Ocular Immunoglobulin G4-Related Disease. A Case Series.

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Introduction

Immunoglobulin G4-related disease has emerged over the last decade as a systemic, chronic, inflammatory disorder that can present to the Ophthalmologist.

Its pathophysiology is not, as yet, completely understood. Molecular mimicry with cross reactivity between antibodies against bacterial peptide sequences and the body's autologous proteins in a genetically predisposed individual may be explanatory.

Objective

Through the adjacent case descriptions we aim to describe some of the common features of Immunoglobulin 4-related disease.

Case Series

We present the cases of three patients with Immunogobulin G4-related orbitopathy.

Prevalence 62 - 100 per 1000 000
Annual incidence 0.28 – 1.08 per 100 000
Male usually > female but may be equal in head and neck disease

An extensive number of organs have been described as being involved in IgG4 related disease and include, amongst others:.

Pancreas
Kidneys
Bile ducts
Salivary glands
Thyroid gland
Lymph nodes
Pericardium
Blood vessels
Lungs
Brain and meninges
Pituitary
Breast
Prostate
Skin

Other peripheral blood findings may include;

Elevated CRP
Low complement
Peripheral eosinophilia
Elevated IgE

Table 1. The cases of three patients thought to have Immunnogobulin G4-related ocular disease are presented. The key features of their clinical examination the extraocular manifestations of their disease,, and the findings at orbital imaging and the histological analysis of orbital tissue samples are given.

	Case 1	Case 2	Case 3
Age and Gender	46 years Male	28 years Male	31 years Female
Presenting feature	Proptosis Eyelid fat prolapse	Proptosis Eyelid swelling	Eyelid swelling
Medical history	Lymphadenopathy	Asthma Pulmonary nodules Sinusitis Myocardial Infarct	Optic neuritis
IgG4 *			1.68g/L
Radiology	Fat stranding. Medial orbital 'masses'	Rectus muscle enlargement	Lacrimal gland enlargement
Histopathology	Lymphoid cells including plasma cells Fibrosis Obliterative phlebitis		Lymphoid cells, predominantly well formed lymphoid follicles
Treatment	Rituximab	Rituximab	Intra-orbital steroid Rituximab

Figure 1. The clinical appearance of each of our patients is shown. The key radiological findings for each case as already described in Table 1. are also shown in computed tomography images of the orbit for cases 1 and 3 and a magnetic resonance image of the orbit for case 2.

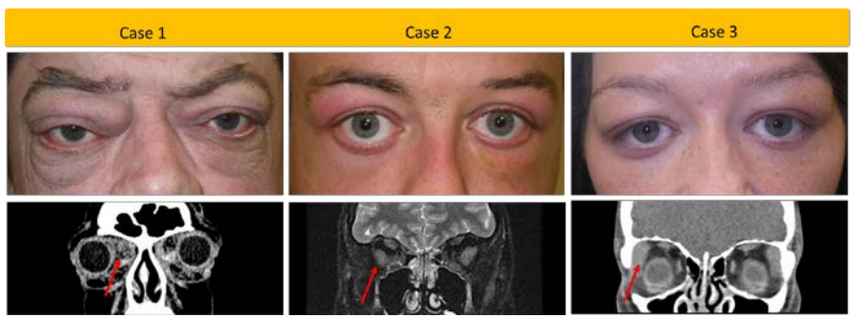
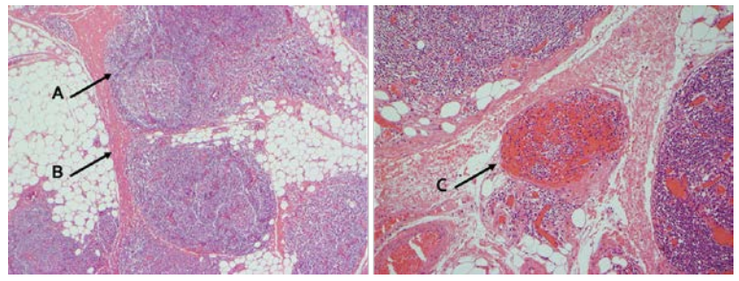


Figure 2. The key pathological features of IgG4 related disease are shown. **A** = Dense lymphoplasmacytic infiltrate, **B** = Storiform fibrosis **C** = Obliterative phlebitis.



Other pathological findings in IgG4 related disease might include:

Phlebitis without obliteration
Tissue eosinophilia
Non necrotizing arteritis

Spontaneous remissions have been reported.

Watchful waiting with close follow up examinations may be an option in patients without organ dysfunction and with disease in locations unlikely to cause complications.

When vital organ are involved aggressive treatment is necessary as IgG4 related disease can rapidly lead to organ dysfunction and failure.

Glucocorticoids are the mainstay of treatment and maintenance therapy.

Rituximab is a very specific agent which interferes with the immunological processes thought to underlie IgG4 disease.

Relapses do occur.

Conclusions

Immunoglobulin G4-related disease is being diagnosed with increased frequency. It should be considered in the differential diagnosis of anyone presenting with orbital pathology.

The work-up requires clinical examination, serological analysis, imaging and histology from affected tissue. It must be distinguished from infections, malignancy and other systemic diseases.

Interdisciplinary collaboration is important for proper diagnosis and treatment.