LETTER TO THE EDITOR

Oral lichen planus after certolizumab pegol treatment in a patient with Crohn’s disease

Dear Sir,

Lichen planus (LP) is a relatively uncommon inflammatory dermatosis of the mucocutaneous surfaces that can present with a variety of clinical manifestations and, most commonly, affecting middle-aged adults. The disease course may be short or chronic, although most cases may resolve after 1 month to 7 years. The real prevalence of LP is unknown, but is estimated to be 1% in the USA.1 The pathogenesis of LP is not entirely understood. In general, activated T lymphocytes are recruited to the dermal–epidermal junction and induce apoptosis in basal keratinocytes. Both CD4+ and CD8+ T lymphocytes are found in the lichenoid infiltrate of LP, with a predominance of the latter cell type being present in established lesions.1

Ten to 20% of patients with LP demonstrate both oral and cutaneous lesions. Oral lichen planus (OLP) manifestations occur in approximately 2% of the general population, while cutaneous lesions occur in 0.4%. We report a rare case of oral lichen planus development as paradoxical adverse events in a patient treated with certolizumab pegol for steroid-dependent Crohn’s disease.

In our center a 59-year-old man with a long history of ileocolonic CD, non responder to azathioprine, methotrexate and infliximab, was treated with certolizumab pegol (CP), as compassionate use, for steroid-dependent disease (adalimumab was still off label in Europe for CD treatment). The dosage was 400 mg subcutaneously at weeks 0, 2 and 4 followed by a scheduled regimen every 4 weeks. The patient achieved a complete free-steroid but 2 years after the first dose he developed a painful and irregular lesion on the buccal mucosa covered with a fibrinous exudate. After a biopsy (Fig. 1), and according to an expert dermatologist, the final diagnosis was OLP probably induced by CP that was discontinued. Topical corticosteroids were effective for complete mucosal healing and at the last visit the lesions were in remission.

OLP may present anywhere in the oral cavity and up to six different clinical patterns are recognized: reticular (often asymptomatic), popular, plaque, atrophic, erosive, and bullous. Erosive LP is the second most common form of OLP. It is a painful condition with lesions irregular in shape and covered with a fibrinous exudate. The periphery of the lesion is frequently surrounded by reticular or finely radiating keratotic striae.2 It has been reported that atrophic and erosive forms of LP can undergo malignant transformation although this risk remains controversial and different research groups have proposed distinct approaches and interpretations.3 This risk may be because of the atrophic nature of the mucosa rather than the specific disease.

A range of topical and systemic medications have been shown to improve the symptoms associated with LP and to hasten the resolution of LP. Topical steroids are first-line therapy in mucosal LP while systemic glucocorticoids are effective in treating erosive oral and vulvovaginal LP (more commonly in conjunction with topical glucocorticoids). Topical retinoic acid, cyclosporine, tacrolimus, and pimecrolimus have been shown to be effective in treating erosive and plaque-like oral lesions. In the last 5 years, also, the efficacy of two biological agents (efalizumab, alefacept) was reported in the treatment of LP.4

Figure 1  Epidermis with hyperkeratosis and hypergranulosis. The papillary derma with band-like inflammatory infiltrate with melanin-containing macrophages (Panel A: 4×; panel B: 20×).
Interestingly should be noted that development of drug-induced form of LP had been reported in the literature (beta blockaders, methyldopa, penicillamine, quinidine, etc.)\(^5\) and, as discussed in a recent review by Asarch et al.,\(^6\) in the last years some authors had described the development of LP-like eruption using tumor necrosis factor-\(\alpha\) antagonists for the treatment of Crohn’s disease (CD), psoriasis, rheumatoid arthritis or ankylosing spondylitis. This form usually develops insidiously and can affect any area of the body surface.

Certolizumab pegol is a pegylated humanized Fab’ fragment of an anti-TNF monoclonal antibody, with a high affinity for TNF-\(\alpha\), which is effective in the treatment of patients with CD, either naive or previously treated with infliximab.\(^7,8\) Mild and severe side effects were described after CP use\(^9\) but to our knowledge there was no evidence with regard to OLP development in CD patients. The published literature does not offer a clear explanation of the mechanisms that underlie the onset of anti-TNF\(\alpha\)-induced OLP.

In conclusion: 1) OLP development is a possible adverse event in inflammatory bowel disease patients treated with anti-TNF\(\alpha\) drugs including CP; 2) when OLP is diagnosed biologics should be discontinued starting standard therapies to resolve the lesions; 3) switch to another biological agent should be considered on the base of clinical symptoms and according to the dermatologist maintaining a strict follow-up of patients due to the controversial malignant potential of OLP.

References