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Effectiveness of Certolizumab Pegol in Chronic Anterior Uveitis Associated to Crohn's Disease and Ankylosing Spondylitis☆

Efectividad del certolizumab pegol en el tratamiento de la uveítis anterior crónica asociada a enfermedad de Crohn y espondilitis anquilosante

Dear Editor,

The increasingly widespread off-label use of anti-tumor necrosis factor alpha (TNF-α) drugs has changed the therapeutic panorama of uveitis when topical or systemic treatment with corticosteroids and classic immunosuppressive drugs failed to control the disease.

Certolizumab pegol is an anti-TNF-α drug approved by the FDA for use in Crohn's disease in 2008, and for rheumatoid arthritis by the EMEA and FDA in 2009. Recently, a series of 7 cases of uveitis treated with certolizumab pegol was published. This is one of them.[1]

The case is a 33-year-old patient affected since 2003 by recurring episodes of acute alternating unilateral anterior uveitis and HLA-B27 positive spondyloarthropathy, the reason for which he was in treatment with infliximab at doses of 3 mg/kg/body weight every eight weeks. Until 2004, he had suffered recurrent episodes of acute alternating unilateral anterior uveitis which came to be controlled with topical steroids. During this year the pattern of ocular involvement was changing, with anterior uveitis episodes becoming more frequent and associated with bilateral episcleritis/scleritis, while presenting the onset of digestive symptoms, being diagnosed with Crohn's disease after a colonoscopy and biopsy. Treatment was established, therefore, with oral prednisone azathioprine and infliximab and dosages increased to 5 mg/kg/body weight every 6 weeks. In 2010 recurring ocular and intestinal flares lead to a change of anti-TNF drug to adalimumab 40 mg weekly. After initial control, the patient presented a flare of uveitis and ileitis after one year. In October 2011 the uveitis unit switches the patient to a third anti-TNF drug, certolizumab pegol 400 mg initial dose and 200 mg every 2 weeks for maintenance, with negative Tyndall result and resolution of synechiae from the second dose, but without resolution of intestinal manifestations. He is admitted for an ileal resection surgery in January 2012. The biological treatment was suspended due to the surgery and the patient presents a severe flare of uveitis in the right eye (AV 0.5, synechiae, Tyndall 3+). The patient is treated with oral and topical corticosteroids. After surgery in February 2012, treatment with certolizumab pegol and azathioprine is resumed. The patient is currently inactive with good visual acuity (VA 1.0) and no flares up until March 2014 when a flare of unilateral uveitis which was controlled with topical treatment (Table 1).

In some cases of anterior uveitis associated with spondyloarthropathies, systemic treatment is necessary to control inflammatory activity and flares (Fig. 1). Uveitis associated with Crohn's disease has somewhat different characteristics, leading to a more chronic form, sometimes more aggressive, and even middle and posterior eye involvement, unlike uveitis associated with ankylosing spondylitis.[2] Among classical immunosuppressants used for treating anterior uveitis the literature suggests methotrexate[3,4] and sulfasalazine as effective[5] as well as anti-TNF-α drugs. However, due to high cost and off-label use, they are used as second line therapy. There are papers describing case series and isolated cases of patients with anterior uveitis treated with anti-TNF-α.[6–9]

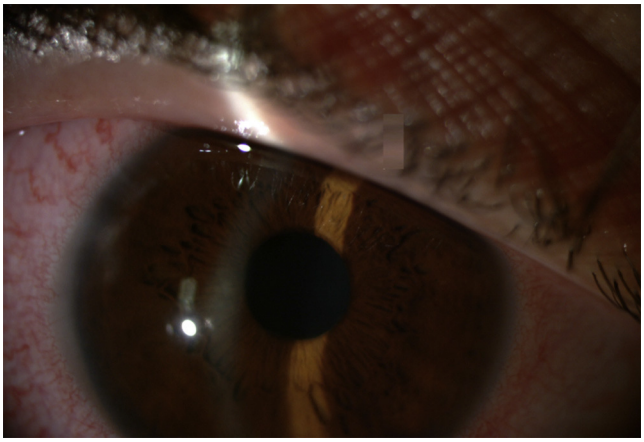

Fig. 1. Anterior uveitis with perikeratic injection.

Table 1
Pattern of Uveitis and Treatments Received.

	2003–2010	2010–2011	2012–2014
Uveitis pattern	URAAU	CAU	CAU
Anti-TNF-α	Infliximab	Adalimumab	Certolizumab
Immunosuppressive therapy	Azathioprine	Azathioprine	Azathioprine
Adjuvant treatment	Periocular infiltration oral corticosteroids	Periocular injections oral corticosteroids	Ileal resection

URAAU, unilateral recurrent acute anterior uveitis; CAU, chronic anterior uveitis.

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Certolizumab Pegol is a pegylated anti-TNF drug without an Fc fragment. PEGylation involves the addition of polyethylene glycol as a 'transporter', which gives advantages from the pharmacokinetic point of view.[10,11] This could explain its effectiveness when other anti-TNF drugs have failed.

Uveitis is a condition that can have serious consequences. Therefore, the capacity to use a new drug for treatment is very encouraging. Although studies are needed to confirm efficacy and safety, the therapeutic response in this patient suggests that certolizumab pegol could be an effective therapeutic alternative for these patients.

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Pneumonitis Induced by Methotrexate in a Patient With Seronegative Rheumatoid Arthritis☆

Neumonitis inducida por metotrexato en una paciente con artritis reumatoide seronegativa

Dear Sir,

Methotrexate-induced pneumonitis is a serious (mortality: 13%–20%)[1] but uncommon (0.3%–7.5%)[2,3] complication of treatment with this folic acid antagonist in patients with rheumatoid arthritis (RA) and other diseases. The typical onset is characterised by an acute picture of nonproductive cough, dyspnoea, and fever, within the first year of treatment, most commonly during the first months (mean: 36–78 weeks),[4] and irrespective of scheduled dose, patient's smoking habit, and gender. The following risk factors have been identified: advanced age, extra-articular manifestations of rheumatoid arthritis (mainly pulmonary involvement), diabetes, and elevated creatinine levels.[5] If this condition is suspected, methotrexate should be immediately discontinued, and respiratory support and systemic steroids at medium-high doses should be initiated; it is also recommended to associate a broad-spectrum antibiotic, with coverage for *Pneumocystis jirovecii*,[6] until the infectious origin is ruled out.[1]

We present the case of a 68-year-old female patient, who in February 2013 was diagnosed with seronegative rheumatoid arthritis in the context of high blood pressure and type II diabetes mellitus with secondary sensorimotor axonal polyneuropathy. We started oral treatment with prednisone 30 mg/day and methotrexate 10 mg/week. After eight weeks, a partial improvement was observed; for this reason, methotrexate dose was increased to 15 mg/week and steroid dose was reduced.

Two months later, the patient presented at the ER of our hospital with 24-h-course dyspnoea, cough, sweating, nausea, fever, and dizziness. Physical examination: BP 92/56 mmHg, HR 110 bpm, SaO_2 86%, T 38.4 °C, glycaemia 178 mg/dL, Glasgow index 15/15, negative meningeal signs, tenderness on abdominal palpation. Of the complementary tests, the most significant data include: ECG: sinus tachycardia 100 bpm with isolated ventricular extrasystole; abdominal ultrasound: normal; chest X-ray: bilateral diffuse alveolar consolidation and cardiomegaly (the X-ray performed before treatment start was reported as normal); haemogram: haemoglobin 11.4 g/dL, haematocrit 34.4%, MCV 104 fL; coagulation: Quick's test 51%, D-dimer: 5109 ng/mL; gasometry: lactic acid 5.8 mmol/L, pH 7.52; creatinine: 1.8 mg/dL (normal values in previous tests); procalcitonin 0.11 ng/mL; pro-BNP: 9130 pg/mL; urine sediment: normal. The patient was admitted to the Intensive Care Unit, where respiratory support (Mk-reservoir 12 lpm and, subsequently, CPAP) and empiric antibiotic therapy with imipenem, along with low doses of noradrenaline and methylprednisolone IV, were initiated; methotrexate was discontinued. Serial blood culture and urine culture were negative, and the echocardiography was normal. Bronchoalveolar lavage was not performed.[7] After 48 h, an improvement in her condition and the laboratory values was observed; for this reason, she was transferred to the ward, where two days later she was asymptomatic and oxygen therapy was no longer required. A pulmonary CT was performed (Fig. 1A) where the presence of a predominantly peripheral bilateral extensive ground-glass opacity was confirmed, associated with minimum subpleural lung consolidations in the right lower lobe; the preserved lung parenchyma was normal. The patient was discharged with oral steroid treatment (0.5 mg/kg) for control at the outpatient offices; oral sulfasalazine was added, and it was discontinued a few weeks later due to hair loss, abdominal pain, and palpable purpura in abdomen and upper part of limbs.

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