Recurred Post-intubation Tracheal Stenosis Treated with Bronchoscopic Cryotherapy

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Abstract

Post-intubation tracheal stenosis accounts for the greatest proportion of whole-cause tracheal stenosis. Treatment of post-intubation tracheal stenosis requires a multidisciplinary approach. Surgery or an endoscopic procedure can be used, depending on the type of stenosis. However, the efficacy of cryotherapy in post-intubation tracheal stenosis has not been validated. Here, we report a case of recurring post-intubation tracheal stenosis successfully treated with bronchoscopic cryotherapy that had previously been treated with surgery. In this case, cryotherapy was effective in treating web-like fibrous stenosis, without requiring more surgery. Cryotherapy can be considered as an alternative or primary treatment for post-intubation tracheal stenosis.

Key words: bronchoscopy, cryotherapy, endotracheal intubation, tracheal stenosis

(Intern Med 55: 3331-3335, 2016)
(DOI: 10.2169/internalmedicine.55.6421)

Introduction

Post-intubation tracheal stenosis is the most common type of tracheal stenosis these days (1). With the introduction of an endotracheal tube with a high-volume low-pressure cuff in the 1970s, the risk of post-intubation tracheal stenosis has decreased, but its incidence is still reported to range from 6% to 21% (2, 3), remaining a complicated problem. The standard care for tracheal stenosis is tracheal resection with end-to-end anastomosis; however, not all patients seem to benefit from the surgery (3-5). In particular cases, endoscopic procedures can be used instead of open surgery (6, 7). However, these endoscopic procedures may require repeated interventions. If stenosis recurs after a primary intervention, treatment becomes complicated, and the prognosis tends to be poor (8). We herein report a case of recurrent post-intubation tracheal stenosis that was successfully treated with bronchoscopic cryotherapy performed in a patient who had already undergone tracheal resection with end-to-end anastomosis for a previous event of post-intubation tracheal stenosis.

Case Report

A 42-year-old woman was referred to the department of pulmonology at our institution for dyspnea after undergoing tracheal resection with end-to-end anastomosis to treat post-intubation tracheal stenosis. Three months prior, she had been under endotracheal intubation for three weeks at another hospital while being treated for neurogenic edema, which resulted from rupture of a cerebral-artery aneurysm. However, this history was under-recognized, and her dyspnea and wheezing were regarded as asthmatic symptoms. She was taking systemic and inhaled corticosteroids before the identification of tracheal stenosis. Despite these medications, her symptoms worsened; considering her previous history of intubation, tracheal computed tomography (CT) was performed. The CT image showed irregular luminal narrowing of the trachea, with the smallest diameter measuring 3.84 mm (Fig. 1). Tracheal resection with end-to-end anastomosis was performed, and fiber-optic bronchoscopy showed no serious complications one week after the operation (Fig. 2). However, three weeks after the operation, the patient experienced reoccurrence of dyspnea, as well as stridor.
At this point, the patient was referred to our department of pulmonology for evaluation of dyspnea.

On physical examination, her blood pressure was 130/89 mmHg, heart rate was 110 beats/min, temperature was 36.7°C, respiration rate was 24 breaths/min, and S\textsubscript{ao2} was 98%. Auscultation revealed stridor and wheezing. A chest radiograph showed no lung parenchymal lesions. Pulmonary function tests were not possible due to the sequelae of the ruptured aneurysm.

Bronchoscopy revealed recurrent tracheal stenosis that had formed web-like fibrosis above the previous anastomosis site in the upper trachea (Fig. 3A and B). The diameter of the lesion was approximately 5 mm. Her general condition was unfavorable for a possible repeat surgery. We therefore decided to perform cryotherapy with flexible bronchoscopy at the site of the stenotic lesion (Fig. 3C and D). Under conscious sedation with midazolam (0.07 mg/kg), a flexible cryoprobe was inserted through a working channel of the bronchoscope (BF-1T 260™; Olympus, Tokyo, Japan) via the trans-oral route. The cryotherapy unit consisted of a cryomachine (ERBOKRYO CA; ERBE, Tubingen, Germany) and flexible cryoprobe (ϕ 2.4 mm, length 900 mm). Cryogen was nitrous oxide. The tip of the cryoprobe was positioned directly on the web-like stenosis. A freeze-thaw course was repeated 6 times, as follows: 3 times in the 12 o’clock direction, 3 times in the 3 o’clock direction. The duration of each freezing cycle was 30 seconds. The procedure was finished within 30 minutes. After the procedure, 80 mg of methylprednisolone was administered by intravenous injection for 2 days. The patient experienced no immediate complications, and the follow-up sessions of bronchoscopy performed at one-week intervals showed gradual improvement of the lesion with luminal enlargement up to 10 mm in diameter. After one month, airway patency was consistently well maintained (Fig. 4), and the patient was stable without dyspnea, stridor, or wheezing. Tracheal CT taken two years after cryotherapy showed no further stenosis at the old lesion site (Fig. 5).

Discussion

The treatment of post-intubation tracheal stenosis requires a complex approach (6). Curative surgery is proposed for patients with good general condition (3-5). However, depending on the type of stenosis, endoscopic procedures can provide good results without complications (6, 7). Further, advances in endoscopic procedures have expanded treatment options to include both surgical and non-surgical candidates (6, 7). Endoscopic procedures include laser excision, balloon dilatation, stent insertion, electrocautery, argon-plasma coagulation, topical application of mitomycin C, and cryotherapy.

Cryotherapy is a technique where a cryoprobe is inserted through the working channel of the bronchoscope to create a freeze-thaw effect on target tissue. This process induces coagulation necrosis of selected tissue and destruction of the lesion (9). Available cryogens are nitrous oxide, carbon dioxide, and liquid nitrogen. Cryotherapy has been used to treat malignant and benign airway tumors and to remove granulation tissues, foreign bodies, and blood clots. There are two methods of tissue removal in cryotherapy. The first

Figure 1. (A, B) Initial tracheal computed tomography shows luminal narrowing of the trachea where the narrowest diameter=3.8 mm.

Figure 2. Bronchoscopy conducted one week after the tracheal resection with end-to-end anastomosis revealed only mucosal ulceration at the anastomosis site, but no other complications such as re-stenosis were found.
Figure 3. (A, B) Bronchoscopy conducted one month after tracheal resection and end-to-end anastomosis showed concentric stenosis beyond the anastomosis site in the upper trachea. The diameter of the lumen was 5 mm, which was equivalent to maximal opened diameter of a forcep. After the forcep passed forward through the stenotic lesion, hypoxia occurred. (C, D) Bronchoscopic cryotherapy was performed on the weblike fibrous stenosis. After six repeats of a freeze-thaw course, each with a 30 second duration, immediate results from the cryotherapy appeared to be effective.

Figure 4. Bronchoscopy was performed one month after undergoing cryotherapy. The web-like stenosis has been improved with luminal diameter over 10 mm (arrow: previous web-like stenosis site, arrow head: previous anastomosis site).

involves repeat freezing and thawing to induce tissue necrosis. The second is a pulling-out method, extracting frozen tissue which is attached to a cryoprobe. While the pulling-out method carries a risk of hemorrhage, Franke et al. demonstrated that cryotherapy has a low risk of bleeding even when using the pulling-out method (10). Vasoconstriction of
cooled tissue may account for the reduced amount and duration of bleeding after cryotherapy. Indeed, the hemostatic, analgesic, and anti-inflammatory effects of cold have been known for centuries (9).

Because of its selective tissue destruction, cryotherapy is less likely to affect the cartilage, collagen, or fat tissues in the airway; thus, the risk of perforation is low. Compared with laser therapy, which is commonly used to treat post-intubation tracheal stenosis through rigid bronchoscopy, cryotherapy is less likely to cause hemorrhage or perforation, is less expensive, and is relatively simple to perform (9). Balloon dilatation is another common treatment option, but it requires repeated procedures to achieve satisfactory results and shows a high relapse rate compared to cryotherapy (9, 11). Airway stenting can be considered in patients with long-segment stenosis (over 1 cm) and accompanying cartilage damage or extrinsic compression. Complications of stent insertion include migration, obstruction, and granuloma formation. In addition, relapse is a frequent problem after stent removal (6, 12).

Post-intubation tracheal stenosis mainly occurs at the cuff site due to loss of regional blood flow. After an ischemic injury, the healing of damaged tissue can be associated with the development of web-like fibrosis within 3 to 6 weeks (11), as in our patient’s case. Web-like fibrosis shows membranous concentric stenosis of short segments (less than 1 cm). Patients with post-intubation tracheal stenosis tend to present with web-like fibrous stenosis, while post-tracheostomy patients mainly present with stenosis that resulted from excess granulation tissue around the stoma site (13). The efficacy of cryotherapy in treating post-intubation tracheal stenosis is unclear due to a lack of previous studies. Furthermore, due to the tissue selectivity, cryotherapy has rarely been used to treat post-intubation tracheal stenosis with web-like fibrosis. If the type of post-intubation tracheal stenosis is found to be web-like, a mucosal-sparing technique including laser resection with or without dilatation is generally recommended (6, 14). Nevertheless, in our present case, cryotherapy was effective in treating the web-like fibrous stenosis, and no re-intervention was necessary throughout the two years of follow-up and beyond.

Risk factors for post-intubation tracheal stenosis have been reported to be prolonged intubation period, high cuff pressure, traumatic intubation, history of intubation, secretion infection, excessive corticosteroid use, hypotension, old age, female sex, diabetes mellitus, severe respiratory failure, autoimmune disease, obstructive sleep apnea, and history of radiation therapy for oropharyngeal or laryngeal cancer (2, 11, 15). In the present case, the patient’s predisposing factors were a female sex, a prolonged intubation period of three weeks, and the use of corticosteroids for longer than six weeks. Estrogen increases the level of transforming growth factor-β1, and the deposition of type I and type II collagen induces fibrosis. This mechanism contributes to female predominance in post-intubation tracheal stenosis (11, 15, 16).

According to one study, when tracheal intubation lasts longer than 11 days, the prevalence of tracheal stenosis increases to 12% compared to 5% prevalence for intubation between 6 and 10 days (17). Another study found that even an 18-hour intubation could cause tracheal stenosis (18). Typically, stenosis symptoms arise between 2 and 24 weeks after extubation (19), and in the present case, the patient’s symptoms started three weeks after extubation. Because her intermittent dyspnea and wheezing were thought to be a manifestation of asthma, 62.5 mg of methylprednisolone was administered and tapered over a 1- to 2-week interval; her total steroid course lasted 6 weeks. A brief improvement in symptoms was followed by a worsening of dyspnea, wheezing, and stridor. In previous studies, corticosteroids were demonstrated to be effective in treating tracheal stenosis due to its anti-inflammatory effects (20, 21). However, our patient experienced progressive symptoms of stenosis, which is consistent with the findings from previous studies that prolonged use of corticosteroid at a moderate to high dose is a predisposing factor for tracheal stenosis (13, 16). Corticosteroids may have accelerated the progression of

Figure 5. (A, B) Tracheal computed tomography was taken two years after receiving cryotherapy. The trachea shows stable airway patency with the smallest tracheal lumen diameter enlarged to 10.3 mm.
stenosis in our patient. However, the causal relationship is not clear. Thus, in this case, the impact of corticosteroids on the course of post-intubation tracheal stenosis remains controversial.

Given the increase in survivorship among ICU patients, post-ICU care has become an increasingly important issue for improved quality of life. If patients with a history of intubation present with any respiratory symptoms, tracheal stenosis should be strongly suspected, as the diagnosis can be challenging. Symptoms can develop over a wide time frame, from within two days to longer than several months. Patients usually remain asymptomatic until the diameter of the airway narrows to just over 30% of its original lumen (22). Typical stridor is usually not evident until the diameter of the tracheal lumen narrows to less than 5 mm (19). Simply a dry cough and difficulty raising sputum may be a sign of moderate tracheal stenosis (13). Accordingly, careful evaluation should be carried out in high-risk patients, along with preventative efforts, including cuff-pressure monitoring, early extubation, and enhanced infection control. Furthermore, a routine check-up with bronchoscopy is recommended in patients with predisposing factors (2). Many patients after extubation are too vulnerable to receive surgical management. In such circumstances, bronchoscopy is a good option for diagnosis and treatment of post-intubation tracheal stenosis.

In conclusion, bronchoscopic cryotherapy is a convenient, low-risk, easily performed modality that can be considered as an alternative or primary treatment for post-intubation tracheal stenosis. Risk assessment in mechanically ventilated patients and close monitoring after extubation are crucial for prevention of post-intubation tracheal stenosis. Further studies validating the efficacy of cryotherapy in post-intubation tracheal stenosis are needed.

The authors state that they have no Conflict of Interest (COI).

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