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Case Report

IgG4 related disease masquerading as a sinonasal mass: a case report and review of literature

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ABSTRACT

IgG4-related disease (IgG4-RD) is a relatively new autoimmune fibroinflammatory disease. Most seen to affect the pancreas and biliary tract, IgG4-RD of the nose and paranasal sinuses is very rare. Known to have tumour-like clinical presentations, they can present with varying levels of dysfunction of the organs they affect. In the paranasal sinuses, it can present with nasal block, discharge, bleeds, and sometimes, with symptoms that arise as a consequence of bony erosions and subsequent extension of the disease. We present a case of a 52-year-old lady, who presented with a painful swelling over the malar region with discoloration of the overlying skin. Radiological evaluation helps to check for bony erosions and soft tissue infiltration. Histopathology with immunohistochemistry helps to confirm the diagnosis of IgG4-RD. Most patients benefit from a long course of oral steroids and regular follow-ups, that help to prevent recurrence and ensure a good quality of life for the patient.

Keywords: IgG4- related disease, Sinonasal IgG4, Paranasal IgG4

INTRODUCTION

IgG4-related disease (IgG4-RD) is a fibro-inflammatory condition characterized by several features: a tendency to form tumefactive lesions in multiple sites; a characteristic histopathological appearance; and often, but not always elevated serum IgG4 concentrations.[1]

The earliest recognition of IgG4-RD in the form of elevated serum IgG4 levels corelating with inflammatory sclerosing lesions in the pancreas causing autoimmune pancreatitis was made by Hamano et al in 2001.[2] They first described elevated Ig G4 levels in sclerosing pancreatitis characterized by irregular narrowing of the main pancreatic duct, lymphoplasmacytic inflammation of the pancreas with hypergammaglobulinemia and that responded to glucocorticoid treatment.

IgG4-RD also presents with fibrosis, contributing to organ dysfunction. It is known to affect multiple organs including the pancreas, salivary glands, lacrimal glands, retroperitoneum, kidneys, lungs, thyroid and others. Understanding the extent of disease and monitoring multiple organs is crucial for a comprehensive management of IgG4-related disease.

IgG4-RD of the head and neck region is relatively rare, and that of the nose and paranasal sinuses is even more uncommon.[3] Patients present with varying symptoms like nasal obstruction, nasal bleed, nasal discharge, and other symptoms like loss of perception of smell, swelling over

the face or ophthalmological symptoms. Diagnosis is confirmed by histopathology and immunohistochemistry. Management often requires long term oral steroid usage and immunomodulators with frequent follow-ups and monitoring.

CASE REPORT

A 52-year-old female patient presented to our out-patient department with a history of swelling and brownish-black discoloration in the right malar region associated with pain for 3 years. There were no other nasal or orbital symptoms. Patient was a known hypertensive and hypothyroid and was on medications for the same. Clinical examination showed a hyperpigmented brownish-black discoloration of the right side of dorsum of the nose and adjoining malar region with local tenderness (Figure 1a). Anterior rhinoscopy showed a bulge in right middle meatus. On nasal endoscopic examination, mucosal edema and a soft tissue mass arising from the middle meatus was noted. Patient had undergone nasal endoscopic biopsies two times in the past two years at different centers and each time it was reported to contain chronic inflammatory tissue.

A comprehensive diagnostic workup of the patient was done with relevant blood and radiological investigations. A non-contrast computed tomography (CT) scan of the paranasal sinuses revealed a heterogenous opacification of the right maxillary sinus with erosion of the right nasal bone, extending to the medial and anterior wall of the right maxillary sinus and inferiorly, to the right superior alveolar arch (Figure 2). Opinion was sought from the department of rheumatology in view of long-standing inflammation and possibility of immunogenic origin. After counselling, the patient underwent endoscopic sinus surgery. The maxillary sinus and middle meatus showed dense fibrotic granulation tissue. Disease clearance was done and tissue samples were sent for histopathology and immunohistochemistry. Histopathological evaluation was reported as inflammatory granulation tissue with an excess of plasma cells with significant fibrosis (Figure 3a). Immunohistochemistry of the tissue revealed infiltration of sheets of IgG4 positive plasma cells (Figure 3b) in a background of sheets of IgG plasma cells (Figure 3c). Serum IgG4 levels were elevated at 2.87 g/l. We made a diagnosis of IgG4 related disease based on clinical features, elevated serum IgG4 levels, radiological findings and pathological findings.

Multidisciplinary management with the department of rheumatology was initiated, and patient was started on corticosteroid therapy with tapering doses of prednisolone. She was also advised to use routine measures like topical saline and Fluticasone furoate nasal sprays. On follow up, a flaring up of the disease was noted after tapering the steroid dose. The patient was given two doses of intravenous infusion of rituximab 1000 mg in an interval of 15 days and she showed good response. The patient has recovered well and is on regular follow-ups and is now maintained on low dose prednisolone 2.5 mg daily and injection rituximab 1 gm every 6 months. The pain and the skin discoloration have got significantly ameliorated and she is comfortable (Figure 1b).

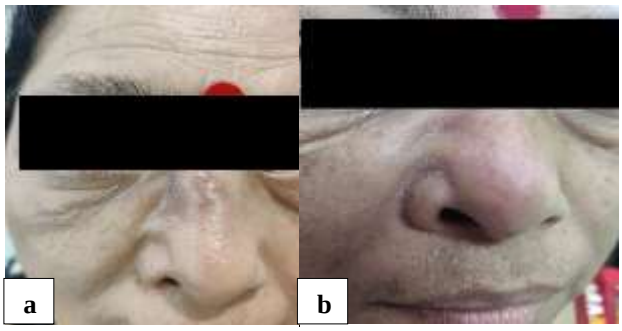

Figure 1: (a) Preoperative picture showing swelling and hyperpigmentation in right malar area, and (b) post treatment picture showing resolution of swelling and hyperpigmentation.

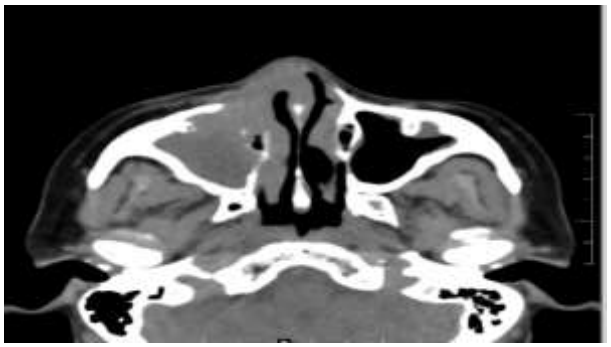

Figure 2: CT scan paranasal sinuses axial view showing opacified right maxillary sinus with bony erosion.

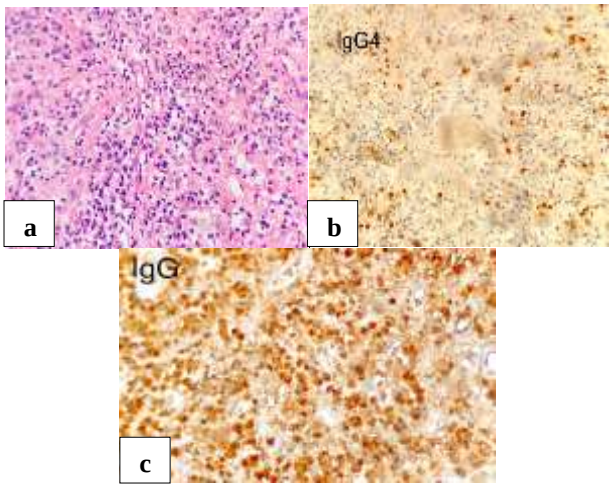

Figure 3: (a) Photomicrograph showing dense plasma cell rich infiltrate, HE at 400X, (b) photomicrograph showing sheets of IgG positive plasma cells, IgG immunostain at 400X, and (c) photomicrograph showing increased numbers of IgG4 positive plasma cells, IgG4 immunostain at 400X.

DISCUSSION

IgG4-related disease is an autoimmune fibro-inflammatory condition. It is known to have a tendency to form tumour-like lesions in various sites in the body. It also has a distinctive histopathological appearance, and in most cases, elevated serum IgG4 levels.[1]

It was observed that many of these patients had extra-pancreatic lesions that contained a high ratio of IgG4 cells, involving different organ systems in the body. Hence the concept of IgG4- related disease, as a group or spectrum of disorders was put forward. Most organs in the body have now been found to be affected by IgG4 disease.[1]

The diagnosis of IgG4-related disease is based on histology. According to the "consensus statement on the pathology of IgG4-related disease" there are three main criteria based on the histopathological features of the disease. These are dense lymphoplasmacytic infiltration with an increase of IgG4 positive plasma cells, fibrosis with areas having a storiform pattern, and obliterative phlebitis. Two out of three are required to make a diagnosis.[1]

Hamano et al were the first to come out with a study which concluded that there was an association with raised IgG4 levels in the plasma and sclerosing pancreatitis, an entity which would often be confused with pancreatic cancer at that time.[2]

IgG4-RD in the head and neck region is very rare, and there is very limited literature available on it. The most common site of presentation of IgG4-RD in head and neck region is the orbit, followed by the submandibular gland, with many patients having involvement of more than one site, both within the head and neck region, as well as elsewhere in the body.[3]

Common orbital manifestations included periorbital swelling, eyelid swelling, and proptosis. Salivary gland and lacrimal gland involvement were very common and included submandibular, parotid gland, and lacrimal gland enlargement, infiltration, and formation of pseudotumours. Lymphadenopathy was a particularly common presentation in the head and neck. The majority of cases received some form of medical management comprising of high-dose corticosteroids. Patients had excellent response to medical therapy alone with full remission rate of 90%.[3]

IgG4-related disease is a multi-organ immune-mediated condition which links many disorders previously regarded as isolated, single-organ diseases without any known underlying systemic condition. The extent of fibrosis is an important determinant of responsiveness to immunosuppressive therapies. IgG4-related disease generally responds to glucocorticoids in its inflammatory stage, but recurrent or refractory cases are common.[4] Allergic features may develop in a substantial subset of patients with IgG4-RD, and many patients have long standing histories of allergy, such as allergic rhinitis, nasal polyps, and asthma. Mild to moderate peripheral eosinophilia and high serum IgE concentrations are also common in these cases.[5]

Dosen et al have described two patients with lesions showing a histological picture of fibrosis and lymphoplasmacytic infiltrations with abundant IgG4 positive plasma cells at hitherto unreported symmetrical nasal locations.[6] The symmetrical complex, in their study, consisted of one central lesion in the anterior nasal septum and the two others in each of the lateral nasal walls. The lesions extended from the anterior part of the inferior concha into the vestibulum and caused severe nasal obstruction.

Kaur et al have described cheek swelling, pain and visual disturbances as the presenting features.[7] Serum IgG4 levels were mildly elevated. Storiform fibrosis, obliterative phlebitis and plasma cell infiltration were seen in varying proportions. Destruction of bone and subepithelial mucoserous glands were present.[7]

Management of IgG4-RD usually requires some combination of surgical debridement of the involved area, along with oral steroids and other immunosuppressive agents to ensure long term remission of the disease.[8] The otolaryngologist or rhinologist should have a high index of suspicion for this disease process when considering patients who present with new-onset symptoms of chronic sinusitis, particularly middle-aged adults without a longstanding history of sinonasal complaints or patients with refractory disease despite appropriate surgical intervention. Recommended diagnostic workup that includes CT sinuses without contrast, serum IgG4, and biopsy of the involved sinus tissue, if feasible. Steroid monotherapy is usually sufficient to prevent recurrence in sinonasal IgG4-RD. Rituximab is an important consideration with recurrent disease after steroid monotherapy.[8]

Our patient underwent an endoscopic sinus surgery for tissue sampling and disease clearance, following which the patient was started on long term oral steroid course, once the diagnosis of IgG4-RD was confirmed.

CONCLUSION

IgG4 related disease of the paranasal sinuses, is an important, albeit rare pathology encountered in otorhinolaryngology practice. There needs to be a high index of suspicion about this disease to be able to differentiate it from other similar entities, like sinonasal malignancies and other auto-immune diseases of the paranasal sinuses. Pathological evaluation of the affected tissue becomes extremely crucial in confirming the diagnosis of IgG4-RD. Surgical debridement forms only as a tool for diagnosis and decreasing the disease load, and systemic therapy with long term oral steroids and immunosuppressive drugs forms the essence of

management of this entity to give the patient long term disease control.

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REFERENCES

1. Deshpande V, Zen Y, Chan JK, Yi EE, Sato Y, Yoshino T, et al. Consensus statement on the pathology of IgG4-related disease. Mod Pathol. 2012;25(9):1181-92.
2. 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;344(10):732-8.
3. Mulholland GB, Jeffery CC, Satija P, Côté DW. Immunoglobulin G4-related diseases in the head and neck: a systematic review. J Otolaryngol Head Neck Surg. 2015;44(1):24.
4. Kamisawa T, Zen Y, Pillai S, Stone JH. IgG4-related disease. Lancet. 2015;385(9976):1460-71.
5. Takano K, Yamamoto M, Takahashi H, Himi T. Recent advances in knowledge regarding the head and neck manifestations of IgG4-related disease. Auris Nasus Larynx. 2017;44(1):7-17.
6. Døsen LK, Jebsen P, Dingsør B, Haye R. IgG4-Related Nasal Pseudotumor. Case Rep Otolaryngol. 2015;749890.
7. Kaur K, Kakkar A, Manchanda S, Chatterjee P, Kaur H, Mishra D, et al. Sinonasl Ig-G4 related disease: a rare and emerging entity broadening the differential diagnosis in the sinonasal universe. Eur Arch Otorhinolaryngol. 2021;278(8):2883-90.
8. Wilson CP, Brownlee BP, El Rassi ET, McKinney KA. Sinonasal immunoglobin G4—related disease: case report and review. Clin Case Rep. 2021;9(12):e05095.

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