Certolizumab in a patient with severe psoriasis and concomitant hepatitis C virus infection

Diana Velázquez Tarjuelo, MD,[a] and Pablo de la Cueva Dobao, MD[a,b]
Madrid, Spain

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INTRODUCTION

The treatment of psoriasis has benefited in recent years from the introduction of biological drugs that target specific components of the immune system. Some of these drugs block the excess production of tumor necrosis factor (TNF)-α in the skin or joints, thus, helping stop the inflammatory cycle of psoriatic disease. However, it has been suggested that anti–TNF-α agents could be associated with exacerbations of concomitant viral infections, an effect that could have potentially serious consequences in patients with hepatitis C virus (HCV) infection. TNF-α activates the immune system in response to viral infection, and the use of anti–TNF-α drugs in patients with chronic HCV could promote or reactivate viral replication. However, there are numerous reports that confirm the safety of anti–TNF-α biological drugs (eg, adalimumab, infliximab, and etanercept) in patients with psoriasis or psoriatic arthritis and concomitant HCV infection, suggesting that the risk of reactivation of the infection is low.[1-4] Further, TNF-α overexpression in the liver of chronic HCV patients can also lead to an increase of serum levels of transaminases and liver fibrosis, and these drugs could have a potentially beneficial effect in controlling these disorders.[5]

Certolizumab is a recombinant humanized antibody specific against TNF-α and approved for use in psoriasis, psoriatic arthritis, axial spondyloarthritis, and rheumatoid arthritis.[6] PEGylation of the antibody increases its half-life and makes it more hydrophilic, therefore, improving its ability to penetrate into inflamed tissues. In vitro it causes no effects such as degranulation, loss of cell integrity, apoptosis, complement-dependent cytotoxicity, and antibody-dependent cell-mediated cytotoxicity.[7,8]

Abbreviations used:

HCV: hepatitis C virus
PASI: Psoriasis Area and Severity Index
TNF: tumor necrosis factor

A recent retrospective study of rheumatoid arthritis patients found that receiving certolizumab for 1 year versus other TNF-α inhibitors (etanercept, adalimumab, golimumab, or infliximab) had similar risk with respect to serious infections, malignancies, and cardiovascular events.[8] However, we have not found published data on the effects and safety of administration of certolizumab pegol in patients with psoriasis and concomitant HCV infection.

CASE REPORT

A 64-year-old man had HCV infection diagnosed in 2006 and psoriasis in 2007. In 2007, treatment with interferon and ribavirin was prescribed but was interrupted 11 months later because of severe secondary colitis and the onset of severe psoriasis, failing to stop viral replication, and causing increased transaminase levels (glutamic oxaloacetic transaminase,193 U/L and glutamic pyruvic transaminase, 212 U/L). Initial treatment for psoriasis included topical corticosteroids, topical vitamin D derivatives, and acitretin. Between 2011 and 2014, the patient was treated with etanercept, ustekinumab, adalimumab, and infliximab, in all cases with good

From University Hospital Infanta Leonor[a] and Complutense University.[b]
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Correspondence to: Diana Velázquez Tarjuelo, MD, Department of Dermatology, University Hospital Infanta Leonor, Gran Vía del Este 80, 28031 Madrid, Spain. E-mail: dianavelazquezt@gmail.com.
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initial response but subsequent therapeutic failure. In the case of infliximab, the presence of antidrug antibodies and absence of drug in the serum was observed, so a treatment with cyclosporine was started. The patient presented lower and stable hypertransaminasemia (glutamic oxaloacetic transaminase and glutamic pyruvic transaminase levels of 100 U/L), consistent with the concomitant chronic HCV infection and unrelated to the medication. The adverse effects of cyclosporine included significant asthenia and the appearance of muscle and joint pain requiring multiple cycles of prednisone (in the absence of clear signs of psoriatic arthritis). In 2015, treatment with certolizumab pegol (Cimzia) was initiated at the indicated dose for psoriatic arthritis. Following standard procedures, certolizumab administration started with a period of induction (400 mg administered in weeks 0, 2, and 4) followed by a maintenance period (200 mg every 2 weeks or 400 mg every 4 weeks).[6] At the beginning of therapy with certolizumab, and still being treated with cyclosporine and prednisone, the patient had a Psoriasis Area and Severity Index (PASI) score of 6. After 12 weeks of treatment with certolizumab pegol, the response was excellent, achieving a PASI score of 0, which led to the suspension of the treatment with prednisone and cyclosporine. No adverse events from the treatment with certolizumab were observed. Currently, 2.5 years after starting treatment with certolizumab pegol, the patient continues with a PASI score of 0, and antiviral treatment has resumed, this time with sofosbuvir/ledipasvir and ribavirin.

DISCUSSION

In this case, a patient with HCV infection had severe psoriasis after receiving antiviral treatment with interferon.[9] Treatment of psoriasis in these patients is usually challenging, as there is no clear treatment guidance currently in the literature. Certolizumab pegol is a promising treatment for psoriasis because of its rapid reduction of disease activity, long-term therapeutic efficacy, and good safety profile.[7] This effect has been observed in both in bio-naive and non—bio-naive patients, as the case described here. Currently, 2.5 years after the patient started treatment with certolizumab pegol, response to treatment is still excellent (PASI score, 0), with no reactivation of the virus and progressive improvement in serum transaminase levels. The anti—TNF-α activity of biological drugs caused overall improvement in transaminase levels.[5]

The results of a phase 2, placebo-controlled, study in patients with moderate to severe psoriasis treated with certolizumab at doses of 200 and 400 mg showed that 75% and 83% of the patients, respectively, reached a PASI score of 75 by week 12.[10] Two phase 3 clinical trials (CIMPASI-1 and -2) that assessed the efficacy of certolizumab pegol in patients with moderate to severe chronic plaque psoriasis have shown significant, clinically meaningful improvements in PASI and PGA scores when compared with placebo.[11] A third phase 3 study (CIMPACT, ClinicalTrials.gov identifier: NCT02346240) is still ongoing and will evaluate efficacy comparatively with etanercept. However, further long-term extension trials are required to determine the safety of anti—TNF-α agents such as certolizumab in patients with concomitant viral infections.

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