IgG4-Related Disease of the Glottis: A Rare Primary Presentation of IgG4-RD

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Introduction

What is IgG4-related disease?

- A chronic autoimmune disease characterized by fibrotic inflammatory lesions that can involve any organ system.[1]
- Risk factors include smoking history, occupational exposure and male sex assigned at birth.
- Typically impacts multiple anatomic sites, including the kidneys, pancreas, retroperitoneum, salivary glands and orbits.[2]
- Characteristic histology includes lymphoplasmacytic infiltrate, storiform fibrosis, and obliterative phlebitis.[1]
- Strictest histological criteria requires >10 IgG4 positive plasma cells/HPF and >40% IgG4:IgG ratio.[1]
- Serum IgG4 may or may not be elevated.[1]
- IgG4-RD has been reported to involve the larynx, but never the glottis alone.[4-6]

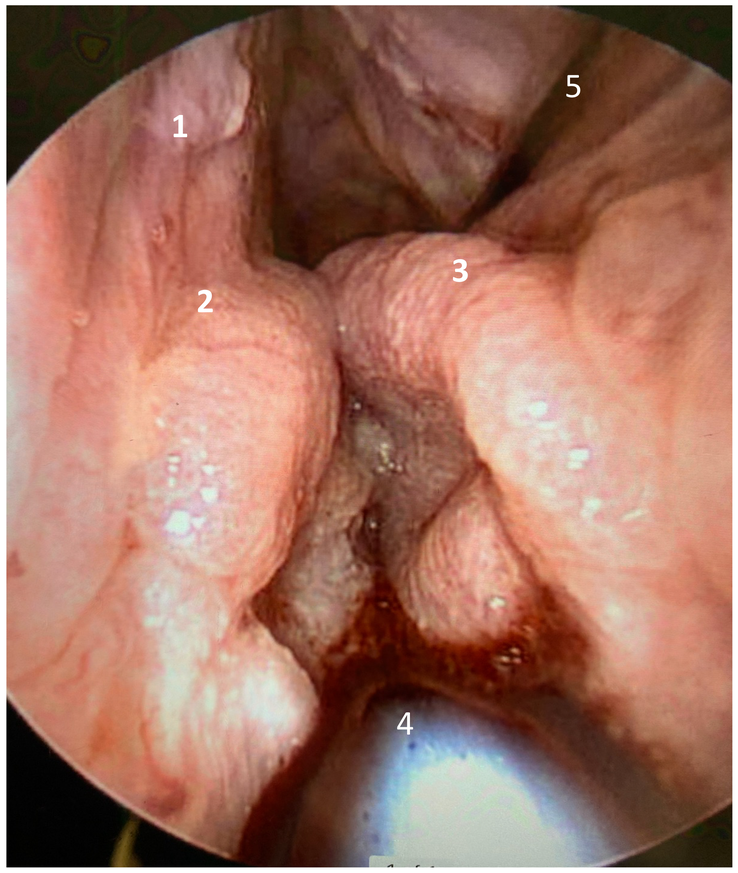

Figure 1. Endoscopic view of the larynx on flexible laryngoscopy.
1: Glottis
2: Left vocal fold lesion
3: Right vocal fold lesion
4: Endotracheal tube
5: Laryngeal suction

Case Presentation

- Chief Complaint: 56 year old male presents with worsening hoarseness, cough, throat clearing and throat pain for one year. He denies dysphagia.
- Medical history: Hypothyroidism, T2DM, HTN, CKD, CAD, PAD, 70-pack year smoking history
- Surgical history: CABG, bilateral lower extremity bypass surgeries one year ago
- Medications: PO methylprednisolone 24mg
- Physical Examination: Raspy voice and bilateral posterior glottic polypoid lesions on flexible laryngoscopy.
- CT neck: Mild soft tissue prominence of nasopharynx reflecting non-involuted lymphoid tissue. Glottis closed on examination.
- Management: Microlaryngoscopy with excisional biopsy of left vocal fold lesion was performed.
- Histopathologic findings included lymphoplasmacytic infiltrates and >200 IgG4+ plasma cells per high power field, with an IgG4+/IgG+ plasma cell ratio of 45%, confirming the diagnosis of IgG4-RD.
- Subsequent PET scan detected no other organ involvement.
- Serum IgG and IgG subclasses within reference ranges.
- Initial management included a 7 day course of steroids which improved the patient's laryngeal symptoms with subsequent relapse upon completion.
- Three month 24mg prednisone taper resulted in the patient noting improvement in hoarseness.

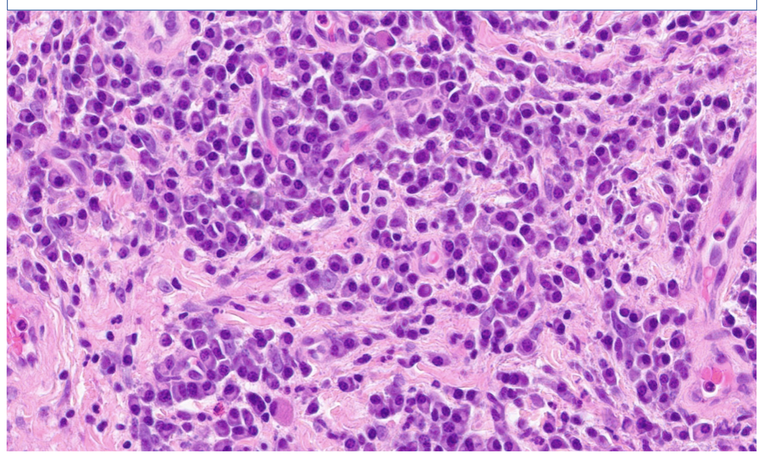

Figure 2. Subepithelial chronic inflammation of lymphoplasmacytic infiltration with polyclonal plasma cells. (Kappa:Lambda ratio of 2:1) on high power, 40X Magnification

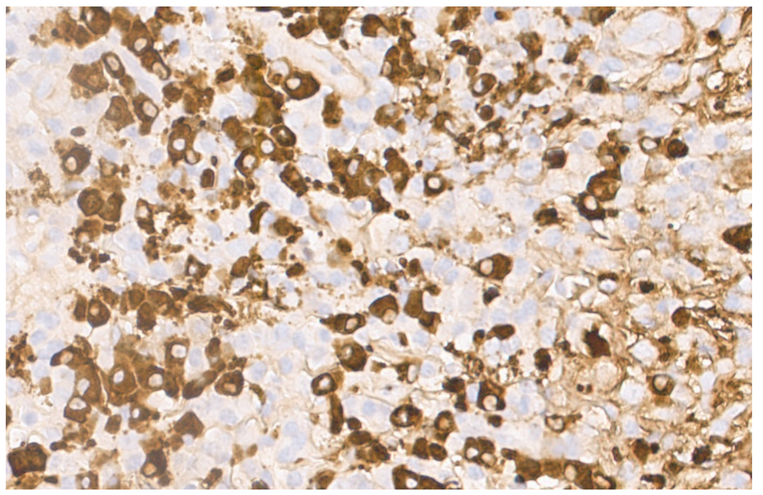

Figure 3. Immunostaining for IgG4. Greater than 200 positive cells per high power field (hpf). 40X Magnification.

Discussion

- Because IgG4-RD mimics benign and malignant conditions, immunohistologic analysis is required to confirm diagnosis.
- Laryngeal IgG4-RD frequently does not exhibit storiform fibrosis and obliterative phlebitis on histopathologic evaluation.[6]
- PET can be helpful in determining multi-system involvement in IgG4-RD.[3]
- Steroid unresponsiveness excludes IgG4-RD.[6]
- First line treatment is initial high-dose glucocorticoids, followed by taper.[5]
- Second-line treatments include methotrexate, mycophenolate mofetil, azathioprine, rituximab, other immunologic therapies.[5]
- Prognosis is favorable, with most patients entering remission with appropriate treatment, however relapse is common.[6]

Conclusions

- IgG4-RD can involve any subsite of the larynx, and can mimic other benign and malignant laryngeal pathologies.
- Prompt tissue biopsy and collaboration with rheumatologist for ongoing medical treatment is critical for successful management of IgG4-RD.

Contact

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