Letter to the Editor

Certolizumab Pegol-induced Palmoplantar Pustulosis: A Case Report and Review of the Literature

Pustulosis palmoplantar inducida por certolizumab pegol: presentación de un caso y revisión de la literatura

Dear Editor,

The biological drugs that target tumour necrosis factor α (TNFα) are now widely used to treat rheumatoid arthritis (RA) and other immunomediated inflammatory diseases. Although they have been shown to be highly effective and to have a good safety profile, they are also associated with adverse cutaneous events, including psoriasis and psoriasisiform lesions. We present a patient diagnosed RA who developed palmoplantar pustulosis (PPP) during treatment with certolizumab pegol (CZP), and we also review the published cases of psoriasis induced by this drug.

A 57 year-old male with a history of diabetes mellitus and arterial hypertension was diagnosed RA at the age of 50 years-old due to his polyarthritis in the small joints of the hands, raised acute phase reagents and positivity for rheumatoid factor and anticyclic citrullinated peptide antibodies. He was treated at first with methotrexate (maximum dose 20 mg/week, subcutaneous), with clinical improvement and good tolerance. However, after 5 years he underwent gradual worsening of the inflammatory symptoms in the hands and persistently high levels acute phase reagents (disease activity measured by DAS28: 5). Due to this it was decided to add CZP (subcutaneous 200 mg every 2 weeks), achieving a good response in the joints and analytical results within the first 2 months. After 3 months of anti-TNFα treatment he visited the emergency department due to a sudden outbreak of converging and painless millimetrical pustular lesions on the palms and soles of the feet (Fig. 1), with no signs of infection or lesions in other locations. Biopsy of a palm lesion was histopathologically compatible with PPP. CZP was withdrawn, but methotrexate was maintained, starting topical corticoid therapy with betamethasone cream. The latter was subsequently changed to clobetasol cream with occlusive bandages and laser sessions, and the lesions disappeared completely 4 months after suspending the anti-TNFα. The patient remained in remission after a 6-month observation period, continuing treatment only with subcutaneous methotrexate 25 mg/week, without the need to recommence the biological treatment.

The appearance of psoriasis de novo or worsening of pre-existing psoriasis is an AE associated with all anti-TNFα drugs, and it may occur at any time (from days until years after the start of treatment), without any variations according to sex or age. Although it has been described in almost all of the diseases treated with anti-TNFα, up to 75% of cases correspond to inflammatory rheumatological disease. A recent meta-analysis that included 216 cases of de novo psoriasis induced by anti-TNFα found the following frequency for each of the following drugs: infliximab 62%, adalimumab...
<table>
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<tr>
<th>Study</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Base disease</th>
<th>PH/FH of psoriasis</th>
<th>Previous treatments</th>
<th>CZP treatment pattern</th>
<th>Type of psoriasis</th>
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<tr>
<td>Shelling et al.</td>
<td>78</td>
<td>M</td>
<td>RA</td>
<td>No/no</td>
<td>MTX, ETN</td>
<td>400 mg every 2 weeks, sc</td>
<td>PPP</td>
<td>10 weeks with ETN 6 weeks with CZP</td>
<td>Improvement following the suspension of CZP and high power topical corticoid treatment</td>
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<td>Koizumi et al.</td>
<td>71</td>
<td>W</td>
<td>RA</td>
<td>No/no</td>
<td>MTX, IFX</td>
<td>200 mg every 4 weeks, sc</td>
<td>PPP → CPP</td>
<td>122 days until the development of PPP 157 days until the development of CPP</td>
<td>No response following suspension of CZP and topical corticoid treatment Rapid improvement of the lesions (one week) with oral etretinate (20 mg/day), but without completely disappearing</td>
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<td>Eickstaedt et al.</td>
<td>14</td>
<td>M</td>
<td>CD</td>
<td>No/no</td>
<td>IFX</td>
<td>ND</td>
<td>PsoP</td>
<td>29 months with IFX 3 months with CZP</td>
<td>Remission of the first outbreak following suspension of IFX topical treatment with triamcinolone and calcipotriene and dressings with acetic acid Remission of the second outbreak after suspension of CZP and topical treatment with hydrocortisone Remission of the first outbreak after suspension of IFX and topical treatment with triamcinolone and hydrocortisone Remission of the second outbreak after suspension of CZP and treatment with MTX and topical hydrocortisone Remission of the first outbreak after suspension of ADA and topical treatment with hydrocortisone and betamethasone Remission with topical treatment with flucinolone and calcipotriene Remission after suspension of CZP and topical treatment with triamcinolone Start of IFX and oral PDN for CD, no recurrence of PsoG</td>
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<tr>
<td>Fischer et al.</td>
<td>38</td>
<td>M</td>
<td>CD</td>
<td>No/no</td>
<td>PsoP/no</td>
<td>ND</td>
<td>PsoG</td>
<td>One week until development of PsoG</td>
<td>Improvement following suspension of CZP and treatment with topical corticoids Complete remission of the lesions with CSA (3 mg/kg/day) and oral acitretin (10 mg/day) Initial improvement in pustular lesions with suspension of CZP and oral PDN 30 mg/day Improvement of PsoG with MTX (25 mg/week), that had to be changed to 6-MP Recurrence of PsoG that improved with UBV phototherapy and topical treatment with betamethasone and calcipotriene</td>
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<td>Mocciaro et al.</td>
<td>42</td>
<td>W</td>
<td>CD</td>
<td>No/no</td>
<td>MTX, IFX</td>
<td>400 mg every 4 weeks, sc</td>
<td>PPP + PsoP</td>
<td>29 weeks until development of PPP</td>
<td>No response after suspension of CZP and treatment with topical corticoids</td>
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<td>Klein et al.</td>
<td>26</td>
<td>W</td>
<td>CD</td>
<td>No/no</td>
<td>ND</td>
<td>ND</td>
<td>PsoG</td>
<td>4 months until the development of PPP</td>
<td>Initial improvement in pustular lesions with suspension of CZP and oral PDN 30 mg/day Improvement of PsoG with MTX (25 mg/week), that had to be changed to 6-MP Recurrence of PsoG that improved with UBV phototherapy and topical treatment with betamethasone and calcipotriene</td>
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<tr>
<td>Protic et al.</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>NE</td>
<td>ND</td>
<td>Remission after suspension of CZP and topical treatment with betamethasone and cobalatol and laser sessions</td>
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<td>The current case</td>
<td>ND</td>
<td>ND</td>
<td>RA</td>
<td>No/no</td>
<td>MTX</td>
<td>ND 200 mg every 2 weeks, sc</td>
<td>NE</td>
<td>ND</td>
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Rather reflecting any difference between these drugs, this may be due to the higher number of patient-years of exposure to the first anti-TNFα approved, in comparison with CZP and golimumab, and it is now considered to be a class effect of these drugs.2,3

In our review of the literature (PubMed) we found 9 cases of CZP induced psoriasis, 2 in RA and 7 in Crohn’s disease (Table 1). The cases which occurred in RA corresponded to PPP; in the first of these it was a recurrent AE (the first event after etanercept),4 while in the second it appeared de novo and progressed to generalised pustular psoriasis (GPP).5 CZP was withdrawn in both cases and after dermatological treatment the patients showed good clinical evolution of the lesions. All of the cases which arose in Crohn’s disease were de novo (3 with CZP as the first anti-TNFα and 3 in which it was the second) and the types of psoriasis they had were: plaque psoriasis (3),6 guttata psoriasis (1),7 PPP + plaque psoriasis (1),8 PPP + guttata psoriasis (1)9 and one unspecified type (1).10 In 5 cases CZP was suspended, 4 cases had a good response to topical corticoid therapy and 2 cases also required photochemotherapy and acitretin.

The types of anti-TNFα-induced psoriasis described the most often in the literature are: plaques 44.8%, PPP 36.3%, GPP 10.9% and guttata 8%.3 The high frequency with which PPP occurs in patients treated with anti-TNFα in comparison with the general population (an incidence of 0.12%) suggests that this is a specific AE of these drugs. Although suspension of the treatment is not always indispensible, severe forms such as PPP and GPP may respond better if the anti-TNFα is withdrawn.5

To conclude, CZP may be associated with the development of induced psoriasis, as is the case with other anti-TNFα drugs, regardless of their indication, and PPP is one of the most frequent forms of presentation.

References


Lourdes Villalobos-Sánchez, Carmen Larena-Grijalba, Adela Alía-Jiménez, Walter Alberto Sifuentes-Giraldo

Servicio de Reumatología, Hospital Universitario Ramón y Cajal, Madrid, Spain

* Corresponding author.
E-mail address: lurdesvs@hotmail.com (L. Villalobos-Sánchez).