

An Unexpected Cause of Amaurosis Fugax

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Abstract

IgG4-RD is an increasingly recognized group of immune-mediated conditions that share specific pathologic, serologic, and clinical features. It is a systemic inflammatory disorder that typically causes tumor-like swelling of involved organs, a lymphoplasmacytic infiltrate with predominance of IgG4-positive plasma cells with a variable degree of fibrosis, and elevated levels of serum IgG4. Lacrimal and orbital involvement is rare and when present is referred to as IgG4-related ophthalmic disease. Biopsy is the gold standard for diagnosis. The optimal treatment strategy has yet to be determined but glucocorticoids and rituximab have shown success. We report a case of amaurosis fugax and orbital inflammatory pseudotumor as an unusual presentation of IgG4-RD. IgG4-RD though rare, is likely underdiagnosed and often misdiagnosed. It is important that physicians are aware of the clinical spectrum of IgG4-RD as recognition and accurate diagnosis is crucial and early treatment may induce remission and prevent progression.

Introduction

Amaurosis Fugax is a visual complaint that has many underlying causes. We report a case of amaurosis fugax and orbital inflammatory pseudotumor as an unusual presentation of IgG4-RD. Clinical diagnosis of IgG4-RD is highly variable and early diagnosis is crucial to prevent systemic involvement and long term complications.

Case Report

An 80 year old Caucasian male presented complaining of a two-month history of transient visual loss. He additionally complained of jaw claudication and headaches. Visual disturbances began in the left eye with blurry vision followed by complete visual loss described as a “curtain being pulled over left eye.” Vision spontaneously returned after about 15 minutes. Recurrence of symptoms occurred in the left eye one week later followed once again by spontaneous return of vision. The patient reported ten additional episodes of similar visual loss along with double vision involving both eyes. Additional clinical history includes longstanding bilateral proptosis and periorbital cutaneous lesions previously diagnosed as necrobiotic xanthogranuloma (NXG) [1]. Symptoms had remained relatively stable for 10 years until he noted persistent enlargement and swelling of his orbits as well as parotid glands. Examination revealed significant bilateral proptosis with periorbital edema, with enlargement of the lacrimal and parotid glands. MRI with and without contrast of the brain and orbits (Figures 1 and 2) revealed bilateral proptosis with marked thickening and diffuse enhancement of the bilateral medial rectus muscles and bilateral inferior rectus muscles, left-sided greater than right. Additionally inflammation of the bilateral lacrimal glands also known as dacryadenitis was present. In comparison to an MRI performed 3 years prior, the changes involving appeared to be chronic. Patient’s labs are listed in Table 1. Of note was a significant elevation in IgG, IgG SC4, along with elevated ESR and CRP.

Patient Lab Values			
IgG	2957 mg/dL (700-1600 mg/dL)	ESR	51 mm/hr (0-20 mm/hr)
IgG SC4	320 mg/dL (4-86mg/dL)	CRP	20 mg/L (0-10 mg/L)
ANA	Negative	C3/C4	Normal
SSA/SSB	Negative	ANCA	Negative
RF/CCP	Negative	CBC/CMP/TSH	Normal
TSH	Normal	SPEP	Normal

Table 1: Relevant patient lab values. Reference values in parentheses.

Differential diagnosis for the amaurosis fugax and proptosis in this patient was IgG4 related disease with signs and symptoms of orbital inflammatory pseudotumor and Mikulicz’s syndrome, giant cell arteritis, transient ischemia attack, vasculitis, and NXG. The patient was started on prednisone 60 mg daily with dramatic improvement in proptosis and orbital edema within a few days. A temporal artery biopsy was negative and ruled out giant cell arteritis. The biopsy was performed two days after starting prednisone. The accuracy of this biopsy is not affected as long as the biopsy is performed within two weeks of starting steroids [2]. CT and MRI of brain were negative for CVA and cardiac echocardiogram was normal. Given these negative tests and a clinical presentation of marked proptosis that nearly resolved with prednisone, TIA was ruled out. The patient was referred for oculoplasty and orbital biopsy to confirm the diagnosis of orbital inflammatory pseudotumor and evaluation for IgG4-RD. He remains on 10 mg prednisone daily and follows up regularly. Currently, we are considering adding rituximab as a steroid sparing agent. This patient

satisfied the first two diagnostic criteria listed in Table 2 confirming a diagnosis of Immunoglobulin G4-related disease [3].



Figure 1: T2 weighted MRI brain/orbits. Bilateral proptosis with marked thickening and diffuse enhancement of the bilateral medial rectus muscles (yellow arrows) and bilateral inferior rectus muscles present. Additionally, inflammation of the bilateral lacrimal glands is present (red arrow).

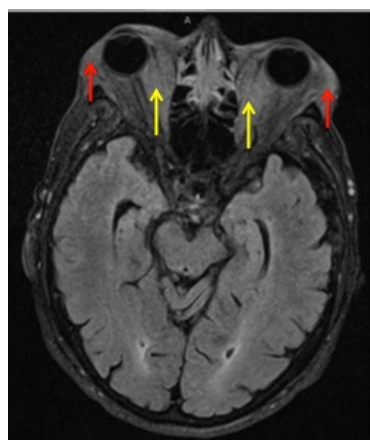


Figure 2: T1 weighted MRI brain/orbits. Bilateral proptosis with marked thickening and diffuse enhancement of the bilateral medial rectus muscles (yellow arrows) and bilateral inferior rectus muscles present. Additionally, inflammation of the bilateral lacrimal glands is present (red arrow).

3. Histopathological features including lymphocyte and IgG4+ plasma-cell infiltration with typical tissue fibrosis or sclerosis

Table 2: Diagnostic criteria for IgG4+ Mikulicz's disease adapted from Masaki Y et al. [7].

Discussion

IgG4-RD is an increasingly recognized group of immune-mediated conditions that share specific pathologic, serologic, and clinical features [4]. It is a systemic inflammatory disorder that typically causes tumor-like swelling of involved organs, a lymphoplasmacytic infiltrate with predominance of IgG4-positive plasma cells with a variable degree of fibrosis, and elevated levels of serum IgG4 [5]. It most often presents with infiltration of a single organ and most often affects males over the age of 60. It classically presents as a "lymphoplasmacytic sclerosing pancreatitis," now known as type 1 (IgG4 related) autoimmune pancreatitis. Other frequently involved sites include the liver, thyroid, salivary, or lacrimal glands, bile ducts, aorta, retroperitoneum, and lymph nodes. Lacrimal and orbital involvement is rare and when present is referred to as IgG4-related ophthalmic disease [4-7]. Biopsy is the gold standard for diagnosis. The optimal treatment strategy has yet to be determined but glucocorticoids and rituximab have shown success [8]. We report a case of amaurosis fugax and orbital inflammatory pseudotumor as an unusual presentation of IgG4-RD. Though rare, IgG4-RD is likely underdiagnosed and often misdiagnosed. It is important that physicians are aware of the clinical spectrum of IgG4-RD as recognition and accurate diagnosis is crucial and early treatment may induce remission and prevent progression.

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Diagnostic Criteria for IgG4+ Mikulicz's disease

1. Symmetrical swelling of at least 2 pairs of lacrimal, parotid, and submandibular, glands continuing for more than three months

And

2. Elevated Serum IgG4 (>135 mg/dl)

Or