IgG4-Related Recurrent Periorbital and Sinonasal Eosinophilic Angiocentric Fibrosis

Alison Van Dyke, MD, Ph.D[1], Manju Prasad, MD[1], David Shield, MD[2], John Persing, MD[3], Flora Levin, MD[2], Adebowale J Adeniran, MD[1]

Departments of [1]Pathology, [2]Ophthalmology, and [3]Plastic Surgery, Yale School of Medicine, New Haven, CT

ABSTRACT

Eosinophilic angiocentric fibrosis (EAF) is a rare, progressive tumor-like lesion of the sinonasal and orbital region of unknown etiology. It is characterized histologically by mixed inflammatory infiltrate predominated by eosinophils and concentric perivascular fibrosis. Although benign, it tends to recur following resection and is not amenable to anti-inflammatory therapy. Recently, EAF has been included in the group of IgG4-related diseases, an entity affecting many organ systems and characterized by IgG4-positive plasma cell infiltrate. We present a 53 year-old man with history of nasal obstruction caused by EAF that was resected 8 years ago, and with the chief complaint of double vision. Review of systems was significant for right-sided hearing loss, recurrent nasal congestion, and tearing. Right eye proptosis with lateral displacement of the globe and widening of the nasal bridge were present. The patient underwent anterior and medial orbitotomy with right periorbital, right middle turbinate, and left nasal tumor resection. Grossly, the 3 cm periorbital mass consisted of tan-red firm tissue focally surfaced by mucosa with a tan cut surface. Microscopic examination revealed complete distortion of normal architecture by fibro-collagenous onion-skinning around small-caliber arterioles with a dense, mixed inflammatory infiltrate consisting of numerous eosinophils, lymphocytes, plasma cells, and scattered neutrophils. This morphological presentation was characteristic of EAF. The plasma cell infiltrate was diffusely positive for IgG4. At present, the patient's proptosis and diplopia in primary gaze have resolved. This case provides further support for EAF as a member of the IgG4-related diseases and has implications for potential directed medical treatment.

BACKGROUND

What/Where: EAF is a tumefactive lesion of the upper respiratory and sinonasal tracts and, less commonly, subglottis[1]. It is characterized by areas of onion-skin pattern, whorling fibrosis around small caliber vessels and mixed inflammatory infiltrate including numerous eosinophils.

Who: First thought to affect the young and women more than men, further case series reviews reported a female–to–male ratio of 1.3 with most cases arising in middle age.

Disease Course: The disease course is indolent and progressive with potential sinonasal and orbital bony erosion that can cause disfigurement, ocular symptoms, and problems associated with sinonasal obstruction.

Therapies: EAF lesions are largely described as being unresponsive to steroidal, cytotoxic, and most immunosuppressive regimens.

Etiopathogenesis: First thought to arise in the setting of atopy and other allergic conditions, EAF has recently been included in the group of IgG4-related diseases (IgG4-RDs).

CASE REPORT

THE PATIENT:
- 53 year-old Iranian male

CLINICAL PRESENTATION:
- *Chief Complaint:* Double vision

- *Review of Systems*
  - **+** Mild limitation of right eye extraocular movements
  - **+** Constant diplopia
  - **+** Right eye proptosis (slowly progressive)
  - **+** Tearing
  - **+** Congestion
  - **-** Ophthalmodynia
  - **-** Decreased vision

MEDICAL HISTORY:
- Hypertension
- Recurrent sinus infections & otitis media
- Eosinophilic angiocentric fibrosis
  - 8-9 years ago
  - Presented w/ nasal obstruction
  - Status-post excision in Iran

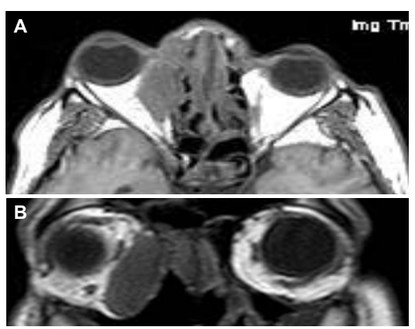
SURGICAL HISTORY – Head & Neck:
- Deviated nasal septum repair
- Right dacryocystorhinostomy – nasolacrimal duct obstruction
- Right tympanostomy – otitis media

ALLERGIES:
No known allergies

SOCIAL HISTORY:
No alcohol, tobacco or illicit drug exposure

PHYSICAL EXAMINATION:
- Right eye exophthalmos
- Nasal bridge widening & obstruction

WORK UP & PROCEDURE



FIGURES 1: Imaging demonstrating right eye exophthalmos & lateral deviation.

WORK UP & PROCEDURE - continued

SURGICAL PROCEDURE:
- Subtotal resection of EAF mass:
  - Right orbit & nose
  - Right lateral rhinotomy
  - Left nasal mass debulking

PATHOLOGY

GROSS DESCRIPTION:
- Perioribtal Mass:
  - Tan-red, firm tissue
  - 3 x 2.5 x 1 cm aggregate
  - Tan cut surface

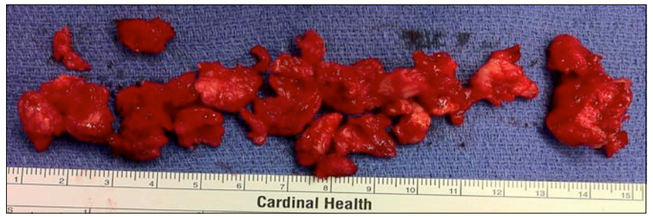


FIGURE 2: Surgical Specimen: Right orbital and nasal mass.

MICROSCOPY: H&E
- Distortion of normal architecture by fibroinflammatory lesion
- Onion-skinning fibrosis around small-caliber vessels with frequent luminal obliteration
- Variably dense, mixed inflammatory infiltrate (numerous eosinophils)
- ***Absence of:***
  - Granulomas, foreign-body giant cells, or necrosis

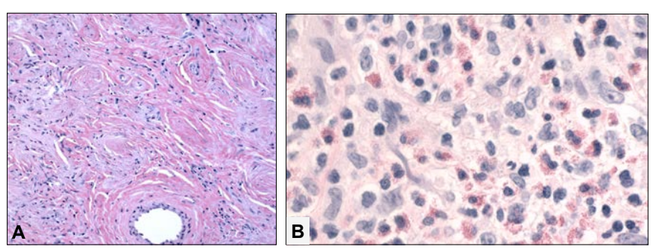


FIGURE 3: Hematoxylin and eosin stain of right middle turbinate mass showing perivascular onion-skin whorling fibrosis (**A**) & mixed inflammatory infiltrate including dense eosinophils (**B**).

***Diagnosis*: EOSINOPHILIC ANGIOCENTRIC FIBROSIS**

ADDITIONAL STUDIES

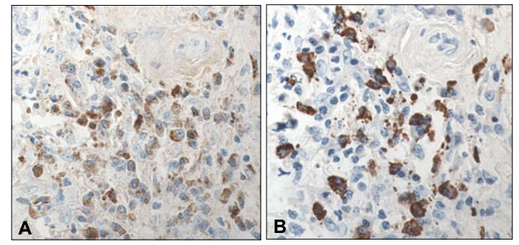


FIGURE 4: IgG4 immunostain of right middle turbinate mass showing dense plasmacytic infiltrate (**A**) and >10 IgG4+ plasma cells per high power field (**B**).

POST-OPERATIVE STATUS
- Diplopia in primary gaze – resolved
- Nystagmus - stable
- Hypoglobus

DISCUSSION

In 2003 Kamisawa et al described a systemic IgG4-related autoimmune disease in association with autoimmune pancreatitis with an infiltration of IgG4+ plasma cells in the pancreas, peripancreatic tissue, bile duct, gallbladder, hepatic portal area, gastric and colonic mucosa, salivary glands, lymph nodes, and bone marrow[2]. Since then, two Japanese study groups have convened to ascertain what constitutes an IgG4-RD[3]. They include: mass lesions/swelling in single/multiple organs, elevated serum IgG4 concentrations (≥135 mg/dL), and/or marked lympho-plasmacytic infiltrate and fibrosis with an IgG4+:IgG+ ratio >40% and >10 IgG4+ plasma cells/HPF. Since its initial description as a disease entity, EAF has also recently been included in the group of IgG4-RDs[4]. Furthermore, responsiveness of IgG4-RD patients to rituximab with disease quiescence has been reported[5].

CONCLUSIONS

The common etiopathogenesis, including genetic and exposure factors, underlying EAF and other IgG4-RDs needs to be elucidated to further identify potential therapeutic interventions.

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