IgG4-Related Disease Involving the Ear: A Case Report

Case Report

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Abstract

IgG4-related disease is a chronic inflammatory disease with widespread clinical presentation. It mimics various malignant, infectious, and inflammatory conditions, leading to confusion in diagnosis and management. Otological manifestations, though relatively rare, can lead to significant complications.

A 45-year-old male with a recent history of ventilation tube placement in the right ear presented with a sensation of imbalance associated with profound hearing loss. He was managed in line of acute otitis media with labyrinthitis with steroids and antibiotics and removal of the ventilation tube. He returned in one week and presented with right-sided lower motor neuron-type facial paresis. Computed tomography images of the temporal bone showed a soft tissue density lesion in the right middle ear cavity extending to the mastoid antrum. He underwent a right cortical mastoidectomy with decompression of the facial nerve. Histopathology and immunohistochemistry of granulation tissues from the middle ear and the mastoid revealed evidence suggestive of probable IgG4 disease.

IgG4-related disease is a relatively new entity, and its pathogenesis has not been properly understood. IgG4 subclass has been involved in this disease resulting in fibro-inflammatory conditions leading to tumor-like masses or fibrosis of the affected organs. Treatment includes glucocorticoids and immunosuppressant medications.

Keywords: IgG4 related, chronic inflammation, facial nerve palsy, vertigo

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Introduction

IgG4-related disease presents with widespread unspecific symptomatology. It is an immune-mediated chronic inflammatory process and mimics various malignant, infectious, and inflammatory conditions (1). This leads to a diagnostic dilemma and inadequate management of the condition. In otolaryngology, salivary and lacrimal gland involvement is more common. The condition has favorable outcomes if treatment is initiated early. Recurrences are common and delay in treatment can lead to severe multi-organic complications (2). Otological manifestations, though relatively rare, can also lead to significant complications.

Case Presentation

A 45-year-old male with no chronic illnesses presented with a history of sensation of imbalance for four days. He had a history of ventilation tube insertion in his right ear one month before. On examination, the tympanic membrane was dull on the right side and the ventilation tube was in-situ. The audiogram revealed profound sensorineural-type hearing loss

on the right side (Figure 1). Magnetic resonance imaging of the brain revealed normal findings. Systemic examination and investigations were done to rule out other conditions. He was admitted with intravenous antibiotics and steroids in line of labyrinthitis. His ventilation tube was removed. The sensation of imbalance gradually improved and was discharged after one week of hospital stay.

He presented again one week later with a right-side lower motor neuron-type facial paresis (House-Brackmann Grade III) (3). He was admitted with intravenous antibiotics and steroids. Computed tomography images of the temporal bone showed a soft tissue density lesion in the right middle ear cavity extending to the mastoid antrum (Figure 2). He underwent a right cortical mastoidectomy with decompression of the facial nerve. The surgery revealed granulation tissues in the middle ear and mastoid cavity. The tympanic and mastoid segments of the facial nerve were traced and found intact. The dural plate, the sinus plate, and the dome of the lateral semicircular canal were intact. The ossicles were intact and mobile. Granulation tissue was sent for histopathological examination. Gene Xpert of the tissue specimen came out to be negative. Right middle ear granulation tissue biopsy reports revealed keratinizing stratified squamous epithelium bony tissue and fibrocartilaginous tissue fragments showing abundant lymphoplasmacytic infiltration without evidence of granuloma, obliterative phlebitis and malignancy (Figure 3).

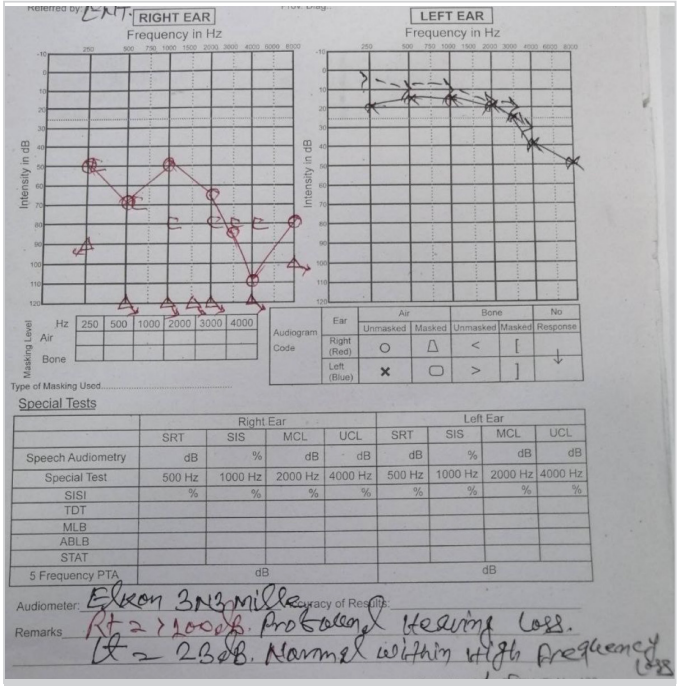

Figure 1. Audiogram of the patient showing profound sensorineural hearing loss in right side

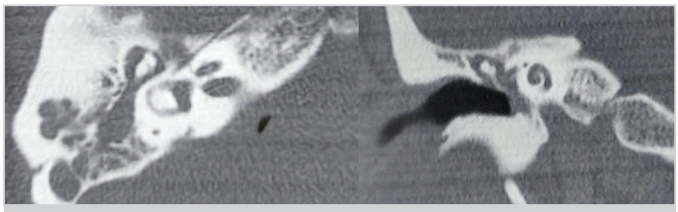

Figure 2. Axial and coronal computed tomography scan of the patient showing soft tissue density lesion in the middle ear, the aditus and the mastoid antrum

Immunohistochemistry showed 50/hpf plasma cells with IgG4 expression and 80/hpf plasma cells with IgG expression. The IgG4/IgG ratio was 62.5%. Diagnosis as probable IgG4 disease was done. He was started on oral steroids and methotrexate along with rituximab injection after consultation with a rheumatologist. After six months of diagnosis and initiation of treatment, his facial paralysis has gradually been recovered and there is no sensation of vertigo. The condition of hearing loss is static.

Systemic screening was done after the disease was diagnosed and no other focus was seen.

An informed consent form was signed by the patient to publish this case.

Discussion

Facial paralysis usually occurs due to Bell's palsy or a traumatic temporal bone fracture. Radiographic evidence of penetrating injury to the nerve, as in open full-thickness incision in trauma-induced paralysis, is an indication for surgical exploration, decompression, and repair with primary neurorrhaphy or grafting, depending on the situation. Apart from this, the treatment of a facial nerve palsy secondary to trauma is similar to that of Bell's palsy. Surgical intervention is considered in patients with Bell's palsy or traumatic facial nerve palsy who have complete paralysis within 14 days of onset, show more than 90% degeneration on electroneurography testing, and have no electromyographical

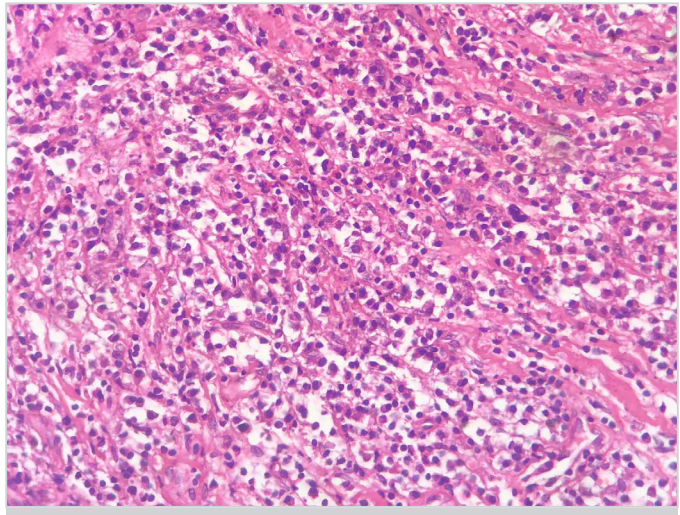

Figure 3. Microscopic image of tissue showing dense inflammatory infiltrates and fibrosis (Hematoxylin and Eosin, 40x)

activity (4). In our center, however, mastoid and tympanic segment decompression is performed on all patients who undergo mastoid exploration due to facial paralysis, regardless of the degree of paralysis. Therefore, in the presented case, the first mastoid exploration and subsequent decompression of the tympanic and mastoid segments of the facial nerve were performed.

IgG4-related disease was first described with involvement of the pancreas more than two decades ago. Since then, it has been practically reported in almost all organs in the head and neck.

The first otological involvement was described in 2010 and since then mastoid has been the most frequent location to be involved in the ear (5).

Below 5% of the total IgG antibody is said to be of IgG4 type in healthy individuals. IgG4 response is initiated after prolonged and recurrent exposure to antigens. One distinctive feature of the IgG4 antibody is its capacity for a half-antibody exchange reaction, whereby the IgG4 antibody readily creates disulfide bonds within the hinge region of its heavy chains. Dissociation of non-covalent bonds allows the chains to separate and randomly recombine leading to the formation of asymmetric antibodies with two different antigen-binding sites. Consequently, the resulting bispecific IgG4 molecules are incapable of cross-linking antigens, thereby forfeiting their ability to generate immune complexes. Also, unlike other IgG subclasses, its amino-acid difference leads to an ineffective complement activation pathway (6).

Pathogenesis of IgG4-related disease has not been clearly understood. But as the name suggests, the IgG4 subclass has been involved in this disease resulting in fibro-inflammatory condition leading to tumor like masses or fibrosis of affected organs. It has been proposed that a collective effect of cytotoxic T lymphocytes and IgG4 antibody causes inflammation leading to fibrotic phase in which pro-fibrotic cytokines are secreted. Resultant activated fibroblasts deposit extracellular matrix, giving rise to dense stratal reaction which is responsible for distorting tissue architecture. This distortion can lead to organ dysfunction and may also culminate in organ failure (7).

Revised comprehensive diagnostic criteria for IgG4-related disease is based on clinical/radiological component, serological evaluation, and pathological assessment (8).

Clinical/radiological criteria: presence of diffuse or localized swelling in one or more organs Serological criteria: serum IgG4 levels greater than 135 mg/dL.

Pathological criteria: presence of at least two of following three criteria:

a. Dense infiltration of lymphocyte and plasma cells combined with fibrosis,

b. Ratio of IgG4-positive plasma cells to IgG-positive cells greater than 40% with more than 10 IgG4-positive plasma cells per high power field,

c. Presence of characteristic tissue fibrosis, especially storiform fibrosis or obliterative phlebitis.

Definitive diagnosis consists when all clinical/radiological, serological and pathological criteria are met. Positive pathological criteria along with clinical/radiological features are classified as probable IgG4-related disease. Positive serological criteria along with clinical/radiological features are classified as possible IgG4 disease.

In the management of active, untreated cases, glucocorticoids serve as the primary choice for inducing remission in all patients. Combination of glucocorticoids with steroid-sparing immunosuppressive agents such as methotrexate, azathioprine, 6-mercaptopurine, mycophenolate, tacrolimus and cyclophosphamide may be required right from the onset of treatment. This approach is chosen because glucocorticoid monotherapy may prove ineffective in controlling the disease and long-term glucocorticoids carry a significant risk of adverse effects. After a successful course of induction therapy, some patients may derive benefits from ongoing maintenance therapy with low dose glucocorticoids or steroid sparing agents (9). Induction of remission is usually done over 2-3 months and maintenance of therapy may take 6–12 months (10). Administering rituximab every 6 months as part of a maintenance therapy regimen has proven to be effective in preventing IgG4-related disease relapse (11).

IgG4-related disease is a relatively new entity, and its pathogenesis has not been properly understood. It can mimic common conditions and a high degree of suspicion is required for identification of the disease. Diagnosis is important as it has favorable prognosis if treatment is initiated early. Recurrences are common and delay in management may lead to severe complications. Adequate awareness is necessary regarding the disease condition among healthcare workers.

Informed Consent: An informed consent form was signed by the patient to publish this case.

Authorship Contributions

Surgical and Medical Practices: R.B.P., Concept: K.D., Design: U.A., Data Collection and/or Processing: U.A., Analysis and/or Interpretation: K.D., Literature Search: U.A., Writing: U.A.

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Main Points

- IgG4-related disease presents with widespread unspecific symptomatology.
- It can mimic various malignant, infectious, and inflammatory conditions leading to confusion in diagnosis and management.
- Diagnosis is based on clinical features, radiology, serology, and histopathology.
- Treatment includes glucocorticoids and steroid-sparing immunosuppressive agents.
- Recurrences are common and delays in management can lead to severe complications.

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