Worsening of posterior scleritis and orbital pseudotumor in a patient with granulomatosis polyangiitis with rituximab-A case report

Kalpana Babu, B G Dharmanand[1]

We report a case of exacerbation of posterior scleritis and orbital pseudotumor in a patient with granulomatosis polyangiitis, with initial rituximab infusion. Modifications in rituximab protocols including reduction in maintenance dose for subsequent infusions with increase in premedication dose of intravenous methyl prednisolone may be useful to prevent periinfusional flares. In this case report, we highlight a rare occurrence and modification in rituximab protocol to prevent post-infusional flare of inflammation.

Key words: Granulomatosis polyangiitis, orbital pseudotumor, refractory scleritis, rituximab

In recent years, rituximab is being increasingly used in India in treatment of autoimmune diseases like granulomatosis polyangiitis (GPA). This case report, first from Indian literature, describes exacerbation of posterior scleritis and orbital pseudotumor in a patient with GPA with initial infusion of rituximab. We also describe modifications in the rituximab infusion protocol successful in eliminating post-infusional flares.

Case Report

A 59-year-old male presented to us with pain especially on eye movements and diminution of vision in left eye after a history of receiving rituximab infusion 3 weeks ago. The induction doses of rituximab included 2 doses of 1000 mg given at 2 weeks interval with premedication of 125 mg intravenous methyl prednisolone. Review of his records reveal a diagnosis of ANCA proven GPA of 13 years. He had received >31 gm of intravenous cyclophosphamide over these years, which is close to safe maximum cumulative dose of 36 gm. He was also diagnosed as systemic hypertension.

Access this article online

Quick Response Code:

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_1644_20

Department of Uveitis and Ocular Inflammation, Vittala International Institute of Ophthalmology, Prabha Eye Clinic and Research Centre, [1]Department of Rheumatology, Vikram Hospitals, Bengaluru, Karnataka, India

Correspondence to: Dr. Kalpana Babu, 504, 40th Cross, Jayanagar 8th Block, Bengaluru - 560 070, Karnataka, India. E-mail: kalpanababumurthy@gmail.com

Received: 24-May-2020 Revision: 21-Jun-2020
Accepted: 16-Jul-2020 Published: 20-Aug-2020

He had refractory scleritis (4 years duration) and orbital pseudotumor resulting in proptosis (2 years duration) in left eye (OS) and was on tab azathioprine (1.5 mg/kg body weight) and oral steroids (20 mg/day). Relapses in inflammation were noted on lowering the dose of oral steroids to less than 20 mg/day.

On examination, his BCVA was 6/9, 6/12 in OD and OS respectively. Proptosis was seen in both eyes (OS > OD). Slit lamp examination revealed diffuse scleral congestion (OS) with healed areas of old peripheral ulcerative keratitis from 1-3'o clock hours (OS). Fundus examination showed few pigmentary alterations in the posterior pole in both eyes and a pocket of subretinal fluid (SRF) in the posterior pole with occasional vitreous cells in the left eye. Ultrasonography showed increased choroidal thickening (2.29 mm in OS vs. 1.70 mm in OD) with presence of T sign in the left eye. EDI-OCT (OS) also confirmed choroidal thickening and the presence of SRF inferotemporal to the fovea. Apart from staining near the fovea, no areas of significant dye leakage were noted on FFA and ICG. MRI orbits and cranium showed heterogeneously enhancing soft tissue lesions with irregular margins in superior and lateral aspects of right orbit (measuring 2.8 cm superoinferiorly, 1.9 cm transversely and 3.3 cm anteroposteriorly) and superior, lateral and inferior aspects of left orbit (measuring 4 cm superoinferiorly, 2.3 cm transversely and 3.7 cm anteroposteriorly) with extraconal, intraconal and preseptal extensions encasing superior and lateral recti muscles (OS > OD) and abutting optic nerve in the left eye suggestive of granulomatous disease. Left superior ophthalmic vein was not visualised while partial encasement was seen on right side. [Fig. 1].

His symptoms of pain and blurred vision (OS) improved on increasing the dose of oral steroids to 50 mg/day with recovery of BCVA to 6/9. Though his symptoms improved, the SRF persisted on OCT. At 3 months follow up, as the SRF continued to persist (on 25 mg/day of oral steroids), he received 3 pulse doses of intravenous methyl prednisolone (1 gm/day). The SRF in the left eye had disappeared at the end of 4 months [Fig. 2] along with a decrease in choroidal thickness (1.7 mm).

A modification in the rituximab protocol was made for the subsequent dose (2nd dose) of rituximab to avoid a post-infusional flare. This included a maintenance dose of 500 mg of rituximab along with 250 mg intravenous methyl prednisolone. There was no exacerbation of ocular inflammation after the 2nd dose. At 4 months follow-up, post 2nd dose of rituximab, the eye is doing well with no relapses of ocular inflammation and a BCVA of 6/6(OU). The oral steroids have also been successfully tapered to 7.5 mg/day with continuation of azathioprine at 125 mg/day without any relapse in inflammation.

Cite this article as: Babu K, Dharmanand BG. Worsening of posterior scleritis and orbital pseudotumor in a patient with granulomatosis polyangiitis with rituximab-A case report. Indian J Ophthalmol 2020;68:1986-8.

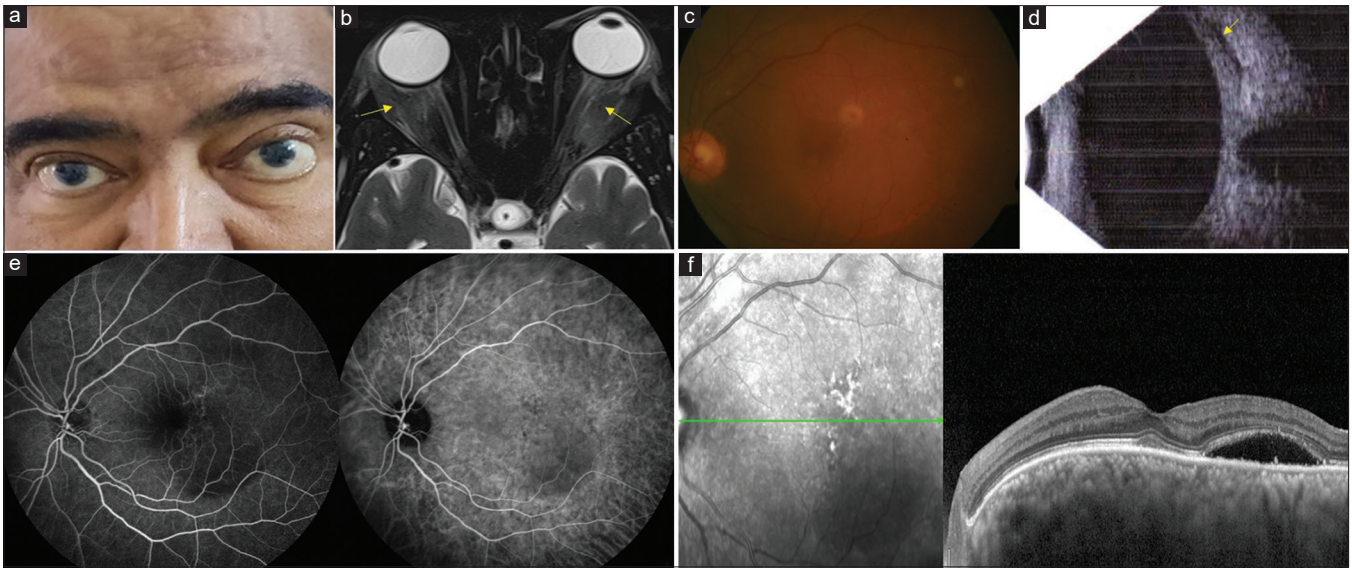

Figure 1: Composite photograph showing bilateral proptosis (a) more prominent in the left eye, MRI orbits showing bilateral, orbital, heterogeneously enhancing soft tissue lesions with irregular margins in superior and lateral aspects shown as yellow arrows, encasing superior and lateral recti and even abutting the optic nerve in the left eye (b), fundus photograph showing pocket of subretinal fluid inferotemporal to the fovea (c), ultrasonography showing increased choroidal thickening with fluid in sub tenon's space shown as yellow arrows (d), fluorescein angiography and indocyanine green angiography showed no active dye leakage (e) and EDI-OCT showing extensive choroidal thickening with subretinal pocket of fluid (f)

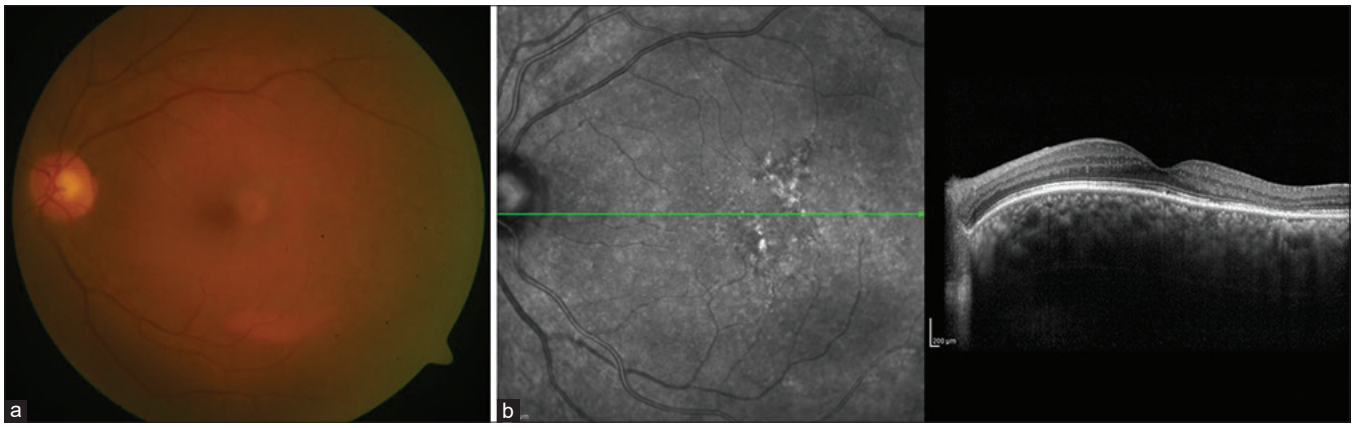

Figure 2: Fundus photograph showing disappearance of the pocket of subretinal fluid (a) and EDI-OCT showing disappearance of subretinal fluid with decrease in choroidal thickness (b)

Discussion

ANCA associated vasculitis includes GPA formerly known as Wegener's granulomatosis. Scleritis and orbital pseudotumor can occur in GPA. Classically disease remission has been induced with high dose corticosteroids and cyclophosphamide. In some cases, the disease is refractory and relapse rates are high.[1-4] Scleritis is thought to be mediated by the ANCA produced B cells while the granulomatous inflammation as in orbital disease may be mediated more by CD4+ T cells with a T helper 1 cytokine profile.[1,2]

Rituximab (RTX) is a chimeric monoclonal antibody that leads to depletion of peripheral B cells by targeting the CD 20, a cell surface protein expressed on the surface of B cells. Additional effects on T cells via interference in B and T cell interactions also may contribute to its effects.[1,2] The protocols include infusion given as two doses of 1000 mg at a 14 day interval (rheumatologic protocol) or four doses of 375 mg/m2 weekly (oncologic protocol) for induction treatment with the ongoing maintenance therapy of 375 mg/m2 or 500 mg at 4 to 6 months intervals or at 8 doses of 375 mg/m2 weekly (Foster protocol) for reduction remission protocol with monthly maintenance therapy. Premedication includes 100-125 mg intravenous methyl prednisolone.[2]

Our patient experienced a disease exacerbation within 3 weeks of the initial infusion of 1000 mg rituximab. Acute disease flare following rituximab has been reported in literature in autoimmune diseases like Graves' disease and rarely in GPA.[3-5] This effect, though rare, is probably due to the rapid Bcell elimination causing cytokine release, creating a tumor lysis like effect and worsening of inflammation.[4,5] Our patient developed pain especially on eye movements, diminution of vision, diffuse scleral congestion and SRF in the posterior pole in the left eye, 3 weeks post rituximab

infusion. Though the symptoms improved with increasing the dose of oral steroids, the SRF required pulse doses of intravenous methyl prednisolone. A modification was made for the subsequent injection of rituximab which included a combination of lower dose of rituximab infusion (500 mg) and premedication of 250 mg of intravenous methyl prednisolone. This modification prevented any post-infusional flare of ocular inflammation and a successful reduction of oral steroids to 7.5 mg/day.

Conclusion

This case report, first from Indian literature, though rare, describes disease exacerbation post rituximab infusion. Modifications in rituximab protocol may be useful to prevent such post-infusional flares. As rituximab is being increasingly used in autoimmune diseases, this case report sensitises the reader to this adverse effect and further studies may be needed to understand which patients may encounter these effects.

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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. You C, Ma L, Lasave AF, Foster CS. Rituximab induction and maintenance treatment in patients with scleritis and granulomatosis with polyangiitis (Wegener's). Ocul Immunol Inflamm 2018;26:1166-73.
2. Joshi L, Tanna A, McAdoo SP, Medjeral-Thomas N, Taylor SR, Sandhu G, *et al*. Long-term outcomes of rituximab therapy in ocular granulomatosis with polyangiitis: Impact on localized and nonlocalized disease. Ophthalmology 2015;122:1262-8.
3. Suhler EB, Lim LL, Beardsley RM, Giles TR, Pasadhika S, Lee ST, *et al*. Rituximab therapy for refractory scleritis: Results of a phase I/II dose-ranging, randomized, clinical trial. Ophthalmology 2014;121:1885-91.
4. Suhler EB, Lim LL, Beardsley RM, Giles TR, Pasadhika S, Lee ST, *et al*. Rituximab therapy for refractory orbital inflammation: Results of a phase 1/2, dose-ranging, randomized clinical trial. JAMA Ophthalmol 2014;132:572-8.
5. Shih CB, Wang YC, Lai CC. Ocular and orbital exacerbation after rituximab therapy for granulomatosis with polyangiitis. Can J Ophthalmol 2019;54:e237-41.