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Wegener's Granulomatosis Revealed by Bilateral Orbital Inflammatory Pseudotumor: a Case Report and Literature Review

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Abstract **Case Report**

Purpose*:** To describe the chronology and the extent of orbital involvement in a case of granulomatosis with polyangiitis (GPA). ***Methods*:** Descriptive case report and literature review. ***Results*:** A thirty-two years old male consulted with the following complaints: A retro-orbital discomfort in both eyes, a bilateral fast progressive proptosis and a decrease in visual acuity in the left eye. Eye examination revealed a proptosis, ptosis, epiphora and a motility restriction and peripheral corneal ulcer infiltrates with nodular scleritis in the left eye. A palpable orbital mass was located in the sub temporal orbit in both eyes. Orbit magnetic resonance imaging (MRI) unveiled a diffuse and elongated enlargement of both lacrimal glands with enhancing mass in the superior lateral aspect of both eyes globe. The diagnosis of an orbital pseudotumor was suspected. The biological work-up revealed a high blood levels of inflammation markers and antineutrophil cytoplasmic antibodies (c-ANCA). The diagnostic of active systemic granulomatosis with polyangiitis was then made. ***Conclusion: As seen in this case, clinicians should consider a differential diagnosis of granulomatosis with polyangiitis in patients with an orbital pseudotumor mimic aspect.

Keywords: Granulomatosis with polyangiitis, ANCA associated vasculitis, orbital pseudotumor, Rituximab.

INTRODUCTION

Granulomatosis with polyangiitis (GPA), more commonly referred to as Wegener's granulomatosis (WG), is a necrotizing vasculitis that affects small and medium-sized vessels, which is a component of a vast spectrum of disorders entitled the anti-neutrophil-cytoplasmic-antibody (ANCA) associated vasculitides (AAV). Among the three ANCA-associated vasculitides, GPA is the most common.

To diagnose orbital Wegener's granulomatosis (WG) is a challenge. WG is a relapsing multi-organ disease most often affecting the kidneys and respiratory tract. If untreated, the disease can result in renal failure and death [1, 2]. Ophthalmic involvement is quite diverse as it may include scleritis, corneal melting, uveitis, lacrimal duct obstruction and orbital mass [3]. The diagnostic process in orbital WG is complicated by negative and aspecific findings in blood tests, imaging and biopsy [4]. As a result, the diagnostic process takes longer. This may harm the patient as inflammation continues, causing irreversible damage. To improve our diagnostic strategy, we reviewed patients with a bilateral orbital mass in whom WG was in the differential diagnosis. Our aim is to shorten the diagnostic process in WG by identifying diagnostic features that differentiate orbital WG from other orbital inflammatory diseases.

CASE PRESENTATION

The present report describes the case of a thirty-two years old male with just a one year history of knee arthritis who consulted in our ophthalmology department with the following complaints: A retro-orbital discomfort in both eyes, a bilateral fast progressive proptosis and a decrease in visual acuity in the left eye.

RESULTS

On examination his BCVA was 6/7.5 and 6/60 in OD and OS respectively. Masses were present in both lacrimal glands, especially on the left side, spilling down into the inferior part of the left orbit. Masses were woody hard with gross inflammation of the ocular surface overlying it.

The anterior segment showed a proptosis, moderate swelling and erythema confined to the upper eyelid and temporal bulbar conjunctiva, ptosis, epiphora and a motility restriction. The examination also showed a peripheral corneal ulcer infiltrates covering the limb in both eyes (Figure 2) and a nodular scleritis in the left eye with a scleral thinning and visible, bluish uveal tissue.

Right eye fundus exam was within normal limits, but the left eye fundoscopy revealed a slightly elevated optic disc. IOP was 23mmhg (RE) and 27mmhg (LE).

Other than the ophthalmological aspect, the patient was afebrile and without weight loss, but felt lethargic while walking around.

Anterior segment optical coherence tomography (OCT) centered on the nodular lesion showing a thickening of the anterior sclera with hyperreflectivity (Figure 3).

Orbit magnetic resonance imaging (MRI) unveiled a diffuse and elongated enlargement of both lacrimal glands with enhancing mass in the superior lateral aspect of both eyes globe.

Then a biopsy of the left orbital mass was performed and revealed a mixed inflammatory infiltrate consisting of lymphocytes, neutrophils, eosinophils and granulomatous inflammation but no necrosis or vasculitis. The diagnosis of GPA was considered.

The biological work-up revealed as a matter of fact a high blood levels of inflammation markers and antineutrophil cytoplasmic antibodies (c-ANCA), the kidney function test and the urine protein were normal. The diagnostic of active systemic granulomatosis with polyangiitis was then made. The patient had to be transferred into the internal medicine department and the induction therapy of choice was a combination of intravenous methylprednisolone and intravenous cyclophosphamide (total dose: 1 g) plus oral prednisolone (starting dose 40 mg/ day, tapering 2.5 mg every two weeks).

Two weeks later, the clinical evolution of the patient deteriorated with the onset of NYHA stage IV dyspnea and bilateral edema of the lower limbs. Renal function was impaired and a chest CT-scan showed an active alveolar hemorrhage. A transthoracic echocardiography *showed* that his *left ventricular systolic function* was depressed, with a globally reduced ejection fraction of *30*%. The diagnosis of GPA with myocardial and pulmonary involvement was retained.

Induction therapy of rituximab was immediately started, but the patient went into a critical condition and unfortunately end up dying after few days.

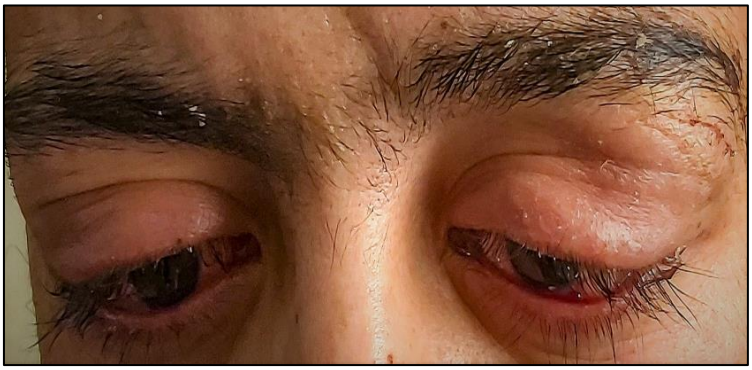

Fig 1: Bilateral mass in the upper external orbital angle with proptosis, upper lid swelling and ptosis

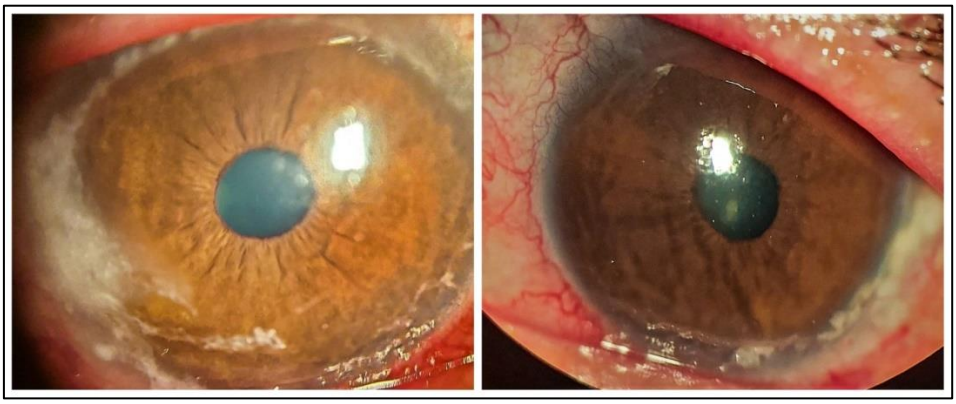

Fig 2: Pictures of the right and left eyes: chemosis, conjunctival hyperhemia, peripheral corneal ulcer infiltrates partially covering the limb zone in both eyes; and a necrotizing scleritis

Fig 3: Anterior segment OCT centered on the nodular lesion showing a thickening of the anterior sclera with hyperreflectivity and few spaces of hyporeflective spots in the deep sclera and focal thinning

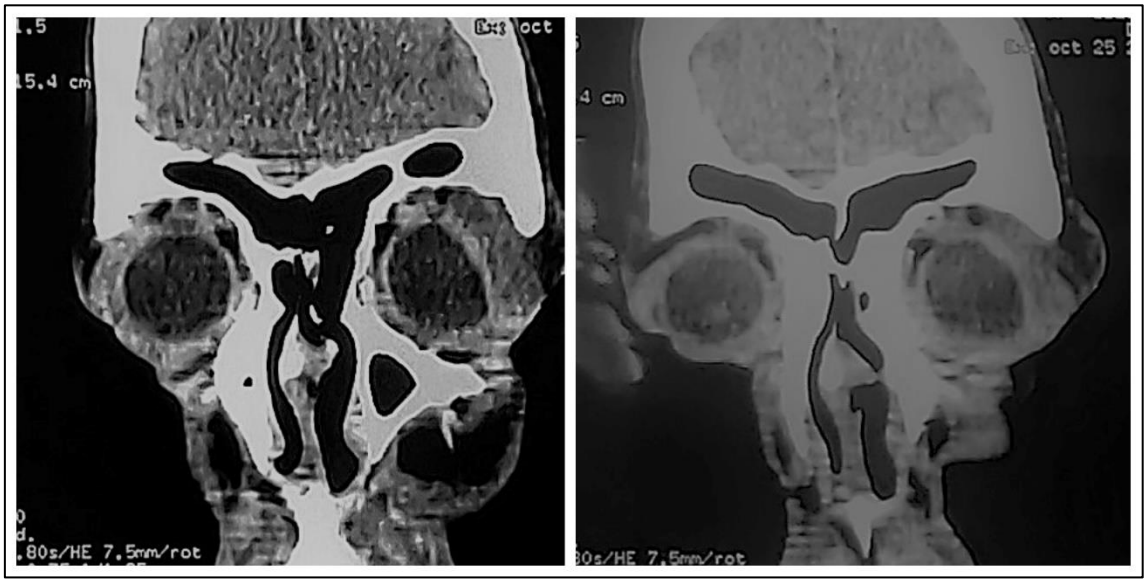

Fig 4: Magnetic resonance imaging (MRI) of the orbit and brain in coronal plane, showing diffuse and elongated enlargement of both lacrimal glands with enhancing mass in the superior lateral aspect of both eyes globe (arrow). Subcutaneous infiltrations are accompanied in the lateral outside of the left orbit

DISCUSSION

Limited forms of granulomatosis with polyangiitis (GPA) are challenging to diagnose. Orbital involvement in GPA is rare and found in about 15% of the cases, representing about 45% of ocular manifestations of the disease and being frequently associated with the limited, benign form of the illness, this orbital inflammation is thought to be mediated by CD4+ T cells with a T helper 1 cytokine profile [5].

Orbital inflammation is a challenging cause of vision loss, pain, diplopia, and even blindness. The differential diagnosis is extensive and includes GPA, thyroid eye disease (TED), sarcoidosis, lymphoma, metastatic disease, histiocytosis, dacryoadenitis, and infection. Orbital involvement in GPA encompasses : lid erythema, proptosis, or orbital mass (69%), obstruction of the nasolacrimal duct (52%), lacrimal sac mucocele (47%), extraocular muscle involvement or diplopia (52%), bony erosion, orbital socket contracture, enophthalmos and compressive optic neuropathy. 80% of the compressive neuropathy cases are due to the presence of an orbital granuloma and 14% of them are related to bilateral lacrimal gland masses [6]. Scleritis and conjunctivitis are most commonly seen. Scleritis can lead to necrotizing anterior scleritis, eventually causing blindness, and seems to be mediated by the ANCA produced B cells. Peripheral ulcerative keratitis (PUK) is the most significant corneal complication of GPA that could lead to corneal melt syndrome. Other manifestations include episcleritis and anterior uveitis [7].

Evaluation of a patient with suspected GPA involves a complete clinical, laboratory, radiological, and histopathological assessment. A thorough clinical evaluation to assess the site and extent of involvement is key while evaluating a patient with GPA. Laboratory evaluation includes a complete blood count, electrolytes, renal function panel, urinalysis, titers of PR3-ANCA and MPO-ANCA, erythrocyte sedimentation rate (ESR), and c-reactive protein (CRP). Radiological evaluation of sinuses, lungs, trachea, and orbits can be performed to assess the sites and extent of involvement. A chest x-ray and computed tomography (CT) scan of the lungs can be done to look for pulmonary lesions and hemorrhage. This could further help in differentiating between GPA and

MPA. Histopathological evaluation, including kidneys, skin, and lungs, can be performed to look for vasculitis and immune deposits [8]. The lung is the most common site for biopsy, and a renal biopsy could be performed, which shows necrotizing glomerulonephritis. Our patient experienced an acute disease exacerbation of multiple manifestations within 4 weeks only.

The main goals of the treatment in GPA are remission induction, followed by maintenance of remission, by using immunosuppressant drugs. Oral corticosteroids alone failed to induce remission [9]. Drugs with proved effectiveness in induction and/ or maintenance of remission are: cyclophosphamide, methotrexate, rituximab, azathioprine, mycophenolate mofetil, 15-deoxyspergualin, cyclosporine, and intravenous immunoglobulin. The cyclophosphamide and high-dose glucocorticoids combination is the standard of care for remission-induction in GPA patients, usually lasting for 3 to 6 months. A randomized controlled trial investigated the efficacy of rituximab in ANCA associated vasculitis, and concluded that rituximab was not inferior to daily cyclophosphamide for induction of remission and may be superior in relapsing disease [10]. In patients without severe disease and no contraindication to methotrexate, methotrexate, in combination with glucocorticoids, is used. Indications for plasmapheresis are rapidly declining kidney function, presence of positive anti-glomerular basement membrane antibodies, or pulmonary hemorrhage complicated by respiratory compromise that does not respond to intravenous glucocorticoids.

CONCLUSION

This case report, though rare, describes an unusual exacerbation of GPA disease evincing that ophthalmologists should consider it as a differential diagnosis of orbital tumors, as it may have different clinical manifestations, even in non-Caucasian population.

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