

Posterior Scleritis in a Teenager Responding to Abatacept

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Abstract

Posterior scleritis is a rare form of scleritis involving the sclera posteriorly to the eye's equator. Accounting for 2% to 12% of all cases, it is probably underdiagnosed. In children it is rarer than in adults. An early diagnosis and an appropriate systemic treatment help to prevent a severe course of this potential sight-threatening disease. In the majority of cases, aggressive therapy with systemic corticosteroids achieves resolution within the first year but long-term immunosuppression is often required to prevent recurrences and preserve vision [1].

Here we report a case of a 14-year-old female who presented a severe relapsing posterior scleritis, cortico-dependent and refractory to repeated increases in the daily doses of Cyclosporine A (CyA) and Mophetilmicophenolate (MMF). On suspicion of poor treatment compliance, blood levels of MMF were measured, confirming that the girl did not take the oral therapy at home. For this reason, MMF was replaced with intravenous Abatacept, which induced a prolonged, although initially delayed, scleritis remission. Then, intravenous infusions of Abatacept were shifted to subcutaneous injections, administered every two weeks and during the following thirty months of follow-up, no other scleritis relapses occurred.

To our knowledge, this is the first reported case of posterior scleritis successfully treated with Abatacept.

Keywords: *Posterior Scleritis; Children; Adolescent; Abatacept*

Introduction

Posterior scleritis, characterized by inflammation of the sclera posterior to the ora serrata, is the rarest type of scleritis. Retrobulbar pain is a hallmark symptom, as well as the engorgement of deep scleral vessels is a typical sign. It can be idiopathic or associated with systemic diseases such as rheumatoid arthritis and Wegener granulomatosis, of which scleritis may be an early clinical manifestation. In children, the largest case series consisted of 13 patients, in which emerged a male predominance and a significant lower association with systemic diseases among the pediatric population. There is not satisfying information regarding systemic treatment, which has mostly been assessed in adults and is based on published recommendations, starting with NSAIDs and followed by oral corticosteroids in those who don't respond [1].

Case Report

A 14-year-old Caucasian female was referred to our Pediatric Ocular Immunopathology Unit for relapsing anterior uveitis despite corticosteroid treatment. She had just been treated with oral prednisone 50 mg/day reduced to 25 mg/day after four days, with subsequent uveitis relapse. Prednisone was re-increased to 50 mg/day, and associated with topical therapy (netilmicin, dexamethasone and cyclopentolate eye drops). A CT-scan of the brain and the orbits was performed and resulted normal. Blood tests such as complete blood count, differential count, white blood cells (WBC), haemoglobin (Hb), platelets, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were also all within normal values. At presentation the best corrected visual acuity (BCVA) was 1.0 in both eyes. Anterior and

posterior segments in the right eye (RE) were normal; in the left eye (LE) there were bulbar conjunctival diffuse redness, diffuse endotheliitis, especially in the medium-inferior sector, and cells 1+ in the anterior chamber, without synechiae. Extraocular muscle movements caused pain and fundus examination revealed an optic disc with blurred and slightly raised margins. In both eyes, intraocular pressure was normal. A B-Scan ultrasonography was performed and revealed a posterior scleritis in the infero-temporal quadrant of the LE, with the typical T-sign [2].

Oral methotrexate, at a weekly dose of 10 mg/m², was introduced as steroid-sparing immunosuppressive agent. Because of an acute severe weakness just after assumption of the first dose, the teen and her mother denied to continue the treatment. Four days later, oral cyclosporine at a daily dose of 250 mg/day was administered in the hospital, without any adverse effect. Thus, clinical remission of scleritis was maintained for 2 months.

Nevertheless, a new scleritis relapse occurred after reduction of prednisone to 2.5 mg/day, and cyclosporine was replaced with oral mophetilmicophenolate (MMF) at a daily dose of 360 mg. Three months after the MMF introduction, acute scleritis relapsed again; the patient underwent five methylprednisolone i.v. pulses and an increase of oral prednisone (25 mg/day).

With suspicion of weak compliance, MMF was administrated under nursing observation in the hospital and blood levels of MMF were measured before the drug administration and some hours later. The first resulted lower than expected with a daily assumption of the drug (1.3 mg/L revealed versus 2.3 mg/L expected).

Consequently, a switch to i.v. Abatacept was performed, at the dosage of 10 mg/kg every 4 weeks, after tapering MMF. Remission lasted seven months, then ocular symptoms relapsed during the fourth week after the infusion. The intervals between the infusions were reduced at three weeks, and maintained for six months. When intervals returned to four weeks, an acute relapse occurred needing higher doses of oral prednisone (from 5 to 12.5 mg/day), and Abatacept (600 mg diluted in 100 ml of physiological saline solution every 4 weeks, patient weighting 50 kg). In five months, oral prednisone was slowly tapered and stopped. Twenty-three months after the last scleritis relapse, intravenous infusions of Abatacept were shifted to the subcutaneous injections, with 125 mg administered every week. No other scleritis relapses occurred in the following thirty months of follow-up. Till October 2017 patient was in remission on therapy.

Discussion and Conclusion

Scleritis is classified in 5 categories, according to the anatomic distribution: diffuse, nodular, necrotizing anterior with or without inflammation and posterior scleritis [3]. Posterior eye wall thickening is demonstrated by orbital B-scan ultrasonography, with retrobulbar and perineural fluid producing the pathognomonic "T-sign". In presence of this, other extensive investigations (CT and MRI) could be not needed for the diagnosis [2]. However, since posterior scleritis has a plethora of clinical presentations and posterior segment signs, such as serous retinal detachments, optic nerve involvement, choroidal folds and subretinal mass, differentiation from other inflammatory and neoplastic diseases is mandatory [4]. In a large series of adult patients, the majority had unilateral disease (65%) and there was no association between laterality and systemic diseases or visual loss. However, the concomitant development of anterior scleritis increased the risk of having an associated systemic disease [5]. In the majority of cases, aggressive therapy with systemic corticosteroids achieves resolution within the first year but long-term immunosuppression is often required to prevent recurrences and preserve vision [1]. An autoimmune dysregulation in a genetically predisposed host is presumed to cause scleritis. Immune complex vessel deposition in episcleral and scleral-perforating capillary and postcapillary venules (inflammatory microangiopathy) and cell-mediated immune responses interact as part of the activated immune network, thus leading to scleral destruction. The autoimmune pathogenesis of scleritis is also supported by the frequent association with systemic autoimmune disorders and by the favorable response to immunosuppressive therapy. Treatment include nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids and non-corticosteroid immunosuppressive agents [6,7]. In literature, there are only few studies regarding the use of the latter. Among these, Abatacept, a fusion protein composed of the Fc region of the immunoglobulin IgG1 fused to the extracellular domain of CTLA-4, binds to the CD80 and CD86 molecules, thus preventing the second signal necessary for the T cell activation by the antigen presenting cell. This pathogenesis was supported by a study of

a 12-years-old patient with recurrent pauciarticular JIA and smoldering anterior uveitis, whose right eye became hypotonic, painful and was enucleated, despite treatment with local and systemic corticosteroids and an anti-TNF agent. The histopathologic analyses of the enucleated globe were reviewed and the immunohistochemical findings suggested that JIA-associated non-granulomatous iridocyclitis was a primarily B-cell-infiltrative process [8]. As reported in a previous pediatric case of posterior scleritis, the understanding of the pathogenesis and the presence of clinical trials demonstrating the effectiveness of anti-TNF and anti-B-cell therapy, will probably revolutionize the treatment of refractive and recurrent disease [9]. Here for example, we did not use Infliximab because the patient had previous reactions to injectable MTX. We instead used Abatacept because it is easily administered with infusions, more rapidly and with less systemic reactions compared to Infliximab, and because of the failed compliance to the oral therapy (MMF at home). We have chosen Abatacept also considering a successful previous case of posterior uveitis (a papillitis) that we have treated with this molecule. The hypothesis that some types of scleritis may represent a localized form of vasculitis can support a clinical and therapeutic approach similar to the treatment options used with other autoimmune diseases such as systemic vasculitis [7]. Therapy consists of a first line steroid, the possible addition of a steroid sparing drug and finally the use of biological agents. Among these, TNF-inhibitors and anti-CD20 antibody are used [6]. There is also a novel nanomicellar formulation of cyclosporine A 0.09%, called OTX-101 (Seciera). This has been acquired from Auvenc Therapeutics by Sun Pharma, who recently announced results from a multicenter, randomized, double masked, vehicle-controlled Phase III confirmatory study. After 12 weeks of treatment, OTX-101 showed statistically significant improvements over the vehicle control in Schirmer's score and several key secondary endpoints. It seems also able to reach easily the posterior segment of the eye, thus potentially being useful in posterior scleritis [10].

Our study shows for the first time a case of scleritis successfully in remission with the use of Abatacept, thus showing the importance of new trials in order to find the best treatment approach for scleritis.

Patient Consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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