IgG4 Related Disease of The Larynx Mimicking Malignancy: A Case Report and Review of the Literature

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Abstract

Objectives: Immunoglobulin G4-related disease is characterized by increased serum IgG4 level, enlargement in the relevant organs and histopathologically intense storiform fibrosis, lymphoplasmacytic infiltration rich in IgG4 positive plasma cells, and obliterative phlebitis.

Methods and Results: In this report, a patient who underwent a laryngeal biopsy with a pre-diagnosis of malignancy, but had findings consistent with immunoglobulin G4-related disease in the biopsy sample, is described.

Conclusion: Immunoglobulin G4-related disease can be seen in very rare localizations. It should be kept in mind in differential diagnosis when tissues especially containing inflammation rich in plasma cells are encountered. Clinical, laboratory and pathological correlation is extremely important in the diagnosis of an IgG4-related disease.

Introduction

Immunoglobulin G4-related disease (IgG4-RD) is characterized by increased serum IgG4 level, enlargement in the relevant organs and histopathologically intense storiform fibrosis, lymphoplasmacytic infiltration rich in IgG4 positive plasma cells, and obliterative phlebitis (1). The etiopathogenesis of the IgG4-RD is uncertain (2). It was first reported in the pancreas in 2001 (3). The IgG4-RD may infrequently involve a variety of head and neck sites primarily affecting the submandibular gland and less often seen in the thyroid gland, other salivary glands, lacrimal gland, sinonasal tract, oral cavity, orbit and lymph nodes (4). Whereas, IgG4 RD cases identified in the larynx are very few (2,5-10).

In this case report, we present the probable IgG4-RD of the larynx that clinically mimics malignancy.

Case Report

A 59-year-old male presented to the otolaryngology section with a 5-year history of hoarseness of voice. His medical history included hypertension and stroke. Complete blood count was normal. On neck magnetic resonance imaging revealed a lesion at the level of the supraglottic larynx, extending from the left aryepiglottic fold to the anterior commissure, and obliterating the left piriform sinus. The lesion was 19x14 mm in size and did not cause significant destruction in cartilage structures (Figure 1). The patient underwent laryngoscopic biopsy with suspicion of malignancy.

During the laryngoscopy, it was observed that the movement of the left hemilarynx decreased. A lesion compatible with the submucosal mass, which filled the left band and cord, was observed. The biopsy sample was reported as a piece of mucosal tissue containing chronic inflammation. It was stated that there was no evidence of malignancy. The biopsy was repeated because of the mass persisted.

In the microscopic examination of the last taken incisional biopsy material, intense storiform fibrosis was seen under the mucosal surface. The fibrotic background was accompanied by pronounced lymphoid follicles and intense lymphoplasmacytic inflammatory cell infiltration (Figure 2). There was no evidence of phlebitis. With immunohistochemical studies, it was determined that there were IgG4-positive plasma cells ranging from 40 to 50 in a high power field (HPF) (Figure 3). The ratio of IgG4/IgG positive plasma cells was over 40%. As a result, the patient was considered probable IgG4-RD. The patient was followed clinically without medical treatment.

Discussion

IgG4 related disease can be seen in any organ in the body, but in the larynx has been reported very few cases. When the literature was examined, it was observed that 10 patients, consisting of 7 case reports, had laryngeal IgG4-RD.

The average age of patients in the publications is 54 and the age range varies between 37 and 62. The age of our patient was 59. 33% of the patients were female and 66% were male.

Our patient was male. It was noted that most of the cases were men over 50 years old. It was observed that patients presented with symptoms such as hoarseness, dysphonia, dysphagia, throat discomfort, cough, weight loss, odynophagia, dyspnea, sore throat. Hoarseness was the most commonly seen complaint, as also our patient (2, 5–9). Although concomitant diseases vary, it was seen that one patient was found to be accompanied by retroperitoneal fibrosis which is in the spectrum of IgG4-RD (2).

The diagnosis of IgG4-RD is made based on three main criteria. These are clinical, laboratory, and histopathological features. Clinically, involvement may be seen in one or more organs. Enlargement or organ dysfunction occurs in relevant organs. Elevated serum IgG4 levels are found in the majority of patients. It is expected to be > 135 mg/dl. Histopathologically, storiform fibrosis, lymphoplasmacytic infiltration rich in IgG4 positive plasma cells, and obliterative phlebitis are seen. In immunohistochemical studies, more than 10 IgG4 positive plasma cells are present in the high-power field (HPF). The ratio of IgG4 positive cells to IgG positive cells should be more than 40%. If all three of the clinical, laboratory and histopathological features are available, the diagnosis of the IgG4-RD is definitive. In patients with organ symptoms, if only one of the serological or histopathological criteria exists, the patient has probably IgG4-RD (11).

Serum IgG4 level (> 135 mg / dL) is expected to be high in IgG4-RD. However, many different diseases can increase the level of IgG4, and in 30% of IgG4-RD, the level of IgG4 was found to be normal (12–14). Serum IgG4 levels were noted to be high in 75% of the laryngeal IgG4-RD cases and ranged from 152 to 277 mg/dl (2, 5–8). In our case, serum IgG4 levels could not be evaluated.

IgG4-RD is characterized by histopathologically storiform fibrosis, lymphoplasmacytic infiltration rich in IgG4 positive plasma cells, and obliterative phlebitis. Inflammatory infiltration may be accompanied by eosinophils (13). When the cases were evaluated histopathologically, all of them had intense

lymphoplasmacytic infiltration. Fibrosis was present in 75% of the cases. In one of the cases obliterative phlebitis was observed, while in another, marked eosinophilic infiltration was noted (2, 5–8). While lymphocytic infiltration rich in plasma cells, and fibrosis were evident in our case, obliterative phlebitis was not observed. Eosinophils were not apparent in concomitant infiltration.

The number of IgG4-positive cells required for the diagnosis of IgG4-RD may vary. The IgG4/IgG ratio is as important as the number of IgG4-positive cells (13). It was shown that there were immunohistochemically at least 50 IgG4-positive cells per HPF in the case reports (2, 6, 7). In our case, 30 to 40 IgG4-positive cells were found per HPF.

In our case, IgG4-RD clinically mimicked malignancy because it had a mass effect on the larynx. Histopathologically, the differential diagnosis of IgG4-RD includes multiple myeloma, lymphoproliferative diseases, inflammatory myofibroblastic tumor, multicentric Castleman disease, Erdheim Chester disease, or infectious diseases. The diagnosis can be skipped in small biopsy specimens and localization where IgG4-RD is rare, so it is important to evaluate the case with clinical findings.

Conclusion

We presented the IgG4-RD of the larynx. It should not be forgotten that IgG4-RD can be seen in very rare localization. Accurate diagnosis is important because IgG4-RD responds well to prednisone treatment and prevents unnecessary surgical procedures.

Declarations

- i. Funding: None.
- ii. Conflicts of interest: The authors declare no conflict of interest.
- iii. Ethics approval: Written consent has been obtained from the patient.
- iv. Consent to participate: Not applicable.
- v. Consent for publication: All authors gave consent for the article to be published.
- vi. Availability of data and material: Not applicable.
- vii. Code availability: Not applicable.
- viii. Authors' contributions: All authors contributed to the concept, design, data collection, interpretation, and literature review of the study.

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Figures

Figure 1

T1 weighted and fat-suppressed axial magnetic resonance images of the neck. It was seen a lesion extending from the left aryepiglottic fold to the anterior commissure.

Figure 2

Intense storiform fibrosis and lymphoplasmacytic inflammatory cell infiltration were seen under the mucosal surface (HE x40).

Figure 3

There were IgG4-positive plasma cells ranging from 40 to 50 in a HPF (IHC x400).