IgG4-RELATED DISEASE CAUSING SUBGLOTTIC STENOSIS

Shristi Gautam[1], Ushant Acharya[1], Prashant Tripathi[1], Manish Neupane[1]

[1] Maharajgunj Medical Campus-TU Teaching Hospital, IOM, Maharajgunj, Kathmandu, Nepal

Corresponding author

Ushant Acharya, Maharajgunj Medical Campus-TU Teaching Hospital, IOM, Maharajgunj, Kathmandu, Nepal

Email: ushantacharya@gmail.com

Phone: +9779841775970

ABSTRACT

Immunoglobulin G4-related disease is a fibro-inflammatory condition rarely involving the laryngotracheal tract. We present a 55-year-old female with progressive dyspnoea and voice change, with findings of subglottic stenosis, diagnosed as Immunoglobulin G4-related disease. This case highlights the importance of having a high index of suspicion in the diagnosis of the condition.

Keywords: Airway Obstruction, Immunoglobulin G4-Related Disease, Laryngeal Stenosis, Tracheal Stenosis

INTRODUCTION

Immunoglobulin G4-related disease (IgG4-RD) is a clinical entity, first reported in 2001, that is characterised by dense infiltration of Immunoglobulin G4 (IgG4)-positive plasma cells and varying degrees of fibrosis.[1] It commonly affects the pancreas, salivary glands, orbits, kidneys, and retroperitoneum. Diagnosis is based on clinical, radiological, serological, and histological findings. Laryngotracheal involvement is uncommon and may be misdiagnosed, leading to delayed treatment and progressive airway compromise. Unlike mechanical or infectious stenosis, it responds to immunosuppressants, potentially avoiding invasive surgical procedures. The case report emphasises the importance of maintaining a high index of suspicion for IgG4-RD in such patients.

CASE REPORT

A 55-year-old female presented to the Otolaryngology outpatient department with complaints of progressive dyspnoea and voice changes. She had initially experienced dyspnoea on exertion for 18 months, which gradually progressed to dyspnoea during household activities and was accompanied by a dry cough and easy fatigability. She had consulted a general practitioner, who diagnosed her with allergic bronchitis and prescribed antihistamines. She had partial symptom relief following two months of treatment. However, two months later, she developed progressive change in voice and was referred to our department for further evaluation.

Flexible laryngoscopy revealed a smooth, non-ulcerated subglottic mass, occluding approximately 50% of the airway lumen on the right lateral wall. Bilateral true vocal cords were mobile. The remainder of the larynx appeared normal.

Computed Tomography (CT) scan revealed non-enhancing asymmetric wall thickening in the right lateral subglottic region spanning a length of 17 mm with a maximum thickness of 6.8 mm, causing approximately 50% lumen stenosis (Figure 1).

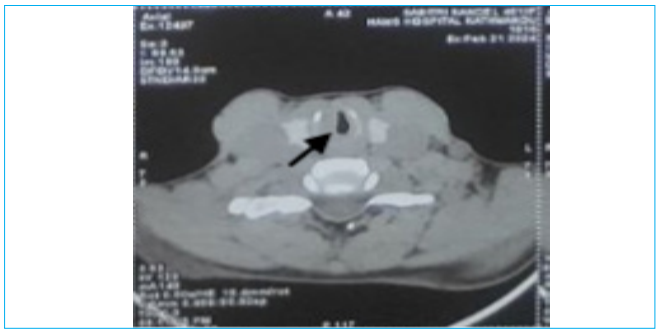

Figure 1: CT scan showing subglottic narrowing (arrow)

Magnetic Resonance Imaging (MRI) of the neck showed a homogenously enhancing lesion, which was relatively well defined with T1 intermediate and T2 high signal intensity, noted in the submucosa of the right lateral wall of the proximal trachea and subglottic larynx with mild diffusion restriction on diffusion-weighted images. Post-contrast images showed homogenous enhancement. The lesion was indenting the tracheal lumen, resulting in up to 70% luminal narrowing (Figure 2).

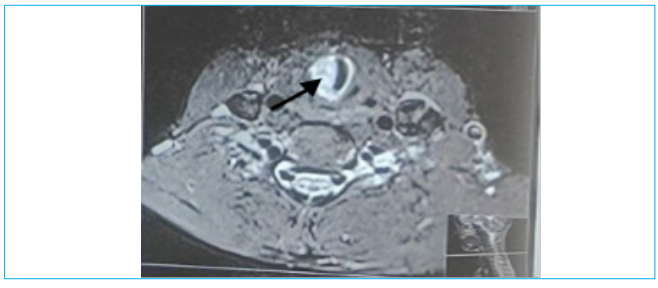

Figure 2: T2-weighted MRI showing subglottic stenosis and a lesion in the right lateral subglottic region (arrow)

The patient was planned for laryngotracheal evaluation and biopsy. Before the surgery, a tracheostomy was done to secure the airway. Laryngotracheal evaluation showed a bulge in the subglottic region in the right lateral wall occluding more

than 50% of the lumen. (Figure 3). Multiple samples of tissue were taken from the swelling and sent for histopathological examination. Decannulation of the tracheostomy tube was done on the third post-operative day.

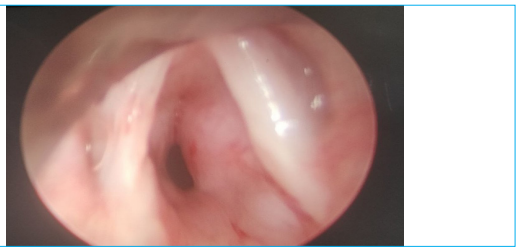

Figure 3: Direct laryngoscopy showing subglottic stenosis

Histopathological report showed mucosal tissue lined by columnar epithelium with underlying stroma showing dense infiltration of lymphocytes and plasma cells along with submucous glands. (Figure 4) Serum IgG4 was within the normal limits. Immunohistochemistry revealed positive staining for IgG4 in 10–15 cells per high-power field, with an estimated IgG4-positive to IgG-positive plasma cell ratio of approximately 40%.

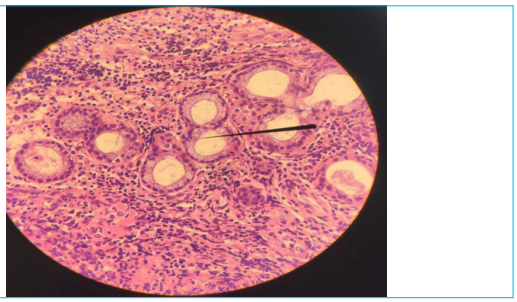

Figure 4: Hematoxylin and Eosin staining showing submucous glands (arrow) and dense infiltration of lymphocytes and plasma cells

The findings were consistent with a probable diagnosis of IgG4-RD. The patient was started on oral prednisolone at 1 mg/kg/day with a tapering dose for 5 months. The patient has improved significantly. Flexible laryngoscopy evaluation showed a significant reduction in the size of the bulge in the subglottic region. (Figure 5) The patient has been on regular follow-up every 3 months.

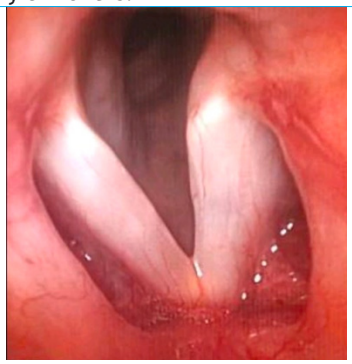

Figure 5: Flexible laryngoscopy of the patient after 5 months of treatment

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

DISCUSSION

IgG4-related disease was first reported in 2001 in Japan in a patient with sclerosing pancreatitis who had elevated serum IgG4 levels.[1] It mimics various inflammatory and malignant conditions. It is a systemic autoimmune condition affecting various organs and is characterised by fibroinflammatory infiltration induced by plasma cells that express immunoglobulin G subclass 4. There is dense lymphoplasmacytic infiltration, storiform fibrosis, and obliterative phlebitis, leading to mass formation in an organ and its dysfunction.[2,3] The condition commonly affects salivary glands, pancreato-biliary system, kidneys, prostate, and retroperitoneum.[2,4] Involvement of the laryngotracheal tract by IgG4 disease is rare, and the subglottic involvement is even more uncommon.[5,6]

The 2020 revised comprehensive diagnostic criteria for IgG4-RD include clinical/radiological, serological and pathological criteria.[7] Clinical/radiological criteria include one or more organs showing diffuse or localized swelling. Serological criterion is the presence of serum IgG4 levels greater than 135 mg/dL. Pathological criteria involve the presence of at least two of the following.

- Dense infiltration of lymphocytes and plasma cells combined with fibrosis,
- Ratio of IgG4-positive plasma cells to IgG-positive cells greater than 40%, and the number of IgG4-positive plasma cells greater than 10 per high-power field
- Typical tissue fibrosis, particularly storiform fibrosis, or obliterative phlebitis.

When all three clinical/radiological, serological, and pathological criteria are met, a definite diagnosis of IgG4-RD is made. Positive pathological criteria along with clinical/radiological features are classified as probable IgG4-RD. Positive serological criteria along with clinical/radiological features are classified as possible IgG4-RD. In this case, clinical/radiological criteria, along with pathological criteria, are met to establish a diagnosis of probable IgG4-RD.

The primary mode of treatment is immunosuppression by corticosteroids. Steroid-sparing immunosuppressive agents such as methotrexate, azathioprine, and 6-mercaptopurine may be considered for patients with adverse effects due to steroids.[8,9] Recurrences are common, and Rituximab is effective in preventing relapses.[10]

CONCLUSION

IgG4-RD presenting as subglottic narrowing is rare, but it should be suspected when other conditions are ruled out. It has an excellent response to medical treatment and can avoid unnecessary surgical intervention and tracheostomy.

ACKNOWLEDGEMENT

Department of ENT-HNS, Department of Pathology, MMC-TU Teaching Hospital, IOM, Maharajgunj, Nepal

REFERENCES

1. Hamano H, Kawa S, Horiuchi A, Unno H, Furuya N, Akamatsu T, et al. High Serum IgG4 Concentrations in Patients with Sclerosing Pancreatitis. N Engl J Med. 2001 Mar 8;344(10):732–8. doi:10.1056/NEJM200103083441005
2. Stone JH, Zen Y, Deshpande V. IgG4-Related Disease. N Engl J Med. 2012 Feb 9;366(6):539–51. doi:10.1056/NEJMra1104650
3. Amor BB, Hajji E, Bayar I, Mesfar R, Saad J, Njim L, et al. Atypical IgG4 related hypophysitis revealed by submandibular sialadenitis: a case report. Endocrine Regulations. 2025 Jan 1;59(1):130–4. doi:10.2478/enr-2025-0014
4. Zhang W, Stone JH. Management of IgG4-related disease. The Lancet Rheumatology. 2019;1(1):e55–65.
5. Maughan EF, Michaels J, Miller B, Weir J, Salama A, Warner E, et al. Primary Immunoglobulin G4-Related Laryngeal Disease: A Case Series and Review of Literature. Clin Med Insights Case Rep. 2020 Jan;13:1179547620960197. doi:10.1177/1179547620960197
6. Nallani P, Guo W, Mayerhoff RM, Meysami A. An unusual presentation of immunoglobulin G4-related disease (IgG4-RD) causing subglottic stenosis. Cureus [Internet]. 2022 [cited 2026 May 22];14(6). Available from: https://www.cureus.com/articles/100701-an-unusual-presentation-of-immunoglobulin-g4-related-disease-igg4-rd-causing-subglottic-stenosis.pdf
7. Umehara H, Okazaki K, Kawa S, Takahashi H, Goto H, Matsui S, et al. The 2020 revised comprehensive diagnostic (RCD) criteria for IgG4-RD. Modern Rheumatology. 2021;31(3):529–33.
8. Khosroshahi A, Wallace ZS, Crowe JL, Akamizu T, Azumi A, Carruthers MN, et al. International Consensus Guidance Statement on the Management and Treatment of IgG4-Related Disease. Arthritis & Rheumatology. 2015 Jul;67(7):1688–99. doi:10.1002/art.39132
9. Kamisawa T, Okazaki K. Diagnosis and Treatment of IgG4-Related Disease. In: Okazaki K, editor. IgG4-Related Disease [Internet]. Cham: Springer International Publishing; 2016 [cited 2026 May 22]. p. 19–33. (Current Topics in Microbiology and Immunology). Available from: http://link.springer.com/10.1007/82_2016_36 doi:10.1007/82_2016_36
10. 10. Campochiaro C, Della-Torre E, Lanzillotta M, Bozzolo E, Baldissera E, Milani R, et al. Long-term efficacy of maintenance therapy with Rituximab for IgG4-related disease. European journal of internal medicine. 2020;74:92–8.