IgG4-Related Otolaryngic Disease: An Under-Recognized Clinical Entity?

Rachel B. Cain M.D.1, Naresh P. Patel M.D.2, Vijayan Balan M.D.3, Thomas V. Colby M.D.4, Devyani Lal, M.D.1

Departments of Otolaryngology – Head & Neck Surgery1, Department of Neurological Surgery2, Department of Hepatology3, Department of Laboratory Medicine & Pathology4

Mayo Clinic, Phoenix, Arizona

Abstract

Objectives: Describe otolaryngic manifestations of IgG4-related disease (IgG4RD) with an illustrative case series.

Study Design: Case series and literature review.

Methods: Review of otolaryngic IgG4RD cases at our institution was conducted.

Results: We present the first otolaryngic case series of IgG4RD from the United States. IgG4RD, a recently described entity affecting multiple organ systems, is typically characterized by tumeffactive lesions, fibrosis, lymphoplasmacytic infiltrate and possible elevated serum IgG4. Clinically, IgG4RD may mimic malignancy or inflammatory processes but histopathology is often non-specific. The disease usually responds to long-term glucocorticoid and immunosuppressant therapy.

Presentation in our IgG4RD patients was initially suspicious for malignancy or invasive infection. Clinical suspicion and repeat pathology review were critical in establishing IgG4RD diagnosis.

Patient #1 presented after multiple non-diagnostic biopsies for cervical lymphadenopathy. MRI for recent retro-orbital pain showed a unilateral enhancing cavernous sinus mass. Review of previous pancreatectomy histopathology revealed IgG4RD (known cause of auto-immune pancreatitis). Review of prior lymph node biopsies also confirmed IgG4RD. Patient #2 presented with headache, vertigo, and an enhancing, infiltrative petroclival mass. Osteomegaly was initially suspected on biopsy. Repeat pathology review showed polyclonal plasmacytosis with increased IgG4-positive plasma cells. Patient #3 presented with massive destruction of the nasal septum and ethmoid sinuses. Lymphoma and vasculitis were suspected. Biopsies showed only inflammation and fibrosis. Repeat review and staining revealed increased IgG4-positive plasma cells.

Once immunosuppressant therapy was initiated for IgG4RD, all patients showed clinical and radiographic improvement.

Conclusions: Otolaryngic IgG4RD may be under-recognized. A high index of suspicion is required to expedite diagnosis, minimize morbidity from multiple biopsies, and initiate treatment.

Introduction

• IgG4-related disease (IgG4RD) is a fibroinflammatory systemic condition recognized in 2003, which is characterized by tumeffactive lesions, a dense lymphoplasmacytic infiltrate rich in IgG4-positive plasma cells, fibrosis, and often but not always, elevated serum IgG4 concentrations.1

• Involvement of numerous organ systems with IgG4RD has been described, including the biliary tree, salivary glands, kidneys, lungs, lymph nodes, meninges, aorta, breast, prostate, thyroid, pericardium, and skin. Exocrine tissue seems preferentially affected.2 The histopathological features are similar across organs, regardless of site.1

• The spectrum of IgG4RD includes Mikulicz’s syndrome, Kütten’s tumor, and Reidel’s thyroiditis, which all share similar pathologic features.1

Cases

Case 1

A 60-year-old man with a history of autoimmune pancreatitis s/p pancreatectomy presented with nasal congestion, cervical lymphadenopathy, and retro-orbital pain. Multiple biopsies of enlarged cervical lymph nodes were non-diagnostic. MRI showed a unilateral enhancing cavernous sinus soft tissue mass. Review of previous pancreas & lymph node histopathology revealed IgG4RD. He was treated with systemic corticosteroids with resolution of symptoms and radiographic evidence of cavernous sinus mass.

Case 2

A 66-year-old man with daily headaches, vertigo, and hearing loss was found to have an enhancing infiltrative process involving the clivus, petrous apices, nasopharynx and paragangyreal tissues on MRI, with bilateral mastoid fluid. Initial differential included lymphoma, osteomegaly, metastasis or granulomatous process. Nasopharyngeal and clival biopsies revealed sclerosis and inflammation, however further review showed polyclonal plasmacytosis with increased IgG4-positive plasma cells. IgG subclass analysis found elevated serum IgG4. His symptoms resolved with initiation of systemic steroids.

Case 3

A 62-year-old woman presented with massive destruction of the nasal septum and ethmoid sinuses causing multiple episodes of epistaxis requiring transfusion. Lymphoma or vasculitis was suspected. Sinonasal biopsies initially revealed only inflammation and fibrosis. Further histopathological review and immunohistochemical staining revealed increased IgG4-positive plasma cells consistent with IgG4RD. Non-progression of her destructive lesion was attained with initiation of systemic steroids.

Discussion

• Chronic sclerosing sialadenitis of the submandibular & parotid glands is a common manifestation of IgG4RD, resulting in unilateral or bilateral swelling.1 Epiphora secondary to bilateral nasolacrimal duct mass-forming lesions from IgG4RD has also been described.2

• IgG4RD can involve the nasal mucosa, resulting in a clinical picture of chronic rhinosinusitis with nasal obstruction, discharge, crusting, & hypoplasia.3 Recurrent mastoiditis with bone erosion from IgG4RD has also been reported.4

• IgG4RD mimics neoplasms, vasculitides, and granulomatous conditions, requiring biopsy for histopathological and immunohistochemical testing. Serum IgG subclass analysis showing elevated IgG4 aids in diagnosis.1

• Lesions are iso- to hypointense on T2-weighted MRI with homogeneous enhancement. Adjacent bone often shows remodeling with erosion or sclerosis.5 FDG-PET is effective for evaluating the presence of systemic lesions, with the uptake of FDG decreasing after steroid therapy.3

• Most patients respond quickly to glucocorticoid therapy. Effective steroid-sparing agents include azathioprine, cyclophosphamide, methotrexate, mizoribine, bortezomb, rituximab1 and mycophenolate mofetil.6

Conclusions

• IgG4RD is an under-recognized disease process that can affect numerous tissues within the head and neck, including the skull base, nose & paranasal sinuses, middle ear & mastoid, thyroid, orbit, salivary, pituitary, and lacrimal glands.

• Features of IgG4RD mimic more common pathologies such as infection and neoplasm.

• A high index of suspicion is required to expedite the diagnosis and initiate appropriate treatment.

References