

Case report

Orbital presentation of systemic vasculitis: a diagnostic and management challenge

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Abstract

Background: Orbital involvement in Wegener's Granulomatosis (WG) is rare and has an overall good prognosis. **Case:** A 60-year-old hypertensive Indian female presented with vision loss and painful proptosis of left eye. Orbital incisional biopsy suggested necrotising small vessel inflammation. The saddle nose deformity and pedal nodulo-ulcerative lesions further consolidated the diagnosis of Wegener's granulomatosis. Systemic immunosuppressant provided remission and the only relapse was managed successfully with intravenous Rituximab. **Conclusion:** Wegener's granulomatosis should be kept in the differential diagnosis of painful proptosis with a diffuse orbital mass in an elderly patient presenting with profound vision loss. Newer immune modulating agents are useful adjuncts in preventing relapses of this fatal disease.

Keywords: Wegener's granulomatosis, proptosis, Rituximab, management

Introduction

Proptosis, with or without retrobulbar mass, in elderly population has variable differential diagnosis ranging from inflammatory and autoimmune pathology to a malignant disease. Wegener's granulomatosis (WG) is a rare multisystem inflammatory vasculitis involving small to medium sized blood vessels. Its incidence ranges from 3 to 9.7 cases /million/year. It is more prevalent in Caucasian population with an average age being 40 years (Cotch et al, 1996). Respiratory tract and renal involvement is typical of systemic WG along with head and neck region. Gomes et al (2010) noticed that orbital involvement (proptosis, orbital mass, orbital cellulitis) by WG is rarer (15-35%) than sinonasal involvement (paranasal sinus

mucocele, nasal bone destruction with saddle nose deformity).

High suspicion and early diagnosis of orbital WG by an ophthalmologist is important for management of this life threatening systemic disease as prompt diagnosis becomes life saving. In advanced stages, irreversible orbital fibrosis and multisystem involvement renders the prognosis grave (Pakrou et al, 2006).

Case report

A 60-year-old Indian female presented to Oculoplastics clinic in June 2011 with chief complaints of profound diminution of vision, pain, swelling and redness of left eye for last 3 months. She was a known hypertensive and was on treatment for last 18 months. On ocular examination, her vision was 6/6 in right eye and no perception of light in the left. Intraocular pressure on applanation tonometry was 18 mmHg and 26 mmHg in right and left eye respectively. The right eye was normal with the

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direct pupillary reflex present. The consensual, however, was absent. Left pupil was dilated and non-reacting (both direct and consensual) (Figure 1A). On Hertel's exophthalmometry, left eye had a proptosis of 5mm. The extraocular movements of left eye were restricted in all gazes (Figure 1B). Local examination revealed fullness of left superior orbital sulcus with presence of firm, nontender, diffuse palpable mass in superior orbit whose posterior extent was not reachable. Retrobulbar resistance was raised. Conjunctival vessels were congested and tortuous along with peripheral corneal opacity extending from 3 to 8 o'clock position (Figure 1A). There was 360 degree neovascularisation of iris. Anterior chamber was quiet and grade IV nuclear sclerosis was present. On fundus examination of left eye, multiple old resolving retinal hemorrhages in all quadrants were seen suggestive of a regressed central retinal vein occlusion.

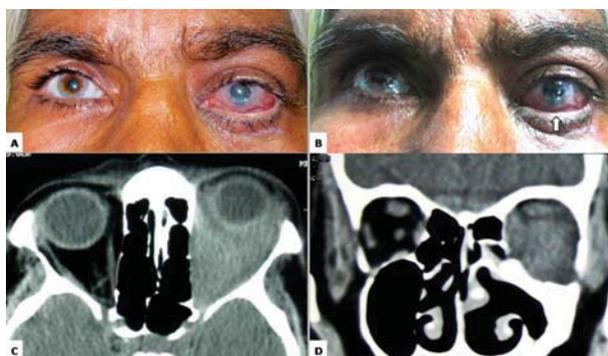


Figure 1

A- Proptosis of left eye with marked conjunctival dilated tortuous vessels, dilated pupil

B- Restricted extraocular movements (frozen globe)

C- CT scan (axial view) shows diffuse, ill defined mass filling almost whole of orbital cavity, no intracranial extension seen

D- Extraocular muscles are not well defined, both intraconal and extraconal compartments are involved

Computer tomography scan showed diffuse, ill defined, moderately enhancing orbital mass filling almost entire left orbital cavity and pushing the globe forwards (Figure 1C, D). There was no bone erosion, sinus invasion or globe compression by the mass. No intracranial extension was noted. Differential diagnosis of orbital lymphoma and orbital metastasis were kept.

Fine needle aspiration biopsy was done which showed few RBCs and inflammatory cells. Meanwhile, the systemic workup did not reveal any occult primary lesion. Systemic investigations, C-ANCA (anti-neutrophil cytoplasmic antibody), RA factor (Latex test) and C-reactive protein, were positive. On retrograde history, the patient had occasional knee joint pain. She had saddle nose deformity along with non healing nodulo-ulcerative lesions on feet (Figure 2E, F).



Figure 2

E- Saddle nose deformity

F- Nodulo- ulcerative lesions on feet

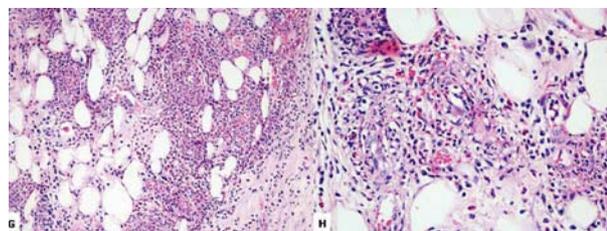


Figure 3:

G (40x magnification) & H (100x magnification) - HPE (H & E stain) shows marked inflammatory cell infiltration, mainly around small blood vessels showing necrosis



Figure 4

I-Reduced proptosis and no conjunctival congestion

J- Mild improvement in extraocular movements

K & L- Healed ulcers of extremities

Incisional biopsy from the orbital mass was carried out and histopathology showed tissue necrosis along with granulomatous inflammatory cells. These cells were predominantly seen around small vessels (Figure 3 G, H). A diagnosis of necrotizing small vessel vasculitis was suggested.

Clinical and histopathological features lead us to the final diagnosis of systemic Wegener granulomatosis with orbital involvement. The patient was started on pulse intravenous Methylprednisolone 1gm (3 cycles) followed by oral steroids (1.5mg/Kg body weight) for 6 weeks with slow tapering. Pain and conjunctival congestion improved after a week of steroids but proptosis remained the same. Intravenous cyclophosphamide (500mg) was prescribed for 6 cycles (every 2 weeks for the first 3 pulses and every 3 weeks for next 3) with 200 mg of prior injection of mesna infusion. Four weeks after the last cycle, intravenous Rituximab infusion was given to prevent disease relapses. She responded very well as the proptosis and orbital congestion disappeared after 6 cycles of cyclophosphamide (Figure I, J) along with healing of foot ulcers (Figure 4 K, L) and relief from joint pains. Her vision remains no light perception in the left eye. The patient is clinically stable and on follow up for more than 12 months.

Discussion

Wegener's granulomatosis is a common systemic vasculitis, which typically involves both arterial and venous circulations of small to medium caliber vessels. Head and neck region is affected in more than 90 % with sino-nasal tract being most commonly involved. WG may affect eye, orbit and adnexal structures in up to 50 % of cases with 7 % having proptosis as chief complaint. Orbital involvement occurs either due to contiguous spread from the paranasal sinuses or due to primary involvement of small vessels of orbit (Fauci et al, 1983).

Ocular complications of WG include proptosis (13%), scleritis/episcleritis (11%), peripheral corneal ulceration (8%), nasolacrimal duct obstruction (7%), optic nerve vasculitis (6%), retinal artery occlusion (5%), conjunctivitis (4%), and uveitis (3%). Poor vision (usually < 6/60) occurs in up to 50% of orbital cases, as a result of ischemic or compressive optic neuropathy. Ophthalmic complications may result from focal vasculitis, granulomatous inflammation, vascular thrombosis, and hemorrhage, or due to chronic inflammation or ischemia. Scleritis reflects the presence and severity of systemic involvement by ischemic disease which can result in limbal ischemia and scleral necrosis (Bullen et al, 1983).

The differential diagnosis for orbital WG includes bacterial or fungal orbital inflammatory infiltration, lymphoma of the orbit, sarcoidosis, Grave's orbitopathy, and orbital pseudotumor (Pakrou et al, 2006). Fine-needle aspiration biopsy (FNAB) has very limited role in the diagnosis of WG because of absence of salient features of this necrotizing small vessel vasculitis. Kalina et al (1992) suggested the histopathological (HP) triad of granulomatous inflammation, tissue necrosis and vasculitis seen in around 50% of orbital biopsies but its absence does not exclude the diagnosis. Similarly, in our case, FNAB was inconclusive while HP guided us to the accurate diagnosis.

Nolle et al (1989) and Rao et al (1995) reported that c-ANCA alone cannot be used for diagnosis in place of tissue biopsy because of its limited positivity (67-85%) rates. But, positive c-ANCA may help in reaching at diagnosis in cases with atypical pathological features. C-ANCA has its value in follow up of patient and monitoring disease activity.

Intravenous Cyclophosphamide is the drug of choice for WG, and is used in form of pulsed treatment followed by oral prednisolone. Methotrexate is used as a remission-maintaining agent but now Infliximab, Rituximab, and 15-deoxyspergualin have also been reported to have long term control over the disease (Pakrou et al, 2006). Due to the chronicity of the disease and frequent relapses, immunosuppressive and immunomodulatory treatment is usually preferred.

WG involving orbit is a rare occurrence and has a good overall prognosis with appropriate and timely management. Diagnosis is routinely guided by the histopathological characteristics of small vessel necrotizing vasculitis in a representative tissue sample.

Conclusion

WG should be kept in the differential diagnosis of an elderly patient presenting with proptosis and vision loss. Rituximab is a useful systemic adjunct to prevent relapses of this disease.

References

Bullen CL, Liesegang TJ, Mc Donald TJ, DeRemee RA (1983). Ocular complications of Wegener's granulomatosis. *Ophthalmology*; 90: 279-290.

Cotch MF, Hoffman GS, Yerg DE, Kaufman GI, Targonski P, Kaslow RA (1996). The epidemiology of Wegener's granulomatosis.

Estimate of the five year prevalence, annual mortality and geographic disease distribution from population-based data sources. *Arthritis Rheum*; 39: 87-92.

Fauci AS, Haynes BF, Katz P, Wolff SM (1983). Wegener's granulomatosis: prospective clinical and therapeutic experience with 85 patients for 21 years. *Ann Intern Med*; 98: 76-85.

Gomes GL, Halpern AS, Souza FH, Shinjo SK (2010). Association between saddle nose deformity and retro-orbital mass in Wegener's granulomatosis. *Acta Reumatol Port*; 35:340-345.

Kalina PH, Lie JT, Campbell RJ, Garrity JA (1992). Diagnostic value and limitations of orbital biopsy in Wegener's granulomatosis. *Ophthalmology*; 99: 120-124.

Nolle B, Specks U, Ludemann J, Rohrbach MS, DeRemee RA, Gross WL (1989). Anticytoplasmic autoantibodies: the immunodiagnostic value in Wegener's granulomatosis. *Ann Intern Med*; 111: 28-40.

Pakrou N, Selva D, Leibovitch I (2006) Wegener's granulomatosis: ophthalmic manifestations and management. *Semin Arthritis Rheum* 35:284-292.

Rao JK, Weinberger M, Oddone EZ, Allen NB, Landsman P, Feussner JR (1995). The role of antineutrophil cytoplasmic antibody (cANCA) testing in the diagnosis of Wegener granulomatosis: a literature review and meta-analysis. *Ann Intern Med*; 123: 925-932.

Sharma A, Kumar S, Wanchu A, Lal V, Singh R, Gupta V, Singh S, Gupta A (2010). Successful treatment of hypertrophic pachymeningitis in refractory Wegener's granulomatosis with rituximab. *Clin Rheumatol*; 29:107-110.

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