Simultaneous Unilateral Presentation of Three Different Ocular Manifestations of Granulomatosis with Polyangiitis

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Abstract

Purpose: To report the simultaneous presentation of three ocular manifestations of granulomatosis with polyangiitis in one eye.

Case Report: A 42-year-old man with a confirmed diagnosis of granulomatosis with polyangiitis was referred to the emergency room with sudden blurred vision. Eye examination showed hyperemic conjunctiva due to necrotizing scleritis in the superior nasal quadrant of the left eye, a mass in the left superior lid, as well as central retinal artery occlusion in the same eye.

Conclusion: This case suggests that unilateral eye involvement may be a manifestation of underlying granulomatosis with polyangiitis.

Keywords: Central Retinal Artery Occlusion; Granulomatosis with Polyangiitis; Lid Granuloma; Necrotizing Scleritis

INTRODUCTION

Granulomatosis with polyangiitis (GPA), also known as Wegener’s granulomatosis, is a rare multisystem disease. GPA is classically characterized by necrotizing granulomatosis lesions in the upper and lower respiratory tract, focal segmental glomerulonephritis, and necrotizing vasculitis. Although its etiology is unknown, organ damage occurs because of small vessel vasculitis and granulomatous inflammation. According to Carol et al study, anti-neutrophil cytoplasmic antibody (ANCA) titers measured by serum immunofluorescence are associated with certain systemic vasculitides.¹

The ANCA test distinguishes two types of immunofluorescence patterns. Diffuse granular fluorescence within the cytoplasm (c-ANCA) is highly specific for GPA and is also detectable with enzyme-linked immunosorbent assay (ELISA). Diffusely granular, cytoplasmic staining pattern under microscopy is caused by autoantibodies directed against proteinase 3. Fluorescence surrounding the nucleus (p-ANCA), an artifact of ethanol fixation, can be caused by...
autoantibodies for several target antigens. This finding is therefore nonspecific and must be confirmed by ELISA for ANCA reacting with myeloperoxidase (MPO-ANCA) because MPO-ANCA testing has a high specificity for small vessel vasculitis. Absolute levels of ANCA do not define disease severity or activity \(^{[1]}\), but changing titers can give a general idea of disease activity and therapy efficacy.\(^{[2]}\) Corneal, nasolacrimal, optic nerve, uveal, retinal, and conjunctival involvement have only been reported in few cases. Visual loss in GPA may result from choroidal, retinal, or optic nerve involvement.\(^{[3,4]}\) In this study, we report a case of GPA with rare synchronous unilateral ophthalmic manifestations.

**CASE REPORT**

A 42-year-old man presented to Feiz Eye Hospital with sudden persistent painless loss of vision in April 2013. He had been diagnosed with GPA 10 months before. His presenting symptoms at that time were high fever and left eye redness along with nasal congestion, sinonasal obstruction, breathing difficulties, and joint pain. Laboratory tests revealed proteinuria. After physical examination, laboratory investigations, kidney biopsy, and imaging studies, GPA was diagnosed. The patient was hospitalized and treated with cyclophosphamide for 14 days. On discharge, he was prescribed high dose corticosteroid (prednisone: 100 mg daily) as a maintenance therapy.

The patient’s symptoms improved until April 2013, when sudden severe visual loss in the left eye caused admission to the hospital. The patient described the sudden appearance of a black spot in his vision that spread all over his left visual field in 1 minute. He also had severe headache, redness of the left eye, and pain for three days.

In the ophthalmologic examination, visual acuity of the right eye was 10/10 and the left eye had only light perception. Relative afferent pupillary defect was positive in the left eye. Slit lamp examination was normal in the right eye but in the left eye there was a 4 mm round, fixed and painless mass in the upper eyelid [Figure 1]. Conjunctiva was hyperemic, and an area of 2 mm necrotizing nodular scleritis in superonasal quadrant was noted [Figure 2]. The cornea, iris, lens and vitreous cavity were normal. Intraocular pressure of the left eye was normal. Dilated funduscopic examination showed a white, swollen retina, particularly in the posterior pole, with a cherry-red spot. There was arterial attenuation and intravascular segmentation of the blood column in the posterior pole, but no emboli were noted [Figures 3 and 4].

The patient’s description of painless, sudden loss of vision and appearance of the cherry-red spot on examination of the fundus indicated. Therefore, we gave him nasal \(O_2\), and performed ocular massage and paracentesis of the anterior chamber. The patient was hospitalized for 7 days and was treated with...
intravenous cyclophosphamide as per internal medicine consult. Aggressive lubrication of the ocular surface and frequent instillation of topical steroids and cycloplegics was prescribed. After several weeks, eyelid nodule and scleritis improved, but vision loss remained.

DISCUSSION

GPA is an autoimmune disease which can progress rapidly and is potentially fatal. It can involve any organ system, including the eyes with different manifestations. Ocular involvement may be an extension from the adjacent paranasal sinuses (contiguous) or as a result of focal vasculitis (non-contiguous). Incidence of ocular involvement in GPA varies from 29% to 79%, Early recognition and subsequent aggressive treatment helps, not only to control inflammation of the eye, but also to prevent potentially life-threatening renal failure. Ophthalmologists may be the first clinicians to encounter GPA patients because ocular manifestations, particularly necrotizing scleritis, may be the first sign of the disease.

Necrotizing scleritis, signified by scleral thinning and a bluish appearance from visibility of the underlying choroid, can lead to scarring, infection, and, in advanced cases, perforation of the globe and phthisis bulbī. Scleritis and episcleritis were noted in 7% and 3.5%, of 140 patients described by Bullen et al, respectively. Visual loss may occur in 85% of individuals with severe necrotizing posterior scleritis, despite aggressive immunosuppression. Visual loss in patients with an established diagnosis of GPA has been documented by several authors, however, visual loss as the primary presentation of the disease has only been reported in a small number of cases.

A more common posterior segment involvement in this disease is retinal vasculitis. As such, we should consider GPA in the differential diagnosis of patients presenting with CRAO and retinal vasculitis. CRAO, a rare event, causes severe visual disturbances and is generally resistant to treatment. Retinal whitening, cherry-red spot, and a pale disc are the characteristic fundus changes associated with CRAO. The prognosis of CRAO is generally poor, and the degree of visual damage is thought to be related to the duration of retinal ischemia and presence of cilio-retinal artery. CRAO results from one or more pathological processes, including retinal emboli, vessel narrowing and thrombosis, arterial spasm, vascular narrowing caused by extravascular disease, and reduced blood flow caused by carotid or ophthalmic artery obstruction. The pathogenesis can be inferred by vasculitis mediated by in part, by stimulatory autoantibodies (ANCA).

In Bullen’s series, 4 of 140 patients (2.9%) had retinitis and only one had a branch retinal vein obstruction. Vasculitis can involve the retina or choroid, be unilateral or bilateral, central or multifocal. It is clinically characterized by perivasculær sheathing, focal arterial and venous occlusion, retinal whitening or ischemia, intraocular hemorrhage, retinal neovascularization, and vitreous hemorrhage. Although ocular manifestations are relatively common in the course of the disease, eyelids and conjunctiva are rarely involved.

Occurrence of CRAO and eyelid involvement, both uncommon manifestations of GPA-related vasculitis, along with the more common necrotizing scleritis in a patient, is an interesting presentation of the disease. This association has not been previously reported. This case suggests that unilateral eye involvement may be a manifestation of underlying granulomatosis with polyangiitis.

Based on its responsiveness to treatment, the eyelid mass seemed to be a granuloma. Ideally, this would have been better confirmed through histological evaluation;
however, we did not perform any further investigations due to patient denial.

Physicians should be aware of the atypical and varied presentations of GPA, which will facilitate the identification and management of this life-threatening disease.

Declaration of Patient Consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of Interest
There are no conflicts of interest.

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