

## Adalimumab for refractory idiopathic scleritis in children

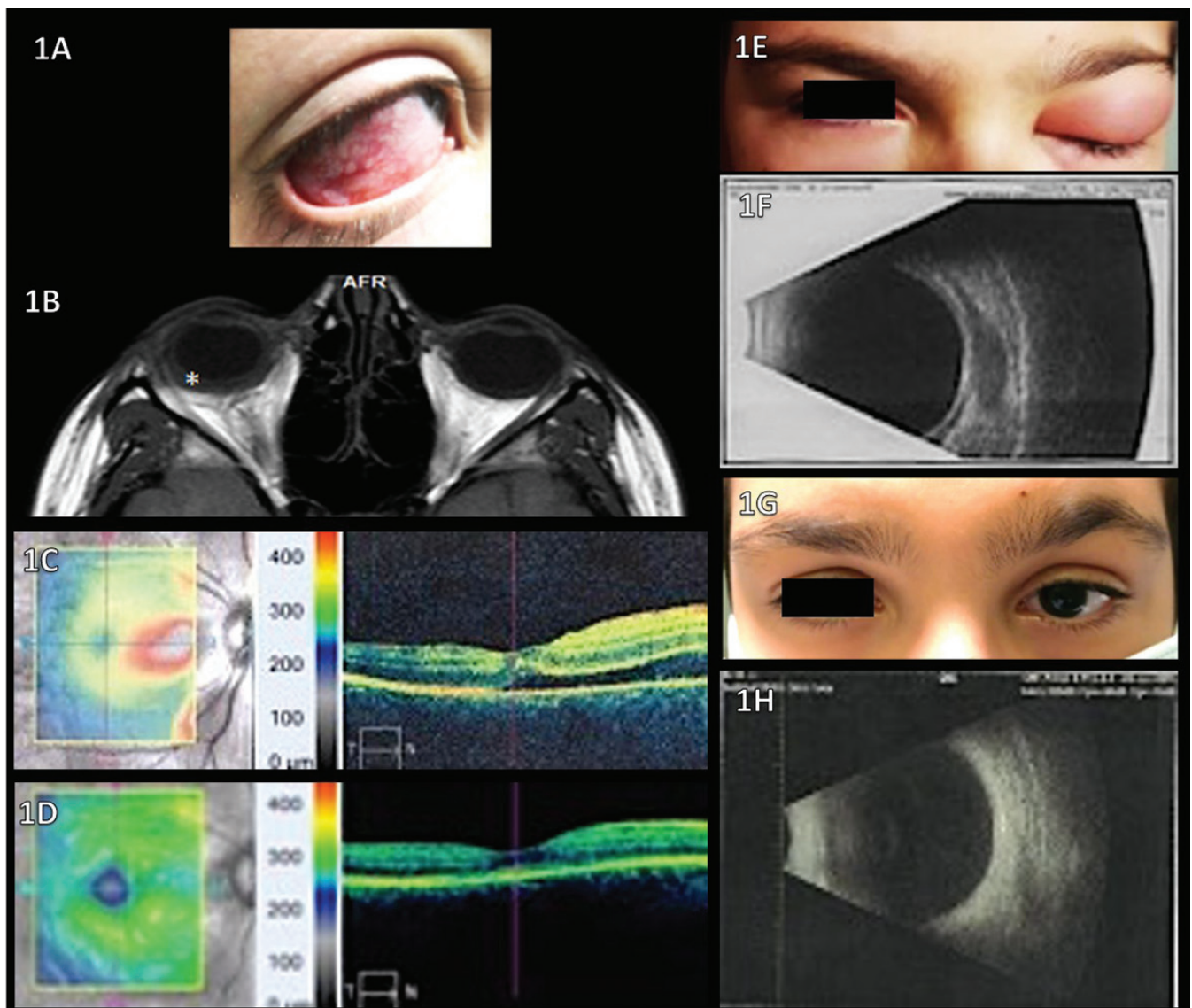
Sirs,

Scleritis is a chronic inflammation of the fibrous outer layer of the eye, ranging from mild to sight-threatening in severity. It can be caused by infectious and non-infectious (mostly immune-mediated) diseases, however in more than half cases it is idiopathic (1). This condition is both rare and poorly recognised in children, therefore a high clinical suspicion is needed in order to start timely a proper treatment (2). In this regard, very few data are currently available to guide therapeutic choices in

paediatric patients. We report two cases of refractory idiopathic scleritis in children who achieved prolonged remission with the tumour necrosis factor (TNF)- $\alpha$  inhibitor adalimumab (ADA).

A 12-year-old girl with right inflammatory orbitopathy, initially diagnosed as orbital cellulitis and treated with systemic antibiotics, presented multiple relapses, characterised mainly by diffuse anterior (Fig. 1A) and posterior scleritis. Her disease was highly responsive to systemic glucocorticoids but refractory to a number of sparing agents, including cyclosporine A, mycophenolate mofetil, cyclophosphamide, azathioprine, rituximab and anakinra. When she came to our attention at 17 years old, she

had severe cortico-dependence. Bulbar ultrasonography showed the pathognomonic T-sign, due to fluid collecting in the posterior episcleral space and extending around the optic nerve. Orbital magnetic resonance imaging (MRI) showed marked thickening of the inferior part of Tenon's capsule and of the uveo-scleral tract (Fig. 1B). Optical coherence tomography (OCT) revealed exudative detachment of the neuroepithelium in the macular area (Fig. 1C). The patient was reassessed through a complete diagnostic work-up, carefully excluding any systemic underlying conditions; HLA-B51 haplotype was found, in the absence of other Behçet's disease manifestations. Therefore, she was started on treatment with



**Fig. 1.** A: Diffuse hyperaemia and vascular congestion as a result of anterior scleritis (patient 1, before treatment); B: marked thickening of the inferior part of Tenon's capsule and of the right uveo-scleral tract (\*asterisk), consistent with posterior scleritis (orbital MRI, patient 1, before treatment); C: exudative detachment of the neuroepithelium in the macular area (OCT, patient 1, before treatment) and D: its resolution after 6 months of therapy with ADA; E: Clinical presentation of posterior scleritis with inflammatory orbitopathy mimicking orbital cellulitis (patient 2, before treatment) and G: complete recovery after 6 months of therapy with ADA; F: retinal-choroidal and scleral thickening and effusion in Tenon's space (B-SCAN ultrasound, patient 2, before treatment) and H: complete resolution of the instrumental picture after 6 months of treatment.

ADA 40 mg subcutaneously every 14 days, with striking improvement of symptoms, to the point that she was able to discontinue glucocorticoids after 3 months. Moreover, complete resolution of the detachment of the neuroepithelium was observed at the 6-month follow-up (Fig. 1D). To date, the girl has been keeping steroid-free ocular remission for 21 months. She gained almost complete recovery of visual acuity (from 6/10 to 9-10/10), limited by the irreversible macular alterations developed over time as a consequence of the scleral and uveo-retinal inflammation.

The second patient was a 12-year-old boy evaluated for a 3-year history of inflammatory orbitopathy, resistant to both methotrexate and azathioprine employed as steroid-sparing agents (Fig. 1E). He was born with bilateral radial agenesis and ulnar dysmorphism, in the context of a dysmorphogenetic syndrome still undefined. The diagnostic work-up had ruled out any systemic condition underlying ocular inflammation. When he came to our observation, he presented growth delay and features of iatrogenic Cushing's disease. He was diagnosed of posterior scleritis with inflammatory orbital involvement based on orbital MRI and B-SCAN ultrasound imaging (Fig. 1F). He started ADA at the standard dosage, which led to rapid clinical and instrumental recovery (Fig. 1G-H) and allowed weaning from glucocorticoids after 3 months of therapy. At the 6-month follow-up visit, resumption of growth was appreciated with a gain of two percentile lines and, to date, he has been stably in remission for 12 months.

The employment of TNF- $\alpha$  inhibitors in the management of non-infectious scleritis in

adult patients results in good efficacy and tolerability, long-term control of ocular inflammation, visual stability and sustained steroid-sparing effect (3-5). Nevertheless, only one case of posterior scleritis in a 13-year-old girl treated with the TNF- $\alpha$  inhibitor infliximab is available in the current literature (6). In our experience, ADA could be a valuable therapeutic option for children suffering from idiopathic scleritis, refractory to conventional immunosuppressive therapy.

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## References

1. SAINZ DE LA MAZA M, MOLINA N, GONZALEZ-GONZALEZ LA, DOCTOR PP, TAUBER J, FOSTER CS: Clinical characteristics of a large cohort of patients with scleritis and episcleritis. *Ophthalmology* 2012; 119: 43-50.
2. MAJUMDER PD, ALI S, GEORGE A, GANESH S, BISWAS J: Clinical profile of scleritis in children. *Ocul Immunol Inflamm* 2019; 27: 535-9.
3. FABIANI C, SOTA J, SAINZ-DE-LA-MAZA M *et al.*: Effectiveness of TNF- $\alpha$  blockade in the treatment of refractory non-infectious scleritis: a multicentre study. *Clin Exp Rheumatol* 2020; 38: 1138-44.
4. RAGAM A, KOLOMEYER AM, FANG C, XU Y, CHU DS: Treatment of chronic, noninfectious, nonnecrotizing scleritis with tumor necrosis factor alpha inhibitors. *Ocul Immunol Inflamm* 2014; 22: 469-77.
5. SHARMA SM, DAMATO E, HINCHCLIFFE AE *et al.*: Long-term efficacy and tolerability of TNF- $\alpha$  inhibitors in the treatment of non-infectious ocular inflammation: an 8-year prospective surveillance study. *Br J Ophthalmol* 2021; 105(9): 1256-62.
6. WEISS K, RIEGER R, KEITZER R, PLEYER U: Successful infliximab treatment of posterior scleritis in a 13-year-old child refractory to other immunosuppressive therapy. *Graefes Arch Clin Exp Ophthalmol* 2007; 245: 1735-7.