Psoriasis Vulgaris Associated with Acne Vulgaris: Differential Effects of Biologicals?

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Sir,

Acne vulgaris and psoriasis vulgaris belong to the most common chronic inflammatory skin diseases. Acne affects approximately 80% of young adolescents and persists beyond the third decade of life in approximately 10% of patients (1). The prevalence of psoriasis in Europe is approximately 3%. In the last few years biologicals have dramatically improved the therapeutic options for psoriasis. In addition, other inflammatory skin diseases can be treated successfully with tumour necrosis factor (TNF)-α inhibitors, for example Behçet's disease, graft-versus-host disease, pyoderma gangraenosum, toxic epidermal necrolysis (2) and SAPHO syndrome (3). With regard to adolescent patients in particular, the coincidence of acne and psoriasis has to be anticipated and both diseases might respond differently to biologicals. However, until now only a few reports on the influence of biologicals on acne vulgaris are available. We report here on a patient with severe psoriasis whose coexistent acne vulgaris was improved drastically when treated with different TNF-α inhibitors.

CASE REPORT

A 40-year-old male patient had had plaque-type psoriasis for 20 years, with the most prominent lesions on his face and genital region, as well as disseminated psoriatic plaques on the rest of the body surface. He had a positive family history of psoriasis, but arthritic symptoms were absent. Since his teenage years he had had severe acne vulgaris on the upper back and shoulders. The patient now requested alternative treatment for his psoriasis since treatment with cyclosporine, fumaric acids esters, methotrexate and psoralen plus ultraviolet-A (PUVA) had failed.

During regular clinical consultations, the Psoriasis Area and Severity Index (PASI) and a photographic documentation of his full body were performed. As an objective parameter of acne severity, an area on his back was defined by pigmented moles. The number of papules and pustules in this area were counted; nodules visually larger than 5 mm diameter and abscesses were sequentially scored 3 times to reflect their greater activity of inflammation. This score is called the Acne Intensity Score (AIS) in this paper (Fig. 1).

Although the acne was initially widespread, inflammation was relatively mild. Within the defined area on the upper back 73 red papules and pustules and 5 nodules were counted; the resulting AIS was 88 (73 + (5 × 3)). After 12 weeks of treatment with efalizumab (initially 0.7 mg/kg, and subsequently 1 mg/kg s.c. once weekly) a 49% reduction in PASI was achieved (from 21.1 to 10.8). However, the acneiform eruptions increased in number and intensity (AIS increased 22%; from 88 to 108). After another 6 weeks of therapy the psoriasis deteriorated again (PASI 12.3) and a combination therapy of efalizumab with cyclosporin A (CSA) (2.5 mg/kg) was started. This regimen resulted in a minor reduction in PASI (to 10.0) and a minor improvement in the acne (AIS 97 compared with 108 before therapy). As the acne was still worse than at the beginning of the antipsoriatic therapy, additional acne-specific therapy was started with topical erythromycin and, 4 weeks later, systemic minocycline (50 mg/day) for 9 weeks. Due to the increased risk of toxicity of CSA in combination with minocycline and the combined immunmodulatory medication with efalizumab, clinical and laboratory controls were performed frequently, but showed normal results. The CSA dose was not increased, for the same reasons.

After 35 weeks of treatment (efalizumab 35 weeks, CSA 17 weeks and minocycline 9 weeks) the acne (AIS 76) and psoriasis (PASI 10.6) persisted. Because of this unsatisfactory result the therapeutic regimen was switched to monotherapy with etanercept, 25 mg s.c. twice a week. After 2 weeks the acne improved dramatically (AIS 49). After 6 weeks the dosage was increased to 50 mg s.c. twice a week due to worsening of psoriasis (PASI 13). After 15 weeks of etanercept therapy the acne was almost healed (AIS 16), but PASI was still 15.9.

For that reason therapy was changed to infliximab (5 mg/kg i.v., week 0, 2, 6, and every 8 weeks). The PASI reduced rapidly in the first 6 weeks (–70%; PASI 5.1) and the acne activity reduced further (AIS 6). After 52 weeks of treatment with infliximab both diseases showed only a little clinical activity (PASI 3.6; –83% from start of therapy; AIS 1; –99% from start of therapy).

DISCUSSION

Acne vulgaris is a skin disease of body regions with abundant sebaceous glands. The main pathophysiolo-

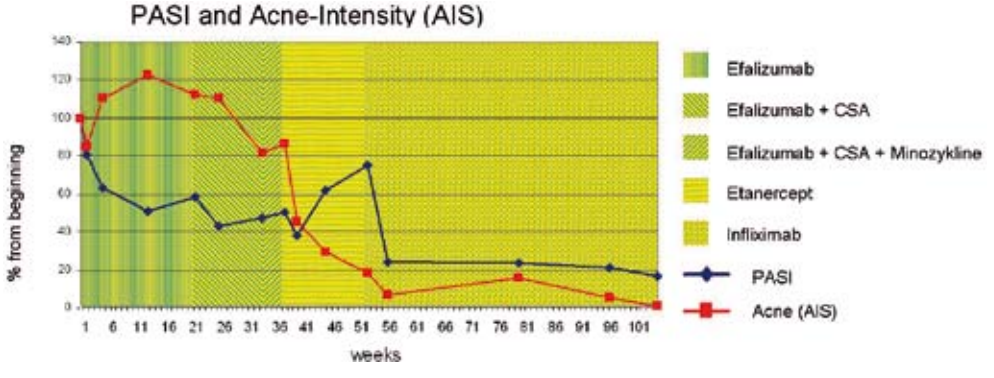

Fig. 1. Progression of Psoriasis Area and Severity Index (PASI) and Acne Intensitiy Score (AIS) during different systemic treatments. CSA: cyclosporin A.

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gical factors are seborrhoea, follicular hyperkeratosis and colonization with *Propionibacterium acnes*. The clinical consequences of these processes are comedones, papules, pustules, inflammatory nodules and abscesses. Common dermatological acne treatments target these pathogenetic factors by comedolytic and antibiotic agents.

Only a few case reports are available on the influence of antipsoriatic medication, as used in our case, on acne vulgaris. CSA has been reported to worsen acne in a patient following kidney transplantation (4). The effects of efalizumab on acne have not been described previously. Regarding TNF-α inhibitors, a single report on etanercept describes a beneficial course in a young patient with severe acne vulgaris (5).

TNF-α seems to play an important role in the pathogenesis of acne; particularly with regard to toll-like receptors (TLR), which are the focus of ongoing investigations of acne. TLR are thought to be a link between innate and acquired immunity. They are expressed on effector cells such as granulocytes and macrophages and can be activated by bacterial ligands such as lipoproteins and peptidoglycans. Jugeau et al. (6) showed in 2005 that *P. acnes* is able to trigger the expression of TLR *in vitro*. Through activation of macrophages by TLR2 the production of TNF-α, interleukins (IL)-1 and IL-8 as well as other proinflammatory cytokines is induced (7). TNF-α boosts the expression of TLR by positive feedback. Accordingly TLR4-expression was reduced by TNF-α-inhibitors, as shown in mononuclear cells and synoviocytes of patients with ankylosing spondylitis (8). Although the influence of TNF-α inhibitors on acne vulgaris has not been investigated, the clinical benefit described in our case could well be explained by a reduction of TLR expression which result in a decreased activation of mononuclear cells.

Although the efficacy of biologicals in other chronic inflammatory skin diseases has been described in case reports, double-blind placebo-controlled clinical studies are available for psoriasis only. Successful treatment of arthritic lesions with etanercept and infliximab has been reported in SAPHO syndrome (3), which includes, by definition, acne-like eruptions. Papules and pustules are also part of PAPA syndrome (Pyogenic Arthritis, Pyoderma gangrenosum and Acne), which has been treated effectively with etanercept (9). However, skin symptoms are not described in detail.

Hidradenitis suppurativa is a chronic inflammatory disease of the apocrine glands with some features in common with acne vulgaris. In 2006, Cusack & Buckley (10) reported on 6 patients with hidradenitis suppurativa who showed a substantial reduction in inflammatory activity with 24 weeks‘ therapy with etanercept. Comparable results with long-term benefits are described for infliximab (11, 12), and in one case for efalizumab (13). In our case, however, efalizumab seemed to worsen the acne lesions.

In addition, a differential clinical effectiveness in treatment for acne and psoriasis could be shown for the two TNF-α blockers used. Whereas both were able to improve acne lesions, only infliximab resulted in an improvement in psoriasis. Hence the inflammatory processes involved in these two diseases are thought to be different, but to include processes in which TNF-α plays a role.

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