CHEST

Successful Total Tracheal Replacement by Cryopreserved Aortic Allograft in a Patient Post-COVID-19 Infection

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This is the first report to our knowledge of a successful total tracheal replacement in a post-COVID-19 patient by cryopreserved aortic allograft. The graft was anastomosed to the cricoid and carina; a silicon stent was inserted to ensure patency. The patient was extubated on the operative table and was immediately able to breathe, speak, and swallow. No immunosuppression was administered. Three weeks after surgery, the patient was discharged from hospital in excellent health, and was able to resume his normal lifestyle, work, and activity as an amateur cyclist. Two months after surgery, the patient assumes aerosol with saline solution three times per day and no other therapy; routine bronchoscopy to clear secretions is no longer needed.

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KEY WORDS: COVID-19; cryopreserved aortic allograft; tracheal replacement

Reconstruction of long-segment tracheal defects is a major unsolved problem in thoracic surgery.[1] Extended tracheal damage is more and more frequent in patients who survive intubation or tracheostomy for COVID-19 disease.[2] In contrast to a post-intubation/post-tracheostomy concentric tracheal stenosis, a more intense and severe peritracheal tissue and tracheal mucosa inflammation, as well as a tracheal cartilage ossification of long segments, are observed during surgical dissection in post-COVID patients, because SARS-CoV-2 also affects the tracheal epithelial cells. Therefore, extensive damage of the trachea could be seen after COVID-19 infection itself. Consequently, an increasing number of post-COVID-19 patients are expected to be referred for tracheal surgery within months or years.

Partial replacement of the trachea, carina, or bronchi by cryopreserved aortic allografts (CAA), without immunosuppression, is a feasible option to produce viable substitutes of airway segments.[3] The feasibility of bioengineered tracheal and bronchial reconstruction using stented aortic matrices has been recently demonstrated.[4] Occasional subtotal tracheal replacement has been reported.[5,6] To our knowledge, this is the first report of a successful tracheal replacement from the cricoid to the carina in a post-COVID-19 patient by CAA.

Case Report

The patient was a 50-year-old otherwise healthy man who contracted SARS-CoV-2 in October 2020. In the ICU, between October and December 2020, the patient underwent orotracheal intubation and subsequent tracheostomy for a total period of 25 days of mechanical ventilation. The patient was discharged from the ICU

ABBREVIATION: CAA = cryopreserved aortic allograft

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without tracheostomy on December 22, 2020. Intensive care procedures, along with the frailty of the airway during COVID infection, resulted in complex tracheal stenoses at three different levels: the first restriction was located at the level of the cricoid ring, approximately 8 mm below the vocal cords, a second stenosis was localized in the middle third of the trachea, and the last involved the distal trachea 1 cm from the carina. Airway caliber was reduced to approximately 70%. These multiple obstructions were associated with extended and severe cartilage involvement, alternating marked tracheomalacia and ossification (Fig 1A). The patient was referred to our center in the ED at the end of January, with respiratory failure and severe *tirage*. After mechanical dilatation by rigid bronchoscopy intended to stabilize the patient, total tracheal replacement by a CAA was planned. The tracheal replacement was scheduled as a life-saving and compassionate procedure, and approval was obtained from the authorities of our hospital, after written consent from the National Transplant Center. A written informed consent was obtained from the patient. Once stabilized by mechanical dilation, the patient underwent complete clinical workup including chest CT scan, multiple bronchoscopy, microbiology on bronchial lavage. A human CAA (17 × 170 mm), not matched by ABO and leukocyte antigen systems, was obtained from a certified tissue bank (Fondazione Banca dei Tessuti, Treviso, Italy). To prevent airway collapse, as described previously,[4] silicon stents (Tracheobronxane Dumon, Novatech) of all available sizes were available in the operating room. After complete monitoring (ECG, invasive BP, peripheral oxygen saturation, cerebral oxygen saturation), general anesthesia was induced intravenously using fentanyl 2 μg/kg, propofol 2 mg/kg, and rocuronium 0.8 mg/kg. Orotracheal intubation was performed with a 6-mm inner diameter microlaryngeal oral endotracheal tube, which was placed in the left main bronchus by videobronchoscope with a 3.8-mm outer diameter. Maintenance of general anesthesia was achieved with desflurane (1 minimum alveolar concentration) and continuous infusion of remifentanil (target-controlled infusion system). A collar cervicotomy and a total median sternotomy were performed to expose the entire trachea, and an extra-long omental flap was prepared laparoscopically. The pre-thyroid muscles were divided on the midline to expose the pretracheal plane. Dissection at this level was extremely difficult because of scar tissue, tracheomalacia, and ossification. The anterior mediastinum was then exposed. Care was taken not to dissect the innominate vessels, which were retracted en bloc with their embedding connective tissue, to prevent tracheo-innominate fistula. The pericardium was incised on the midline, the ascending aorta and arch were retracted to the left, and the carina was exposed. At this point, the entire anterior and bilateral tracheal planes were exposed from the thyroid cartilage to the carina. A decision was made not to encircle the trachea to preserve the membranous portion and interpose the latter between the esophagus and the graft. The recurrent laryngeal nerves were not exposed. The omentum was transposed in the chest through an anterior diaphragmatic incision (Fig 2A). Ventilation was performed in volume-controlled ventilation mode with low tidal volume (4 mL/kg), 5 cm H_2O positive end-expiratory pressure, F_{IO_2} 0.5, a 1:2 inspiratory-expiratory ratio, and a respiratory rate of 15 to 18 breaths/min to achieve an end-tidal concentration of CO_2 <45 mm Hg. Median peak airway pressures ≤20 cm H_2O and maximum peak airway pressures of ≤25 cm H_2O were also maintained.

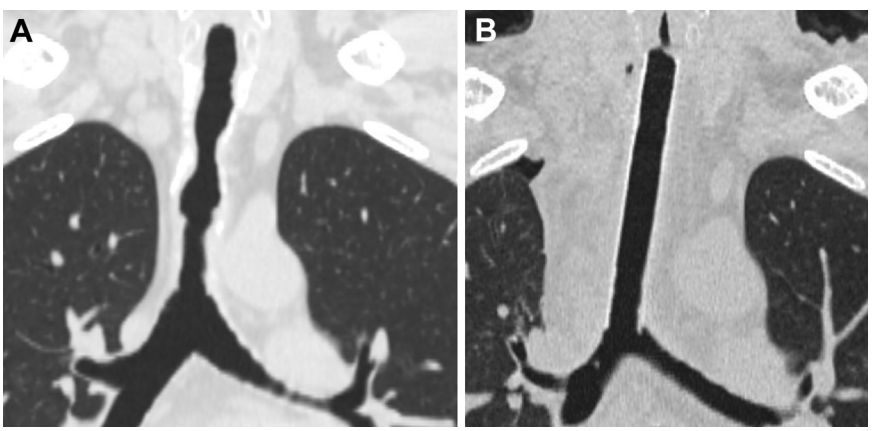

Figure 1 – *CT scan reconstruction of the trachea. A, Preoperative. B, Postoperative.*

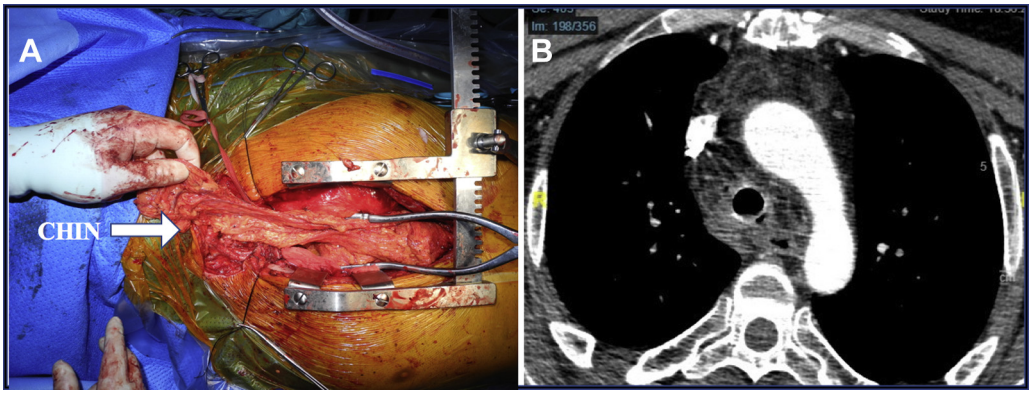

Figure 2 – *A, Extra-long omental flap reaching past the chin. B, Postoperative chest CT scan showing the omental-wrapped aortic graft.*

The trachea was incised 1 cm proximal to the carina and circumferentially divided. The orotracheal tube was retracted below the vocal cords, and the patient was ventilated cross-field by a sterile armored endobronchial tube (5 mm) inserted into the left main bronchus. At this point, the trachea was vertically incised along the midline, and the anterior cricoid ring was divided transversally at the level of the thyro-cricoid membrane. The posterior cricoid mucosa was separated from the cricoid plate as for a subglottic resection.[7] The lumen of the subglottic airway was probed at this level, and a 15-mm silicon stent was deemed appropriate. The lateral wall of the trachea was resected bilaterally, leaving behind the membranous portion, the mucosa of which was cauterized. The aortic graft was prepared according to the protocol.[5,6] Intercostal artery stumps were sutured by 5/0 monofilament. The omental flap was sutured by 3/0 silk transfixed stitches around the aortic graft, thus obtaining a complete wrap. The omental-wrapped graft was then transposed in the tracheal bed from below, under the innominate vessels block (Fig 2). The proximal crico-aortic end-to-end anastomosis was performed by 4/0 monofilament absorbable material; in the posterior portion a running suture was employed, and in the anterior portion interrupted sutures were applied. At this point the aortic-carinal anastomosis was approached. With the patient ventilated by the left main bronchus endobronchial cross-field tube, the posterior portion of the anastomosis was completed with 4/0 monofilament absorbable running suture. The subglottic orotracheal tube was now withdrawn and a second-generation supraglottic device (i-gel laryngeal mask, Intersurgical, UK) size 5 was applied, to reduce airway manipulation and mechanical stress possibly caused by a tube on the freshly sutured and stented airway.[8] A bronchoscope was inserted through the supraglottic device into the patient's airway down to the gaping carinal anastomosis. On the guide of the flexible bronchoscope, a 15 × 100 mm silicon stent (Novatech, France) was inserted in the CAA and advanced upward to cover the crico-aortic anastomosis. All the anterior interrupted sutures were then applied, the patient was hyper-oxygenated by the cross-field endobronchial tube before the latter was removed, and the inferior end of the silicon stent was adjusted to overlap the aortic-carinal anastomosis. Sutures were then tied. Ventilation by the laryngeal mask was resumed with a tidal volume increased to 6 mL/kg, and the anastomoses were tested for air leaks. Both anastomoses were finally carefully covered by omental tissue. Meticulous bronchoscopic toilette and lavage of the airway was done. After proper drainage and closure of the surgical wounds, the patient was awakened in spontaneous breathing, and the laryngeal mask was removed. The patient was able to breathe, speak, and swallow immediately. Cough was effective. Operative time was 4 hours 40 minutes, and blood loss was 250 mL. The patient was able to walk in the first postoperative day. Bronchoscopy for clearance of secretions was performed twice per day for the first week and then daily until discharge. Chest radiography and CT were liberally employed during the hospital stay (Figs 1B, 2B). Pneumonia sustained by *Pseudomonas aeruginosa* occurred on postoperative day 2 and was resolved by antibiotics. Follow-up showed a progressive contraction of the graft (approximately 20%), and the 15 × 100-mm stent was replaced by a 16 × 80-mm stent on postoperative day 18. Three weeks after surgery, the patient was discharged from hospital in excellent health, and he was able to resume his normal lifestyle, work, and activity as an amateur cyclist (Fig 3). Bronchoscopy for clearance of secretions and bronchial lavage were performed twice per week until postoperative day 42 and

Figure 3 – *One-month follow-up: climbing the Etna volcano, Sicily, Italy.*

subsequently every week. Within 6 weeks, bronchoscopic examination through the transparent stent showed a progressive transformation of the pale internal surface of the CAA into a pink, well-vascularized conduit. Two months postoperatively, the patient is able to autonomously clear secretions, and he receives aerosol treatment three times per day but no systemic therapy nor routine bronchoscopy.

Discussion

Experimental and clinical tracheal allotransplantation is challenging because of the difficulty of restoring sufficient blood supply.[9,10] Because the trachea lacks an identifiable vascular pedicle, first-step heterotopic graft revascularization before allotransplantation in the tracheal site has been attempted to provide well-vascularized tracheal sustitutes.[11] Allotransplantation mostly concerned replacement of the cartilaginous tracheal framework or patch tracheal allograft but not the entire complex structure of the trachea. These attempts required immunosuppressive therapy, chimerism with buccal or nasal recipient's mucosa, bio-engineered tissues, and two-step long-term surgery.

The use of CAA as a tracheal substitute proved effective because the biologic aortic scaffold will host tissue regeneration by the recipient's stem cells, as previously described.[4] Biopsy of the CAA at long term demonstrated de novo generation of cartilage and mixed respiratory epithelium within the aortic allograft from recipient cells.[4] This is reported to occur between months 5 and 39 after implantation (mean of 18.2 months),[4] allowing the removal of the silicon stent while preserving CAA rigidity. Preventing airway collapse of the CAA is proved to be necessary because a premature removal of the stent may result in an adverse outcome.[12] However, a prolonged stenting of the airway probably may determine a graft stenosis.[12] This concern will require a close follow-up, pushing for stent removal later then 12 months after implantation and considering potential transversal contraction, together with longitudinal contraction as part of a healing process.

As commented by Valerie Rush,[13] a multicenter clinical trial could demonstrate whether this airway replacement strategy could "challenge that have long bedeviled the field of tracheal surgery," namely, total tracheal reconstruction.

The described technique allows for providing a neo-tracheal conduit stiff enough to propose human airway bioengineering by stented aortic matrices for total tracheal replacement. No immunosuppression is needed, and the postoperative course is straightforward.

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