Immunoglobulin G4-Related Disease Presenting as an Obstructing Tracheal Mass: Consideration of Surgical Indications
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Immunoglobulin G4 (IgG4)-related disease is increasingly recognized in many organs; however, none are described in detail is the trachea. In addition, the role of surgical intervention in the disease has yet to be fully defined. We describe a patient with IgG4-related airway disease presenting as a low tracheal mass, which was treated with tracheal resection and reconstruction. This novel presentation of the disease highlights the importance of including IgG4-related disease in the differential diagnosis of tracheal masses. Further, possible indications for surgical therapy are considered. As the full clinical spectrum of IgG4-related disease continues to evolve, so too must approaches to disease management.

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There is great interest in the recently defined disease entity known as immunoglobulin G4-related disease (IgG4-RD). In this condition, diseases as seemingly diverse as retroperitoneal fibrosis, inflammatory pseudotumor, and Riedel thyroiditis, among several others, share a common classification on the basis of shared histopathologic findings [1]. Much remains unknown about IgG4-RD, including the natural history, pathophysiologic mechanism, exact role of IgG4, and individual organ manifestations [2, 3]. However, it is clear is that IgG4-RD may affect virtually any organ and that prompt recognition and management of the disease is necessary to prevent sclerotic changes and irreversible organ injury [3].

We describe a patient with a tumefactive lesion of the trachea that was found postoperatively to be part of the IgG4-RD spectrum. This case demonstrates a novel organ manifestation of the disease and highlights the need to

Fig 1. Imaging of the tracheal lesion. Preoperative 3-dimensional reconstructed bronchoscopic view of the lesion from (A) high in the trachea and (B) just above the lesion around the level of the carina. (C) A coronal computed tomography image reveals partially obstructive lesion just superior to the carina.
consider IgG4-RD in the differential diagnosis of tracheal masses.

Although medical therapy for IgG4-RD has established efficacy in treatment, the potential role of surgical intervention is not fully defined. Much of the literature to date describes operations for this condition occurring in the setting of misdiagnosis, and such interventions have often been referred to as “unnecessary.” This case study facilitates consideration of circumstances in which surgical intervention may be appropriate.

A 26-year-old Iranian woman presented to Massachusetts General Hospital with shortness of breath after mild exertion and persistent dry cough. Approximately 8 years ago, bronchoscopy first revealed an inflammatory distal tracheal lesion with 90% luminal obstruction. Shortly thereafter, she underwent rigid bronchoscopy with excision of the lesion, followed by laser debridement 6 months later. Pathology records could not be obtained. She was monitored with pulmonary function tests and computed tomography (CT) imaging and remained symptom free until 6 months before presentation. At presentation, bronchoscopy revealed a recurrent lesion with 30% to 40% luminal obstruction.

The patient’s medical history was notable for diet-controlled gastroesophageal reflux disease and latex and specific food allergy to eggplant and red peppers. Results of a preoperative laboratory evaluation were within normal limits, and neither serum IgG nor IgG4 levels were obtained. A CT scan revealed a soft-tissue mass measuring 2.0 × 1.6 × 1.2 cm on the posterolateral wall of the trachea (Fig 1). There was no clinical or radiographic evidence of disease outside of the trachea. The patient underwent tracheal resection and reconstruction. Surveillance bronchoscopy on postoperative days 6 and 12 showed a well-healing anastomosis. She reported considerable symptomatic improvement in the immediate postoperative period.

Examination of the specimen revealed a dense lymphoplasmacytic infiltrate and fibrosis in a storiform pattern (Figs 2 and 3). The infiltrate was composed predominantly of lymphocytes and plasma cells, with interspersed fibroblasts and eosinophils. On immunohistochemistry, fibroblasts were negative for activin receptor-like kinase 1, arguing against an inflammatory myofibroblastic tumor. Immunostaining for IgG4-bearing plasma cells showed abundant IgG4-positive cells (155 per high-power field) and an IgG4/IgG ratio of approximately 0.9 (Fig 4). A single tracheobronchial node was negative for malignancy.

Comment

Histopathologic findings define IgG4-RD and remain the cornerstone of diagnosis [2]. The key observations include a dense lymphoplasmacytic infiltrate dispersed in a storiform pattern of fibrosis, obliterative phlebitis, and a mild to moderate eosinophilic infiltrate. Neither elevated serum IgG4 nor IgG4-bearing plasma cells in tissue are specific markers of the disease, although the latter are necessary but insufficient for the diagnosis [2, 4]. An IgG4/IgG tissue plasma cell ratio greater than 0.4 is highly suggestive of the disease.

Minimum criteria for novel presentations have recently been established, and this case satisfies requirements for the diagnosis of IgG4-RD [5]. Specifically, the histologic findings of a dense lymphoplasmacytic infiltrate, storiform pattern of fibrosis, and IgG4/IgG plasma cell ratio (0.9) all indicate the diagnosis. There was no evidence of malignancy, and no granuloma or neutrophilic infiltrate was observed, both of which are generally inconsistent with the diagnosis [5].

The full breadth of organ manifestations of IgG4-RD has yet to be defined, and to our knowledge, only one other report of isolated tracheal involvement has been published. Virk and colleagues [6] described a patient with idiopathic subglottic stenosis caused by a laryngeal and upper tracheal mass. Whether this lesion was part of the IgG4-RD spectrum remains unclear given that certain seminal histopathologic findings were not addressed, despite finding abundant tissue positivity for IgG4 [6]. Interestingly, their patient also was a young and otherwise healthy woman.
Our case highlights the need for thoracic surgeons to consider IgG4-RD in the differential diagnosis of tracheal neoplasms. Differentiating IgG4-RD of the airway from other tracheal masses is critical given its tendency to respond to corticosteroids and other less invasive treatment modalities.

Several medical treatments are being investigated for IgG4-RD; however, corticosteroids remain the mainstay of treatment. Historically, surgical intervention for the disease has been discussed in the setting of misdiagnosis, and the utility of surgical intervention for IgG4-RD has not been explored.

Surgical intervention for IgG4-RD may be appropriate in select patients with symptomatic disease. A number of studies have documented recurrence of IgG4-RD during and after treatment courses with corticosteroids [7, 8]. Long-standing, more fibrotic lesions of IgG4-RD are generally less responsive to medical treatment and may be ideally suited for surgical resection [2]. Lesions involving critical airway stenosis or circumstances where failure, intolerance, or contraindication of medical therapy exists may be amenable to surgical resection as well. The target lesion must be safely accessible and involve a procedure in which the risk of operative complications is less than the benefit of resection. Surgical resection would likely be limited to a single or few well-defined symptomatic lesions.

Much remains to be learned about the natural history of IgG4-RD. We report a novel presentation of the disease as an isolated tracheal lesion treated successfully with tracheal resection and reconstruction. As more becomes known about IgG4-RD, it is likely that surgery may play a select role in disease management; however, medical therapy will remain the mainstay of treatment.

References
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