Early Surgical Management of Thermal Airway Injury: A Case Series

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Inhalation injury is an independent risk factor in burn mortality, imparting a 20% increased risk of death. Yet there is little information on the natural history, functional outcome, or pathophysiology of thermal injury to the laryngotracheal complex, limiting treatment progress. This paper demonstrates a case series ($n = 3$) of significant thermal airway injuries. In all cases, the initial injury was far exceeded by the subsequent immune response and aggressive fibroinflammatory healing. Serial examination demonstrated progressive epithelial injury, mucosal inflammation, airway remodeling, and luminal compromise. Histologic findings in the first case demonstrate an early IL-17A response in the human airway following thermal injury. This is the first report implicating IL-17A in the airway mucosal immune response to thermal injury. Their second and third patients received Azithromycin targeting IL-17A and showed clinical responses. The third patient also presented with exposed tracheal cartilage and underwent mucosal reconstitution via split-thickness skin graft over an endoluminal stent in conjunction with tracheostomy. This was associated with rapid abatement of mucosal inflammation, resolution of granulation tissue, and return of laryngeal function. Patients who present with thermal inhalation injury should receive a thorough multidisciplinary airway evaluation, including early otolaryngologic evaluation. New early endoscopic approaches (scar lysis and mucosal reconstitution with autologous grafting over an endoluminal stent), when combined with targeted medical therapy aimed at components of mucosal airway inflammation (local corticosteroids and systemic Azithromycin targeting IL-17A), may have potential to limit chronic cicatricial complications.

Acute thermal injuries requiring medical treatment affect nearly half a million Americans each year, with approximately 40,000 hospitalizations and 3275 deaths annually.¹ It is estimated that between 10% and 20% of the inpatient burn admissions in the United States involve concomitant inhalation injury.^{2,3} Inhalation injury itself is an independent predictor of death,⁴ imparting a 20% to 27.6% increase in mortality.⁵⁻⁷ Although the complex pathophysiology of thermal injury to the laryngotracheal complex and lower airways remains poorly understood, acute tissue injury is presumed to result from direct thermal injury compounded by chemical exposure (carbon monoxide, cyanide), reactive immune responses to these processes, as well as secondary infection and hypoxia.⁸ These insults are compounded by local tissue interactions with an endotracheal tube and mechanical ventilation. Chronic complications of laryngotracheal inhalation arise from a combination of cartilaginous framework destruction coupled with mucosal fibrosis.

The acute management thermal airway injury relies on a multidisciplinary approach involving dedicated burn units,

trauma teams, anesthesiologists, pulmonologists, and otolaryngologists. Although these collaborative efforts have translated to significant improvements in outcome over the past 50 years, long-term functional implications for survivors of inhalation injury remain poorly defined.⁸ Insufficient evidence exists to establish the natural history of thermal injury to the laryngotracheal complex or define predictors of functional outcome. With increasing survival driven by primary responders and dedicated burn units, early recognition and treatment of thermal injuries to the laryngotracheal complex is emerging as a key topic for future progress in burn care.^{9,10}

Among the limited published clinical data, the two series widely regarded at the foundation of current clinical practice include 11 patients from Dr. William Montgomery's Massachusetts Ear and Eye Infirmary Otolaryngology service in 1989,¹¹ and 18 patients from Dr. Hermes Grillo's Massachusetts General Hospital Thoracic surgery group in 1993.¹² Both series primarily focus on management of the chronic upper airway complications of thermal injury. The intervening decades since publication of these landmark works have seen extraordinary advances in the science and surgical therapy for benign airway stenosis. Two of the largest shifts have been a trend toward early endoscopic intervention to postintubation airway injuries¹³ and enhanced medical therapy to blunt the component of dysregulated host immune response compounding initial endolaryngeal injury. Our series of three patients illustrates application of these emerging concepts to the management of thermal airway injury, offers novel insights into the cytokine profile of reactive host inflammation, and supports a role for early aggressive endoscopic surgical therapy with mucosal reconstitution and endoluminal stenting.

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CASE SERIES

Case 1

A 24-year-old nondiabetic male carnival “fire-breather” presented to a Burn Intensive Care Unit (ICU) with superficial, partial thickness burn to the face, chest, and left hand comprising 4% of his total body surface area (TBSA). The patient was intubated in the field for airway protection and therefore no specialized airway examination was conducted to grade the patient’s initial inhalation injury. Despite meeting ventilatory parameters, he failed extubation on postinjury day 1 in the Burn ICU secondary to stridor and progressive respiratory distress. He again failed extubation on postinjury day 5 because of progressive respiratory distress and stridor. The otolaryngology service was consulted for emergent airway evaluation.

On evaluation, the patient was in acute respiratory distress, was found to have bilateral true vocal fold immobility, and underwent emergent operative endoscopy. Direct laryngoscopy and bronchoscopy revealed Grade 3 (via Endorf and coworkers’ grading scale¹⁴) mucosal sloughing (in decreasing severity) through the supraglottis, glottis, subglottis, and proximal trachea (Figure 1). In contrast, the carina and bilateral mainstem bronchi had preserved mucosal integrity with diffuse erythema. Notably, the oral cavity and oropharynx were spared tissue injury. Due to the unusual nature of this individual’s injury, we have graded the inhalation injury based on the distal tracheal mucosa and proximal bronchi as the injury to the larynx/glottis is more of a direct thermal injury than the indirect chemical tracheobronchitis that the Endorf grading scale was meant to evaluate. Given the severity of his laryngotracheal injuries, he underwent tracheotomy. Repeat direct laryngoscopy and bronchoscopy 5 days later (postinjury day 10) revealed progressive mucosal sloughing involving the airway from the supraglottis through bilateral mainstem bronchi (Figure 1). Additionally, progressive posterior glottic scar bands were identified. These were lysed, injected with triamcinolone acetate, and delicately mobilized with a control radial expansion balloon catheter (Boston Scientific 15–16.5–18 mm balloon, Marlborough, MA). Biopsies of the glottis and right mainstem bronchus (MSB) were taken at this time to characterize the inflammatory process occurring in the airway. Immunohistochemistry from both biopsies showed abundant subepithelial IL-17A protein (Figure 1).

The patient subsequently underwent serial scar lysis, steroid injection to the bilateral cricoarytenoid joints (CAJ), and subglottis and balloon dilation at 3- to 4-week intervals for the next 6 months. Despite these aggressive efforts, direct laryngoscopy and bronchoscopy at 6 months postinjury revealed bilaterally fixed vocal cords and cicatricial scarring at the bronchial mainstem (Figure 1). Pulmonary function tests at this time revealed significant restrictive lung disease (Figure 1). Supraglottic biopsy at the false vocal fold (FVF) 6 months postinjury confirmed dense reactive fibrosis with abundant acellular collagen when highlighted with blue trichrome staining. During their hospitalization, this patient received both inhaled albuterol and N-acetylcysteine as part of the respiratory protocol of the Burn ICU.

Case 2

A nondiabetic 32-year-old male was admitted to the Burn ICU after sustaining 50% TBSA full-thickness burns to the face, neck, back, chest, abdomen, and bilateral upper and lower extremities during a house fire. The patient was in significant respiratory distress with inspiratory stridor when he was found on the scene. Due to soot and airway edema, they were unable to visualize the airway, and he was initially stabilized with a laryngeal mask airway (LMA). On arrival to the Burn ICU, he was successfully intubated and found to have a grade III inhalation injury.

On postburn day 6, he was taken to the OR for airway evaluation and skin grafting. Direct laryngoscopy revealed significant thermal injury to his glottis and immediate subglottis with anthracotic debris and glottic level edema obstructing the laryngeal inlet (Figure 2). Bilateral palpation of the CAJ demonstrated good mobility. Given the degree of laryngeal edema, he was transitioned to a tracheostomy. He was started on Azithromycin 250 mg PO every other day (QOD) and a BID proton pump inhibitor (PPI), and maintained on this regime for 8 weeks. During their hospitalization, this patient received inhaled albuterol as part of the respiratory protocol of the Burn ICU (PRN for wheezing), however, did not at any point receive any inhaled N-acetylcysteine.

Bedside fiberoptic exam postburn day 10 identified bilateral immobile vocal folds. Operative endoscopy day 17 postburn revealed healing anterior laryngeal mucosa (Figure 2) and posterior glottic mucosal webbing with pronounced granulation tissue. Bilateral CAJ were injected with corticosteroids (2 cc of Kenalog40 TM) and gently mechanically dilated. Bronchoscopy found no subglottic or tracheal mucosal ulceration or stricture, but inflamed mucosa was evident.

On repeat operative endoscopy postburn day 24, his CAJ were again injected with corticosteroids, and the mucosal inflammation in his trachea appeared to be resolving. He underwent repeat endoscopic corticosteroid injection once more on postburn day 32.

When seen in clinic 44 days postburn, his larynx had regained limited abduction (primarily driven by left TVF mobility gains). He was successfully decannulated 2 weeks later.

Case 3

A 40-year-old nondiabetic male sustained a 10% TBSA burn and a grade III inhalational injury during a car fire. His initial hospital course was complicated by acute respiratory failure, requiring extracorporeal membrane oxygenation (ECMO). He was weaned from ECMO to mechanical ventilation with transition from an endotracheal tube to a tracheostomy after 11 days of intubation. After weaning from mechanical ventilation, he was aphonic and had dysphagia to both solids and liquids. The Otolaryngology service was consulted for his voice and swallow on postburn day 24.

Bedside fiberoptic exam postburn day 10 identified bilaterally immobile vocal folds and a 5-mm glottic gap secondary to abundant vocal process granulation tissue. He underwent direct laryngoscopy with cold debridement of his vocal process granulation tissue and corticosteroid injection into the bilateral CAJ (Figure 3). He was started on a PPI BID, and

Figure 1. (A) Postinjury day 5. Direct laryngoscopy from postinjury day 5 revealed diffuse mucosal sloughing throughout the hypopharynx, supra-glottis, glottis, subglottis, and proximal trachea. The carina, bilateral mainstem bronchi showed preserved mucosal integrity with diffuse erythema. Notably, the oral cavity and the majority of the oropharynx were spared. (B) Postinjury day 10. Direct laryngoscopy from postinjury day 5 reveals similar diffuse mucosal sloughing at the level of the glottis and trachea; however, mucosal injury has progressed to the carina and bilateral mainstem bronchi. (C) Postinjury month 6. Direct laryngoscopy 6 months postinjury. Exam revealed bilaterally fixed vocal folds, cicatricial scarring at bronchial mainstem, and significant restrictive lung disease on Pulmonary Function Testing (PFTs preformed via open tracheostomy). (D) Postinjury day 10 immunohistochemistry. Immunohistochemistry from biopsies of the glottis and right mainstem bronchus (MSB) taken on postinjury day 15 demonstrate abundant subepithelial IL-17A protein.

Azithromycin 250-mg QOD via peg tube (and maintained on this regime 21 days). During their hospitalization, this patient received both inhaled albuterol and N-acetylcysteine as part of the respiratory protocol of the Burn ICU.

Repeat operative endoscopy 7 days later showed healing glottic mucosa and 5- × 7-mm exposed cartilage in the subglottis at the prior location of mucosal inflammation.

A split-thickness skin graft (STSG) secured over an Adaptic-covered suprastomal stent (Acelity, San Antonio, TX) (distal limb of a 12-mm Montgomery T-tube [Boston Medical, Shrewsbury, MA]) was placed endoscopically (Figure 3). The stent was secured externally and the indwelling #6 proximal XLT Shiley tracheostomy maintained. The suprastomal stent was removed 2 weeks later in the OR;

Figure 2. (A) Postinjury day 6. Direct laryngoscopy showed significant thermal injury to his glottis and immediate subglottis with anthracotic debris, as well as glottic level edema obstructing the laryngeal inlet. Bilateral palpation of the CAJ demonstrated good mobility. (B) Postinjury day 17. Repeat operative endoscopy day showed healing anterior laryngeal mucosa. Yet the posterior glottis showed mild webbing with pronounced granulation tissue. (C) Postinjury month 2. When seen in clinic 44 days postburn, his larynx had regained limited abduction (primarily driven by left TVF mobility gains).

endoscopy at that time showed improved mucosal coverage above the tracheostomy stoma and healing mucosa in the larynx (Figure 3). Four weeks later he was evaluated in clinic and noted to have return of normal laryngeal movement. Phonatory function was impaired secondary to reduced mucosal wave evident on videostroboscopic exam (Figure 3).

DISCUSSION

Our cases reinforce common teachings about the pathophysiology of thermal airway injury while also suggesting that early endoscopic intervention may provide an opportunity to alter the course of disease. Consistent with prior reports,^{11,12} animal models,¹⁵ and clinical experience, the most severe acute tissue injury occurs at the level of the larynx. This is likely secondary to the glottic closure reflex, activated by the superior laryngeal nerve which closes the glottis, protecting the lower airway from inhalation injury. Additionally, the heat absorption capacity of the proximal upper airway tissue serves to dissipate heat as it travels to the distal airway.^{16,17} Furthermore, the inhalation of aerosolized chemicals and incomplete products of combustion play a role in distal glottic injuries as these particles can travel through the airway before initiating combustion.⁸

Each case, graded by a consistent observer, senior author A.G., demonstrates unique variations of inhalation injury. The first case represents combustible material inhaled along with actual fire, offering an explanation for the progressive extent of tracheal injury. The second case demonstrates burn injury in a house fire, where smoke particulates and thermal injury affect the airway differently from the chemical combustibles in case 1. Case 3 represents burn injury in an enclosed space (car fire) that has a unique impact on the degree of mucosal injury. The differences seen in the pattern of injury support the potentially diverse and complex nature of thermal injuries to the laryngotracheal complex.

The initial extent of injury is far exceeded by the subsequent immune response and aggressive fibroinflammatory healing. In all cases, serial exam demonstrated progressive mucosal inflammation, granulation tissue, and epithelial sloughing even in regions without apparent significant initial injury. This supports the importance of both serial exams, and early efforts to quickly arrest the process of host inflammation. Case 1 demonstrates that IL-17A appears to be an early component of this host inflammatory response. Interfering with the production (or effect) of this cytokine with established reagents (Azithromycin) may have clinical benefit.¹⁸

In case 2, most of the initial tissue injury was localized to the anterior larynx; yet within 10 days of the injury, the

Figure 3. (A) Postinjury day 24. Direct laryngoscopy revealed a 5-mm glottic gap secondary to abundant vocal process granulation tissue, which underwent cold debridement and corticosteroid injection into the bilateral CAJ. Subglottic granulation tissue was also visualized. (B) Postinjury day 31. A split-thickness skin graft secured over an adaptive-covered suprastomal stent (distal limb of a 12-mm Montgomery T-tube) was placed endoscopically. The stent was secured externally and the indwelling #6 proximal XLT Shiley tracheostomy was maintained. The suprastomal stent was removed 2 weeks later in the OR; endoscopy at that time showed improved mucosal coverage above the tracheostomy stoma and healing mucosa in the larynx. (C) Postinjury month 3. Clinical exam with fiberoptic endoscopy showed return of laryngeal function.

posterior larynx evidenced severe cicatricial complications. Similarly, in case 3, the patient's posterior glottic granulation tissue was likely a product of prolonged intubation in the setting of a mucosal injury, which in this case is a thermal injury. Both cases highlight the role an indwelling endotracheal tube plays in promoting tissue injury in the setting of postburn host inflammation. It merits thoughtful discussion of the timing of tracheostomy in this patient population.

Case 3 illustrates how mucosal reconstitution can be easily applied over an endoluminal stent while maintaining the safety of a standard dual-lumen tracheostomy. Placement of an airway stent with a STSG was temporally associated with rapid abatement of mucosal inflammation, resolution of granulation tissue, and return of laryngeal function.

Reports describing management of thermal injury to the laryngotracheal complex are rare. The two series that form the foundation of current clinical practice include 11 patients from Dr. William Montgomery in 1989,¹¹ and 18 patients from Dr. Hermes Grillo's in 1993.¹² The core principles distilled from these two authors experience the following: 1) Strictures of the larynx and trachea related to inhalation injury are associated with prolonged inflammation. 2) Early open tracheal resection should be avoided. 3) In the larynx, when healthy mucosa has been replaced by fibrous tissue, this fibrous tissue must be removed to the level of the perichondrium, and all denuded areas resurfaced with autologous grafts. 4) Silicone

laryngeal stents or tracheal T-tubes play a vital role in supporting airway framework and resisting the contractile forces of mucosal scarring through the prolonged inflammatory phase. 5) As the host inflammatory process resolves, severe complex injuries respond to open surgical reconstruction with potential for functional recovery of a voice, swallowing, and airway prosthesis-free survival.

The patients described by Drs. Montgomery and Grillo were primarily seen with chronic fibrotic airway contractures, several months after their initial injury. Since their insights nearly 30 years ago, new minimally invasive approaches to acute postintubation airway injury have emerged. Based on a cohort of 31 patients managed at The National Centre for Airway Reconstruction in London, Dr. Guri Sandhu's reported on his experience in the early treatment of acute postintubation airway lesions in an effort to modify the natural history of tracheal injury.¹³ In his publication, patients treated acutely required significantly fewer interventions, had a significantly longer intervention-free interval, and did not require external laryngotracheal reconstruction compared with patients treated for mature fibrotic scars. Based on this report, aggressive early intervention in postintubation airway stenosis has gained traction within the surgical community engaged in airway reconstruction. Our case series suggests that similar principles may be successfully applied to thermal injuries of the laryngotracheal complex.

Burn injury has been shown to induce a robust inflammatory response involving a variety of inflammatory mediators depending on the grade of initial injury.¹⁹ Local Th-17 (and therefore IL-17A) response has been shown to be upregulated in animal models of cutaneous thermal injury, however thus far has not been demonstrated in human burn models.^{19,20} Interestingly, upregulation of the IL-17A axis has been implicated in a number of fibroinflammatory human airway diseases, including asthma,^{21,22} cystic fibrosis,²³ and chronic obstructive pulmonary disease.²⁴ Driven by insights from our group on the role of IL-17A in the fibrotic remodeling seen in idiopathic subglottic stenosis,¹⁸ this pathway may play a role in the host response to thermal airway injury. Our first case suggests that an IL-17A response is detectable in human airway mucosa following thermal injury. This is the first report implicating IL-17A in the mucosal immune response to thermal injury. Working on the hypothesis that IL-17A pathway activation in burn injury may offer a novel approach for therapy. Although they were not explicitly evaluated for IL-17A activity, in our second and third patients, we used Azithromycin in combination with early aggressive endoscopic surgical therapy. Azithromycin has been used in airway reconstruction for its proven anti-inflammatory effects (Mike Rutter, personal communication). Reports from the pulmonary transplant literature also detail the ability of Azithromycin to lower local IL-17A levels and limit the fibrotic complications of post-transplant bronchiolitis obliterans.^{25,26} After these efforts, our both second and third patients were able to regain enough laryngeal function to allow successful decannulation.

A mainstay of cutaneous burn management is early, aggressive surgical debridement, removal of nonviable tissue, and epithelial reconstitution with autologous or heterologous sources.²⁷ Besides reducing infection, grafting promotes resolution of the systemic host-inflammatory response. Separately, airway surgeons have employed endoluminal grafting of buccal mucosa, or split-thickness skin for its antifibrotic properties.^{21,22} Our third patient offers an example of application of this minimally invasive endoscopic surgical technique to thermal airway injury. The impressive tissue response, characterized by rapid remucosalization, and prevention of reactive CAJ fibrosis, may be a viable new treatment approach to optimize laryngotracheal functional recovery after thermal injury.

Conclusions based on our series of three patients are clearly limited. Although we present our treatment algorithm as a logical progression based on the experiences of three patients, in reality the superior treatment outcomes in the second and third patients may relate to the lower severity of their injury when compared with the first patient. Additionally, despite the overall good outcomes in the second and third patients, it is possible that their airways would have healed in the absence of any medical or surgical intervention. These limitations aside, we believe our approach of early minimally invasive intervention consisting of endoscopic scar lysis, mucosal reconstitution, and endoluminal stenting (frequently occurring as a concomitant procedure with external surgical skin grafting), coupled with anti-inflammatory local corticosteroids and systemic Azithromycin, offers the potential to limit downstream cicatricial complications with very limited risk to the patient.

CONCLUSION

Patients who present with a history of inhalation injury should receive a thorough multidisciplinary airway evaluation with early otolaryngologic evaluation in severe thermal airway injury. New early endoscopic approaches when combined with targeted medical therapy aimed at components of mucosal airway inflammation (local corticosteroids and systemic Azithromycin targeting IL-17A) may have potential to limit chronic cicatricial complications and should be prospectively explored across our nationwide burn center infrastructure. New surgical approaches aimed at scar lysis, and mucosal reconstitution with autologous grafting over an endoluminal stent may provide long-term benefit for this subset of patients with a potentially devastating injury.

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