Short communication

Rituximab in rheumatoid arthritis-associated peripheral ulcerative keratitis

M. Albert, a, * E. Beltrán, b L. Martínez-Costa a

aServicio de Oftalmología, Hospital Dr. Peset, Valencia, Spain
bServicio de Reumatología, Hospital Dr. Peset, Valencia, Spain

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ABSTRACT

Clinical case: We report two cases of patients affected by longstanding rheumatoid arthritis who developed a severe form of peripheral ulcerative keratitis (PUK). Neither of them had an optimal biological and clinical control of their systemic illness despite being treated with several disease-modifying antirheumatic drugs (DMARDs) and biologic therapy. High-dose systemic corticosteroids were given to treat the PUK without any success. Rituximab resulted in a favourable response with resolution of the corneal lesions and optimal control of their systemic illness.

Discussion: Rituximab may be an additional tool to arrest progressive rheumatoid arthritis-associated PUK that is refractory to other drugs.

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Rituximab en queratitis ulcerativa periférica asociada a artritis reumatoide

RESUMEN

Caso clínico: Se presentan dos pacientes diagnosticadas de artritis reumatoide de larga evolución que desarrollaron una queratitis ulcerativa periférica (QUP) grave. Habían sido tratadas previamente con fármacos modificadores de la enfermedad (FAME) y terapia biológica (TB) sin alcanzar un control clínico-biológico óptimo de su enfermedad. Se trataron inicialmente con corticoides sistémicos a dosis altas sin éxito. Rituximab indujo la regresión de las lesiones corneales y el control de su artritis reumatoide.

Discusión: Rituximab puede ser una alternativa para detener la progresión de la QUP asociada a artritis reumatoide refractaria a otros fármacos.

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Introduction

Peripheral ulcerative keratitis (PUK) is characterized by a significant peripheral corneal thinning, with a high risk of perforation. It can be accompanied by inflammation of the conjunctiva, episclera and sclera. PUK is classified as: 1) slight, with the thinning of corneal thickness between 25% and 50%, and good response to systemic or topical corticoids and nonsteroid anti-inflammatory medication, and 2) severe, with extreme thinning which progresses regardless of systemic corticoids treatment.

Clinical case 1

A 58-year-old sero-positive woman diagnosed with rheumatoid arthritis, erosive and nodular with high rheumatoid factor titles, with a 15-year evolution. She had previously received treatment with various disease modifying drugs such as hydroxychlorokine, sulphasalazine, cyclosporine and leflunomide, withdrawn due to lack of efficacy. She followed basic treatment with methotexate 25 mg/week, prednisone 5-10 mg/day (variable) and infliximab 5 mg/kg/IV/8 weeks with acceptable control of the disease in the past 2 years with low activity but without achieving complete remission.

The evolution exhibited septic arthritis in the right ankle, with a positive sinovial liquid culture for Staphylococcus aureus. Infliximab was withdrawn and treatment with IV antibiotic therapy was initiated.

Three months later the patient visited the practice due to red eye, intense periocular pain and photophobia, exhibiting half-moon peripheral corneal infiltrate with extreme stromal thinning associated to scleritis (fig. 1). A culture of the corneal tissue was negative. With the suspicion of severe PUK, treatment was initiated with oral prednisone 1 mg/kg/day without response. Megadoses of methylprednisolone 1 g/IV/3 days were prescribed, in addition to a surgical resection of the conjunctival tissue adjacent to the PUK and cyanoacrylate adhesive to avoid ocular perforation. The patient responded poorly to this treatment with persistent pain, scleritis and corneal infiltrate. As in addition the disease was poorly controlled, it was decided to initiate perfusion of rituximab 1 g/i.v. in 2 infusions 15 days apart. Three weeks after the treatment a significant clinical improvement was observed, exhibiting corneal leukoma apparently inactive without scleritis (fig. 2). At present the patient maintains treatment with IV rituximab in RA pattern every 8 months with good clinical control.

Clinical case 2

A 52-year-old woman with erosive sero-positive RA, high rheumatoid factor titles citrulinated cyclic anti-peptide antibodies (anti-CCP) of 12 years evolution, with failure...
secondary to infliximab and adalimumab. The patient exhibited red eye, pain and photophobia. Exploration: half-moon peripheral corneal infiltrate associated to scleritis (fig. 3). Corneal tissue culture negative. Treatment was initiated with oral prednisone 1 mg/kg/day and it was decided to change the therapeutic target to rituximab in the usual dosage for RA with methotrexate 25 mg/week. After the first cycle of rituximab, the patient experienced significant improvements with healing of the PUK and initiated clinical remission of the RA. Ten months later, a corneal infiltrate and scleritis reappeared together with articulation clinic. It was decided to maintain treatment with IV rituximab in the RA prescription every 8 months with good clinical control of the ocular and systemic condition.

Discussion

PUK can appear associated to infectious as well as non-infectious diseases, with RA being the disease which is most frequently associated to PUK.1 The above cases exhibited severe PUK as extra-articular expression of evolved RA, with high rheumatoid factor and anti-CCP titles. PUK appeared at a point of the disease in which the clinical and biological control was not the best despite the use of disease modifying drugs and biological therapy (anti-TNF).2 For this reason it was decided to change the therapeutic target to rituximab.

Rituximab is a chimeric monoclonal antibody which specifically joins antigene CD20 expressed in mature pre-B and B lymphocytes. It is also indicated in combination with methotrexate in adult patients for treating active severe RA which exhibited inadequate response or intolerance to other disease modifying drugs, including one or more treatments with anti-TNF.3

Patients with RA exhibit an immediate depletion of B cells in peripheral blood after two perfusions of 1,000 mg of rituximab at a 14-day interval. Recently, a case of severe PUK has been published in a patient under treatment with rituximab.4

Rituximab has also been utilized successfully for treating severe scleritis and PUK associated to RA, Sjögren and to cases resistant to Wegener granulomatosis treated previously with anti-TNF.5

It is important for the ophthalmologist to suspect and diagnose these cases at an early stage and to inform the rheumatologist immediately of the ocular disease as it could be the first sign of potentially life-threatening systemic vasculitis.

Conflict of interest

None of the authors have declared any conflict of interest.

References