole after administration of neostigmine and glycopyrrolate in the setting of probable humoral rejection. We felt comfortable reversing the neuromuscular blockade in this patient given the relatively brief interval since her transplant (*i.e.*, small likelihood of reinnervation) and because no bradycardia or asystole developed after the use of neostigmine and glycopyrrolate when she underwent anesthesia for the Broviac catheter placement a week earlier. We speculate that she developed the cardiac manifestations of humoral rejection over this period; clinically, she did manifest evidence of myocardial dysfunction such as tachypnea and decreased perfusion (although a contemporaneous echocardiogram showed "normal" systolic function). It is also tempting to speculate that the patient's ventricular tachycardia and enhanced sensitivity to cholinesterase inhibition were due to alloantibodies reactive against epitopes on cardiac conducting tissue; it is equally possible that these events were due to local inflammation and ischemia.

If correct, this sequence of events also highlights some of the perioperative and anesthetic management challenges posed by these patients. The clinical signs of rejection can be nonspecific and relatively insensitive. Echocardiograms are suboptimal for detecting rejection, particularly during the initial weeks and months after transplantation, in part because the technique is confounded by changes that occur as a consequence of "normal" recovery from ischemia–reperfusion injury (*e.g.*, increased myocardial mass and edema) and a relative insensitivity to diastolic dysfunction (at least using standard clinical examination techniques); furthermore, it has been our impression that echocardiographic evidence of systolic dysfunction due to rejection can lag behind the parenchymal rejection process. Other techniques to detect rejection, including use of expression microarrays and magnetic resonance methods, remain in various stages of development. As a result, endomyocardial biopsy remains the accepted standard in most centers for surveillance and detection of rejection. It is noteworthy that cellular rejection is typically quite heterogeneous, and thus biopsy (which typically obtains four to seven specimens from right ventricular endocardium only) is potentially a hit-or-miss proposition that can have a false-negative rate of between approximately 20% and 60%. It is also worth noting that a substantial number of pediatric transplant recipients require deep sedation or general anesthesia to tolerate the procedure (and hence obtain a diagnosis) successfully, and thus pediatric anesthesiologists are routinely confronted with providing this care without knowing the rejection or true functional status of the patient. Overall, this case points out the need to maintain a high index of suspicion for the presence of rejection— both cellular and humoral— and its manifestations in cardiac transplant recipients, regardless of their clinical findings. With specific reference to reversal of neuromuscular blockade, it raises the question of avoiding the use of muscle relaxation in instances where antagonism of the blockade will be necessary. Alternatively, using short-acting agents that permit adequate recovery of neuromuscular junction function without use of cholinesterase inhibiting agents or, perhaps in the near future, use of specific combinations of neuromuscular blocking-reversal agents that do not share this side effect profile (*e.g.*, rocuronium–sugammadex), should be considered.

References

1. Kertesz NJ, Towbin JA, Clunie S, Fenrich AL, Friedman RA, Kearney DL, Dreyer WJ, Price JF, Radovancevic B, Denfield SW: Long-term follow-up of arrhythmias in pediatric orthotopic heart transplant recipients: Incidence and correlation with rejection. J Heart Lung Transplant 2003; 22:889–93

2. Park JK, Hsu DT, Hordof AJ, Addonizio LJ: Arrhythmias in pediatric heart transplant recipients: Prevalence and association with death, coronary artery disease, and rejection. J Heart Lung Transplant 1993; 12:956–64

3. Allan CK, Thiagarajan RR, Armsby LR, del Nido PJ, Laussen PC: Emergent use of extracorporeal membrane oxygenation during pediatric cardiac catheterization. Pediatr Crit Care Med 2006; 7:212–9

4. Blanche C, Czer LS, Trento A, Fishbein MC, Doan D, Jordan S, Utley CB, Barath P, Matloff JM: Bradyarrhythmias requiring pacemaker implantation after orthotopic heart transplantation: Association with rejection. J Heart Lung Transplant 1992; 11:446–52

5. Backman SB, Fox GS, Stein RD, Ralley FE: Neostigmine decreases heart rate in heart transplant patients. Can J Anaesth 1996; 43:373–8

6. Beebe DS, Shumway SJ, Maddock R: Sinus arrest after intravenous neostigmine in two heart transplant recipients. Anesth Analg 1994; 78:779–82

7. Bjerke RJ, Mangione MP: Asystole after intravenous neostigmine in a heart transplant recipient. Can J Anaesth 2001; 48:305–7

8. Stewart S, Winters GL, Fishbein MC, Tazelaar HD, Kobashigawa J, Abrams J, Andersen CB, Angelini A, Berry GJ, Burke MM, Demetris AJ, Hammond E, Itescu S, Marboe CC, McManus B, Reed EF, Reinsmoen NL, Rodriguez ER, Rose AG, Rose M, Suciu-Focia N, Zeevi A, Billingham ME: Revision of the 1990 working formulation for the standardization of nomenclature in the diagnosis of heart rejection. J Heart Lung Transplant 2005; 24:1710–20

9. Casarez TW, Perens G, Williams RJ, Kutay E, Fishbein MC, Reed EF, Alejos JC, Levi DS: Humoral rejection in pediatric orthotopic heart transplantation. J Heart Lung Transplant 2007; 26:114–9

10. Kaczmarek I, Deutsch MA, Sadoni S, Brenner P, Schmauss D, Daebritz SH, Weiss M, Meiser BM, Reichart B: Successful management of antibody-mediated cardiac allograft rejection with combined immunoadsorption and anti-CD20 monoclonal antibody treatment: Case report and literature review. J Heart Lung Transplant 2007; 26:511–5

Potential Mucosal Injury Related to Continuous Aspiration of Subglottic Secretion Device

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ASPIRATION of oropharyngeal secretions that pool above the cuff of the endotracheal tube has been one of many factors implicated in the pathogenesis of ventilator-associated pneumonia.[1–3] The advent of continuous aspiration of subglottic secretion (CASS) devices has generated interest in their potential to minimize ventilator-associated pneumonia risk, especially when prolonged tracheal intubation is anticipated.[4–6] However, despite their potential benefits, there may be adverse consequences of device use that may only be recognized as use increases. We report two cases of tracheal injury that may be attributable to the use of a CASS device.

Case Reports

Case 1

A previously healthy 36-yr-old man was admitted to the trauma service with multiple orthopedic injuries, splenic laceration, shock, and hypothermia sustained in a roll-over motor vehicle accident. Tracheal intubation was completed with a Mallinckrodt Hi-Lo Evac® (Mallinckrodt, Inc., St. Louis, MO) CASS endotracheal tube (ETT) in the emergency department. The CASS feature was used according to the manufacturer's published guidelines and maintained with regulated low-wall suction (-20 cm H_2O, or less) within the intensive care unit. During a tracheostomy performed on hospital day 35, the surgeons noted "maceration" of the tracheal mucosa in a linear distribution adjacent to the tracheostomy site. Subsequent fiberoptic evaluation demonstrated a tracheoesophageal fistula, which was confirmed with a barium swallow esophagram. Endoscopy demonstrated that the fistula and tracheal injury extended slightly above where the previous endotracheal tube cuff was in contact with the mucosa along the posterior aspect of the trachea to the level of the cricoid cartilage. During surgical correction, the tracheal origin of the tracheoesophageal fistula was identified at the likely position of the CASS ETT suction port orifice. The patient was subsequently

weaned from ventilatory support and was discharged to a rehabilitation facility after a total of 5 months.

Case 2

A previously healthy 48-yr-old woman was admitted to the trauma service with inhalational injury and orthopedic injuries sustained from a second story fall while fleeing a house fire. The patient's trachea was intubated with a Mallinckrodt Hi-Lo Evac® ETT secondary to reports of inhalation thermal injuries. The CASS device was maintained with regulated low-wall suction (-20 cm H_2O, or less) according to manufacturer's guidelines. After multiple failed attempts at weaning mechanical ventilatory support, the patient underwent a tracheostomy on hospital day 22. Extensive tracheal mucosal injury with a fistulous tract in the posterior wall of the trachea was noted 1.5 cm above the tracheostomy site extending cephalad an additional 2–3 cm. The surgeon felt that the tracheal component of the fistula was above where the cuff of the endotracheal tube was in contact with the trachea, a location not generally seen with tracheoesophageal fistula attributed to endotracheal cuff mucosal injury. Upon further discussion with the surgeon, the injury was localized to the area underlying the suction port of the CASS ETT. Definitive repair of the tracheoesophageal fistula was completed on hospital day 30, and the patient was discharged to a rehabilitation facility on hospital day 44.

Discussion

Oropharyngeal, laryngeal, and tracheal structures in contact with an artificial airway are at increased risk for injury.[7–15] It is well established that risk factors for airway injury include cuff pressures, ETT diameter, duration of intubation, and patient movement. Donnelly *et al.*[12] described tracheal injury in many cases within an hour of ETT placement, and longer intubations resulted in broader and deeper ulceration. It is reasonable to associate tracheal injury and subsequent ulceration observed with artificial airways with increased risk for development of a fistula connecting the trachea and the esophagus.

The suction port of the current CASS endotracheal tube (fig. 1) may add another potential etiology for tracheal injury. An incidental notation of tracheal mucosal injury in sheep at the level of the CASS suction port was reported by Berra *et al.*[6] during their investigation of CASS efficacy. Our two cases of tracheoesophageal fistula along with this report prompted us to investigate the anatomical relation of the suction port in human patients. Retrospective review of the available computed tomography (CT) images from our two patients with tracheoesophageal fistula revealed suction port and mucosal relations that may have been conducive to mucosal
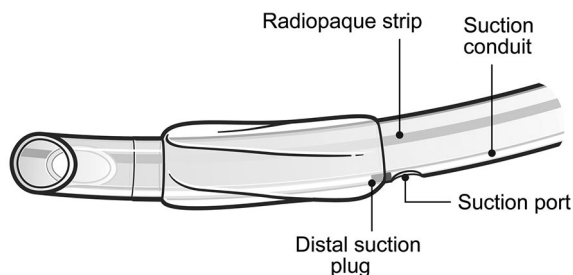
Fig. 1. Picture of continuous aspiration subglottic secretion device with schematic illustrating unique structural components. Suction conduit consists of small diameter lumen incorporated within endotracheal tube posterior wall and opens to trachea at the suction port just proximal to the endotracheal cuff. Distal suction plug consists of radiodense plastic that occludes the suction conduit distal to the suction port, ensuring that suction force is directed at suction port orifice.

injury with tracheal mucosa incorporated into the suction port. To better assess this anatomical relation of the suction port and laryngeal mucosa, a high-resolution CT scan of the neck was obtained in a separate patient who was undergoing pulmonary CT angiography for a suspected pulmonary embolism and who was intubated with an Evac® ETT (fig. 2). This high-resolution CT scan demonstrated invagination of the posterior tracheal mucosa into the suction port orifice of the ETT, and asymmetric inflation of the cuff (figs. 2A and B). Of note in this patient who did not develop clinically apparent tracheal injury is the proximity of the invagination of mucosa into the suction port and the orogastric tube in the esophagus. This tube–mucosa relation is further illustrated in reconstructed CT images (fig. 3). Similar invaginations of tracheal mucosa into the suction port of the ETT were observed in scans from other patients who had the Evac® ETT (not shown).

In an evaluation of 41 autopsy specimens from patients with an *antemortem* artificial airway, Stauffer *et al.*[14] reported mucosal ulceration at the epiglottis in 12%, at the posterior glottic rim in 51%, and at the level of the tracheal cuff in 15%. In both of our cases, the site of mucosal injury was posterior and immediately proximal to the ETT cuff, extending cephalad up to the cricoid cartilage. This distribution of mucosal injury, which is not a commonly reported location for airway injury, corresponds to the position where the suction port

would have been located. The linear distribution of the lesions may be attributed to cephalad–caudad displacement of the suction orifice due to endotracheal tube movement commonly seen with patient positioning and/or ETT adjustments.

There are a few unique features of the CASS ETT that distinguish it from other ETT designs. Most importantly, there is a suction port located in the posterior (dorsal) aspect of the tube at the proximal attachment of the cuff membrane (fig. 1). As recommended by the manufacturer, this port is connected to a regulated suction device not to exceed −20 mmHg to keep the area above the cuff free from pooled secretions that migrate down from the oropharynx. The additional structural elements of the CASS ETT design may further contribute to mucosal injury. To accommodate the suction conduit lumen, the diameter of the ETT has been increased slightly, a factor that has been documented to increase the risk for airway injury.[13] In a case report by Siobal *et al.*,[15] the rigidity of the Hi-Lo Evac® ETT was suspected to have contributed to mucosal injury and subsequent development of a tracheoinnominate artery fistula during the prolonged intubation of a patient with extensive burn injuries. In their evaluation of the CASS ETT, they reported significantly greater tube rigidity compared with other ETTs tested. It is conceivable that decreased flexibility of an ETT could result in increased pressure at points of contact between the tube and the airway, and potentially increase the risk of injury to the airway.

The cuff associated with the Hi-Lo Evac® ETT is of the high-volume, low-pressure type, which seems to be designed to suspend the tracheal mucosa away from the suction port when the cuff is inflated. What we observed, however, was that the ETT cuff assumed an asymmetrical shape because of nonuniform volume distribution (figs. 2C and D). Failure of port orifice suspension would subject the adjacent mucosa to the applied suction force. It is likely that the increased rigidity of the CASS tube places disproportionate pressure along the dorsal aspect of the tube, contributing to the observed cuff asymmetry.

The images we present demonstrate mucosal invagination into the CASS ETT suction port orifice and reveal a potential design flaw. It is possible that mucosal injury is sustained by exposure to prolonged suction and/or a "cheese grater" shearing effect of the suction port orifice against the mucosa with endotracheal tube movement *in situ*. Although the mucosal entrapment within the CASS suction port visualized on CT imaging does not define causality of tracheoesophageal fistula, it is reasonable to identify it as a potential source of mucosal injury. Of certainty is that the etiology of tracheoesophageal fistula is multifactorial. We recognize that the risks of tracheoesophageal fistula must be weighed against the risks of ventilator-associated pneumonia and acknowledge that the Evac® ETT may also be mucosal protective against chemical injury from laryngopharyngeal reflux pooling
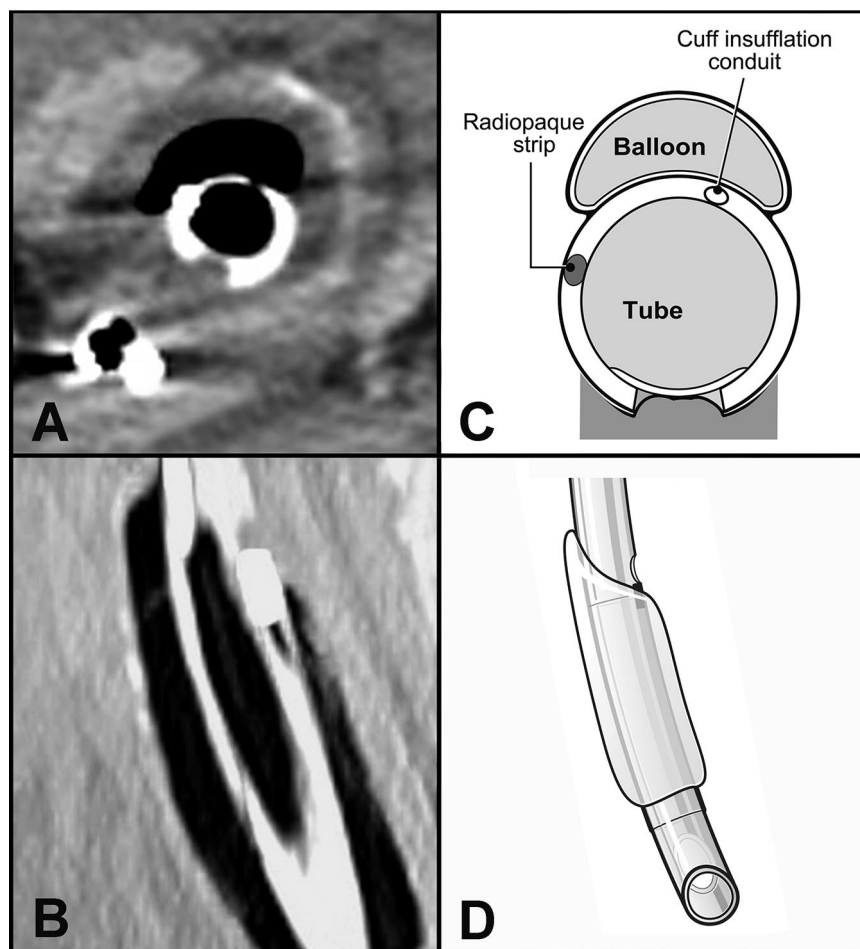
Fig. 2. Cross-section slice of computed tomographic imaging at level of continuous aspiration subglottic secretion suction port (*A*) with corresponding longitudinal section (*B*) with illustrations demonstrating mucosal entrapment (*C*) and asymmetrical volume distribution of endotracheal cuff (*D*) contributing to direct mucosal contact of the suction orifice.

and bacterial colonization of injured mucosa. It is also possible that design modifications and/or intermittent suction protocols[16] may lessen the risk for mucosal injury while maintaining ventilator-associated pneumonia prophylaxis.
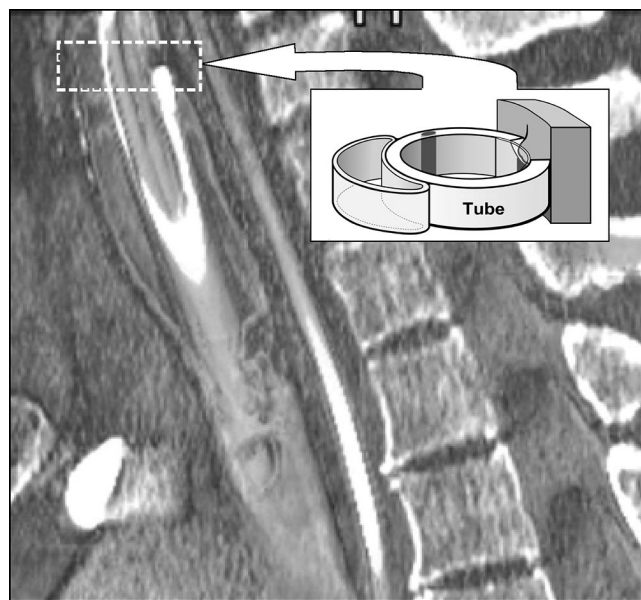

Fig. 3. Three-dimensional computed tomographic reconstruction demonstrating mucosal–suction port relation at −15 cm H₂O suction with invagination of tracheal mucosa into suction port. Schematic overlay highlights the cross-sectional interpretation of tissue–suction port interaction.

References

1. Kollef MH: Prevention of hospital-associated pneumonia and ventilator-associated pneumonia. Crit Care Med 2004; 32:1396–405

2. Diaz E, Rodriguez AH, Rello J: Ventilator-associated pneumonia: Issues related to the artificial airway. Respir Care 2005; 50:900–6

3. Chastre J, Fagon JY: Ventilator-associated pneumonia. Am J Respir Crit Care Med 2002; 165:867–903

4. Valles J, Artigas A, Rello J, Bonsoms N, Fontanals D, Blanch L, Fernandez R, Baigorri F, Mestre J: Continuous aspiration of subglottic secretions in preventing ventilator-associated pneumonia. Ann Intern Med 1995; 122:179–86

5. Kollef MH, Skubas NJ, Sundt TM: A randomized clinical trial of continuous aspiration of subglottic secretions in cardiac surgery patients. Chest 1999; 116:1339–46

6. Berra L, De Marchi L, Panigada M, Yu ZX, Baccarelli A, Kolobow T: Evaluation of continuous aspiration of subglottic secretion in an *in vivo* study. Crit Care Med 2004; 32:2071–8

7. Hamdan AL, Sibai A, Rameh C, Kanazeh G: Short-term effects of endotracheal intubation on voice [published on-line ahead of print August 11, 2006]. J Voice

8. Colice GL, Stukel TA, Dain B: Laryngeal complications of prolonged intubation. Chest 1989; 96:877–84

9. Santos PM, Afrassiabi A, Weymuller EA Jr: Risk factors associated with prolonged intubation and laryngeal injury. Otolaryngol Head Neck Surg 1994; 111:453–9

10. Sue RD, Susanto I: Long-term complications of artificial airways. Clin Chest Med 2003; 24:457–71

11. Weymuller EA Jr, Bishop MJ, Fink BR, Hibbard AW, Spelman FA: Quantification of intralaryngeal pressure exerted by endotracheal tubes. Ann Otol Rhinol Laryngol 1983; 92:444–7

12. Donnelly WH: Histopathology of endotracheal intubation: An autopsy study of 99 cases. Arch Pathol 1969; 88:511–20

13. Bishop MJ, Hibbard AJ, Fink BR, Vogel AM, Weymuller EA Jr: Laryngeal injury in a dog model of prolonged endotracheal intubation. ANESTHESIOLOGY 1985; 62:770–3

14. Stauffer JL, Olson DE, Petty TL: Complications and consequences of endotracheal intubation and tracheotomy: A prospective study of 150 critically ill adult patients. Am J Med 1981; 70:65–76

15. Siobal M, Kallet RH, Kraemer R, Jonson E, Lemons D, Young D, Campbell AR, Schecter W, Tang J: Tracheal-innominate artery fistula caused by the endotracheal tube tip: Case report and investigation of a fatal complication of prolonged intubation. Respir Care 2001; 46:1012–8

16. Smulders K, van der Hoeven H, Weers-Pothoff I, Vandenbroucke-Grauls C: A randomized clinical trial of intermittent subglottic secretion drainage in patients receiving mechanical ventilation. Chest 2002; 121:858–62