Introduction

Immunoglobulin G4-related disease (IgG4-RD) is an immune-mediated fibroinflammatory condition typically involving multiple organ systems.\(^1\) It was first recognised as the etiology of autoimmune pancreatitis with elevated serum IgG4 levels in 2001.\(^2\) Over the last decade, the disease has become diagnosed in several conditions such as sclerosing cholangitis, retroperitoneal fibrosis, tubulointerstitial nephritis, interstitial pneumonia etc.\(^1\) Involvement of the head and neck region is relatively common, occurring as part of systemic disease or in isolation. The most frequently involved sites are salivary glands and the orbit. Here we present the case of a young adult with a laryngeal mass resulted to be an isolated IgG4-RD. Clinical aspects, diagnosis, and treatment are discussed and literature concerning laryngopharynx involvement of IgG4-RD has been reviewed. Authors emphasize that a high index of suspicion and correct diagnostic tools may lead to successful treatment.

Case report

A 36-year-old man was referred to our Operative Unit for investigation of dysphonia and shortness of breath over a period of 2 months. He was otherwise healthy apart from a previous diagnosis of localized borreliosis and a previous hospitalization for cholangitis. Distal-chip evaluation of the larynx revealed a bulky mass of the left-sided supraglottic hemilarynx covered by intact mucosa, partially obstructing the glottis (figures 1a and 1b).

There was no cervical lymphadenopathy and blood exams were unremarkable. With a high index of suspicion for malignancy, an urgent contrast-enhanced computed tomography (CT) scan was obtained and a solid enhancing mass was confirmed. The patient underwent laryngoscopy with narrow band imaging, multiple biopsies and CO2 Laser-assisted debulking with unblocking

Key-words. IgG4-related disease; larynx; pharynx

Abstract. Immunoglobulin G4-related disease (IgG4-RD) affecting the upper aerodigestive tract is rarely reported in the literature. Most commonly affected sites in the head and neck are salivary glands and the orbit. Here we present the case of a young adult with a laryngeal mass resulted to be an isolated IgG4-RD. Clinical aspects, diagnosis, and treatment are discussed and literature concerning laryngopharynx involvement of IgG4-RD has been reviewed. Authors emphasize that a high index of suspicion and correct diagnostic tools may lead to successful treatment.

The authors have no conflict of interests to declare.
aim under general anesthesia. The histological analysis reported lymphoplasmacytic infiltrate with storiform fibrosis. Considering these inconclusive results we decided to submit the patient to a CT-guided biopsy. A thorough histological evaluation revealed polyclonal population of plasma cells who showed significant staining with IgG4, up to 50 stained cells per high-power field. Serological evaluation found a serum IgG4 concentration of 55 mg/dL (range 2.4-121 mg/dL). Positron emission tomography (PET) showed a moderate 18fluorodeoxyglucose uptake (SUV: 4.92) in the left hemilarynx with no evidence of other organ involvement. Based on these findings and according to the more recent diagnostic criteria, a diagnosis of isolated laryngeal IgG4-RD was made. The patient was treated with oral prednisone 0.55 mg/kg daily for 15 days tapering 5 mg every two weeks. Flexible laryngoscopy performed at two months demonstrated excellent treatment response (figures 2a and 2b). Relief of presenting symptoms has been achieved and therapy was well tolerated.

Discussion

Since IgG4 Related Disease has been identified as a clinicopathological entity in 2003 by Kamisawa et al, several studies have been published regarding almost every organ system. Many eponymous conditions described previously in the clinical literature are now recognised to be part of the IgG4-RD spectrum. These include autoimmune pancreatitis, as the archetypal manifestation, primary sclerosing cholangitis, periaortitis, retroperitoneal fibrosis, interstitial pneumopathy, fibrosing mediastinitis, tubulointerstitial nephritis and autoimmune prostatitis. Similarly, some pathologic entities involving the head and neck are now established manifestations of IgG4-RD including: Mikulicz disease, Kuttner tumor, Riedel thyroiditis, fibrosing variant of Hashimoto thyroiditis, pseudotumor orbitae, idiopathic dacryoadenitis, lethal midline granuloma, and pituitary hypophysitis. More recently, involvement of the sinonasal region and middle ear and mastoid region has been described. Authors agree that pharynx and larynx manifestations of IgG4-RD are rare and, to date, scarcely reported in literature. A systematic review on IgG4-RD in the head and neck published by Mulholland in 2015, did not report any pharynx/larynx manifestations. While a review

Figure 1b
Particular showing glottic obstruction

Figure 2b
Particular showing a patent glottic space

Figure 2a
Flexible laryngoscopy performed two months after treatment showing a significant reduction of the laryngeal mass

Figure 2a
Laryngeal IgG4-related disease

published by Takano et al in 2017 found only 2 papers reporting pharynx/larynx involvement. We performed a Medline search (in August 2017) using the terms: larynx IgG4-related disease and pharynx IgG4 related disease. Only articles in English were considered. We found six papers describing IgG4-RD manifestations of the pharynx and the larynx for a total of 9 patients (5 pharyngeal cases and 4 laryngeal cases). Pharyngeal cases involved: palateonsills, the base of tongue and aryepiglottic folds. Laryngeal cases involved: supraglottic region, subglottic region, and subsite failed to be mentioned in one case. Presentation symptoms clearly depend on the site involved but the clinical appearance is somewhat similar: lesions are described as exophytic, lobulated, papilliform and hyperplastic, more often covered by smooth and benign-appearing mucosa. Lesions tend to be diffuse and spreading between laryngeal and pharyngeal subsites. Ulcerative lesions have been described both in the oral cavity and on the palate tonsils. Instead, subglottic lesions showed stenosing behaviour.

Of these nine cases, 4 were isolated lesions, while the other 5 were associated with sclerosing cholangitis, interstitial pneumopathy, skin and genital ulcerations. However, we noticed that some patients did not undergo PET to exclude multiple organ systems involvement. In all cases, the diagnosis was reached by biopsy and histological evaluation. We emphasize that some patients underwent repeated biopsies, multiple surgical procedures, and tracheostomy (in patients with the subglottic disease). Serum IgG4 assay was performed in 7 patients, of which 6 had elevated IgG4 levels and one had normal levels. Every patient was treated with corticosteroid with satisfying results. In two cases steroid therapy failed to be mentioned. Conclusions

The literature on IgG4-RD involving the upper aerodigestive tract is growing steadily. Furthermore, IgG4-RD involving the pharynx and larynx may be more common than currently suggested. When mass-like and hyperplastic lesions are encountered IgG4-RD should be suspected and IgG4 staining in conjunction with serum IgG4 levels should be obtained. Also, pathologic reports of lymphoplasmacytic infiltrate, storiform fibrosis, inflammatory myofibroblastic tumor and plasma cell granuloma should be investigated for IgG4-RD. While radiologic imaging manifestations are nonspecific, biopsy represents the cornerstone of diagnosis. Positron emission tomography should always be obtained to exclude systemic disease. This disease responds well to corticosteroid therapy and patient have a good prognosis. Conventional steroid-sparing medications such as azathioprine and B cell depletion with rituximab demonstrated satisfying results.

A high index of suspicion and a sound diagnostic workup offer excellent chances of cure avoiding major surgery.

References


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