Commentary: Rituximab in scleritis

Over the last few years, there has been an increasing number of reports on the scleritis refractory to standardized therapy. Scleritis can be associated with an underlying systemic disease in up to 50% of patients, with the most common being rheumatoid arthritis (RA) and granulomatosis with polyangiitis (GPA).[1] Management of treatment-resistant scleritis and/or associated systemic disease remains a major challenge. Biological agents have emerged out as a useful alternative in such a scenario. In this current issue of the journal, Murthy *et al*.[2] highlighted the role of rituximab in managing a case of necrotizing scleritis in a patient with GPA.

Rituximab is a chimeric monoclonal immunoglobulin G (IgG) antibody against CD-20, a B cell surface antigen. It has been used successfully in treating various autoimmune

Table 1: Review of literature on the use of Rituximab in scleritis

Author	Number of patients	Dose of RTX/Interval	Aetiology	Relapse (N)
Joshi[5]	20	1 gm/2 week	GPA	12
Cao[10]	15	Variable*	GPA (6) Idiopathic (4) RA (4) Other (1)	3
Suhler[6]	12	500 mg/1 gm, 2 week	Idiopathic (5) RA (4) Systemic Vasculitis (1) GPA (1) Cogan Syndrome (1)	7
You *et al.*[13]	9	Variable*	GPA	2
Ahmed[3]	9	Variable*	GPA	1
Recillas-Gispert[14]	8	1 gm/2 week	GPA	3
Taylor[15]	6	1 gm/2 week	GPA	0
Pérez-JacoisteAsín[16]	4	375 mg/m^2, 4 weekly dose	GPA	NA
Chauhan[7]	3	1 gm/2 week	RA	0
Hardy *et al.*[17]	2	1 gm/2 week	RA	0
Kurz[18]	2	1 gm/2 week	Idiopathic (1) RA (1)	2
Bogdanic-Werner[19]	2	375 mg/m^2 , 4 weekly dose	Idiopathic	0
Fujita[20]	1	375 mg/m^2 , 4 weekly dose	GPA	0
Xu[21]	1	1 gm/2 week	Autoimmune hypophysitis	0
Kasi[8]	1	NA	Necrotizing Scleritis with Idiopathic Orbital Inflammation	0
Caso[22]	1	1 gm/2 week	IgG4-related disease	0
Fidelix[23]	1	1 gm/2 week	SINS	0
Onal[4]	1	1 gm/2 week	GPA	0
Ahmadi-Simab[9]	1	375 mg/m^2, 4 weekly dose	Primary Sjogren's syndrome.	0
Cheung[24]	1	1 gm/2 week	GPA	0
Morarjia[25]	1	1 gm/2 week	GPA	0
Iaccheri[26]	1	1 gm/2 week	RA	1

Interval interval between the doses; GPA Granulomatosis with polyangiitis (Wegener's granulomatosis): RA Rheumatoid arthritis; SINS Surgically induced necrotizing scleritis; Relapse Number of patients showing relapse of scleral inflammation after treatment with Rituximab. *Variable doses: These studies used the following doses - rheumatology protocol: 2 doses of 1 gm (2 weeks apart) every 3-6 months; Institute protocol: 375 mg/m^2 body surface area×8 consecutive weeks, and monthly infusions thereafter and oncology protocol: 375 mg/m^2 body surface area×4 consecutive weeks

diseases, including RA, systemic lupus erythematosus, and GPA. The drug has shown promising results in the treatment of various ocular inflammatory disorders and intraocular lymphoma in recent years. Rituximab has been shown to be efficacious for the management of scleritis by various case reports, a few small case series, and a randomized trial [Table 1].

GPA is an antineutrophil cytoplasmic antibody (ANCA)-associated small-vessel, necrotizing granulomatous vasculitis. Ophthalmic involvement in GPA can occur up to 45% of the patients and can be presenting manifestation of the systemic disease in 16% of the patients. Ophthalmic involvement in GPA includes episcleritis, scleritis, peripheral ulcerative keratitis, uveitis, retinal vasculitis, and orbital inflammation. Scleritis is considered as one of the most common ocular presentations of GPA, and GPA remains the second most common cause of scleritis after RA.[1] Rituximab was reported to be as efficacious and even superior to cyclophosphamide in the management of ocular GPA.[3,4] The response to the treatment with rituximab may show variable responses, especially in cases with granulomatous manifestations of ANCA-associated vasculitis (such as orbital inflammation) and may take relatively longer time to remission in some cases of scleritis.[4,5] Scleral inflammation in GPA is thought to be mediated by ANCA produced by B cells. Depletion of B lymphocytes by rituximab thus helps in the management of scleritis. However, not only ANCA-associated scleritis, rituximab has been found to be efficacious in the management of scleritis secondary to RA and various other autoimmune disorders also.[6-9]

Recurrence of scleral inflammation was reported with rituximab, especially in studies with a longer follow-up period.[5,6,10] The majority of such cases responded to the re-treatment with the same drug.[5,6,10] Rituximab appeared to be superior in terms of safety and efficacy when compared to cyclophosphamide.[3] Stilling-Vinther and Pedersen[11] reported a case of posterior scleritis in a 81-year-old man with multiple comorbidities who developed *Pneumocystis jirovecii* pneumonia following treatment with rituximab and died. There are reports of cystoid macular edema following successful treatment of scleritis with rituximab therapy.[12] Secondary infection was reported in 16% of the patients in a retrospective study, with 8% requiring hospitalization.[5]

Rituximab may be considered as the second-line agents for noninfectious scleritis refractory to conventional immunosuppressive therapy. Further prospective controlled long-term studies may help us to confirm and expand our insight on the use of the drug in patients with scleritis.

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