Adalimumab in the treatment of refractory non-infectious scleritis: 6-month outcomes

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Scleritis is a serious, painful, sight-threatening condition that can significantly impact patients' quality of life and wellbeing. Its management is focused on the control of scleral inflammation using oral corticosteroids and/or corticosteroid-sparing (eg. conventional immunosuppressive) agents. However, a subset of patients does not tolerate or respond to these treatment regimens, which puts them at risk of persisting morbidity and losing vision. In recent years, novel biological therapies have become a highly attractive option for those with refractory scleritis, giving them hope for disease control and thus better outcomes.

One such biological immunosuppressant is adalimumab, which is a fully humanized anti-tumour necrosis factor-alpha (TNF-α) monoclonal antibody. The promising outcomes of scleritics treated with adalimumab have been described in several small case series (1, 2). Since scleritis is a rare disease, affecting roughly 3000 individuals in the United Kingdom (UK) (3), there are no large-scale randomised controlled trials evaluating treatment efficacy. We therefore sought to review the outcome of adalimumab therapy in patients previously refractory to oral corticosteroids and conventional immunosuppressants.

Our retrospective analysis included 15 adults with refractory non-infectious disease initiated on adalimumab between September 2014 and October 2021 at our tertiary referral centre. Figure 1B below describes the breakdown of the different anatomical subtypes. After a loading dose of 80mg subcutaneously, adalimumab was maintained at a standard dose of 40mg every other week, except in one patient who was escalated to 40mg every week at 3.5 months (Figure 2). Patients' baseline characteristics (Figure 1) and 6-month outcomes were analysed to determine the steroid-sparing effect, impact on visual acuity, time to first scleritis flare-up and presence of adverse events. We selected these outcomes as chronic use of high

dose oral corticosteroids is linked to a range of side effects including osteoporosis, diabetes mellitus, weight gain, adrenal suppression, adverse effects on mental health and increased cardiovascular risk (4). Thus, it is best practice for physicians treating autoimmune diseases to reduce the morbidity associated with long-term usage of corticosteroids by tapering and stopping corticosteroid regimes when possible (5). Furthermore, frequent scleritic flare-ups significantly affect patients' quality of life and may lead to ophthalmic complications such as scarring, perforation and visual impairment (4).

On commencement of adalimumab, 46.7% of patients were taking ≤10mg of daily prednisolone, and 26.7% were on ≤5mg. The fraction of patients on ≤10mg and ≤5mg of daily prednisolone increased at 6 months of treatment to 93.3% and 60%, respectively. In terms of disease recurrence, the rate of reactivation on adalimumab was 0.62 flare-ups/patient-year, with 4 patients developing flare-ups during the follow-up period (Figure 2). No patients experienced worsening of their visual acuity, with 27% achieving better vision. Adverse events noted during the follow up period included single episodes of: oral and genital thrush, bleeding gums, pain on injecting adalimumab, headache and nausea.

This case series demonstrates that adalimumab is effective after 6 months treatment in the majority of non-infectious scleritis patients who were previously refractory to conventional therapy.

References

1. Fabiani C, Sota J, Sainz-de-la-Maza M, Pelegrín L, Emmi G, Lopalco G, et al. Effectiveness of TNF-α blockade in the treatment of refractory non-infectious scleritis: a multicentre study. Clinical and experimental rheumatology. 2020;38(6):1138-44.

2. Sharma SM, Damato E, Hinchcliffe AE, Andrews CD, Myint K, Lee R, et al. Long-term efficacy and tolerability of TNFα inhibitors in the treatment of non-infectious ocular inflammation: an 8-year prospective surveillance study. British Journal of Ophthalmology. 2021;105(9):1256-62.

3. Braithwaite T, Adderley NJ, Subramanian A, Galloway J, Kempen H, John, Gokhale K, et al. Epidemiology of Scleritis in the United Kingdom From 1997 to 2018: Population-Based Analysis of 11 Million Patients and Association Between Scleritis and Infectious and Immune-Mediated Inflammatory Disease. Arthritis & Rheumatology. 2021;73(7):1267-76.

4. Okhravi N, Odufuwa B, McCluskey P, Lightman S. Scleritis. Surv Ophthalmol. 2005;50(4):351-63.

5. Smolen JS, Landewé RBM, Bijlsma JWJ, Burmester GR, Dougados M, Kerschbaumer A, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. Annals of the rheumatic diseases. 2020;79(6):685.

Figure 1. Background characteristics of 15 patients with scleritis treated with adalimumab.

Abbreviations: Rheumatoid arthritis (RA), Human leukocyte antigen (HLA), Anti-neutrophil cytoplasmic antibody (ANCA).

Figure 2. Graph representing flare-ups on adalimumab around 6 months of treatment. Due to the nature of variable follow up (i.e. certain patients were not followed up at exactly 6 months), we included flare-ups that occurred up to 14 days after 6 months of treatment. Flare-up was defined as an acute attack of active disease observed on clinical examination +/- presence of symptoms, resulting in an increase of immunosuppressive treatment. Patient 12 experienced an episode of oral and genital thrush and had to pause his adalimumab therapy. Patient 15 was escalated to weekly adalimumab at 3.5 months due to persisting active scleritis despite adalimumab 40mg SC every two weeks.

Data availability

Anonymised data for this study is available from the corresponding author upon reasonable request.

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Competing interests

The authors declare no competing interests.

Author contributions

Design of the study (EB, JV, RL, IY); data collection (EB); data analysis (EB, JL, RL, IY); writing the manuscript (EB); all co-authors contributed to the critical appraisal and review of the manuscript; study supervision (RL, IY).