CONCISE COMMUNICATION

Successful treatment of psoriatic arthritis and comorbid annular atrophic lichen planus with etanercept

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ABSTRACT

Psoriasis vulgaris and lichen planus are distinct T-cell-driven inflammatory skin diseases. Both present in a variety of clinical subtypes. Mucosal or nail involvement may be present. Here, we report the rare concomitant clinical presentation of psoriatic arthritis and annular atrophic lichen planus on the trunk of a 52-year-old male patient. Treatment with sulfasalazine failed to control inflammatory activity; methotrexate and leflunomide were ceased due to side-effects. After confirmation of both diagnoses, we initiated a tumor necrosis factor (TNF)-α-directed therapy with the fusion protein etanercept resulting in significant improvement of both conditions. This case report aims to highlight the rare colocalization of psoriasis and lichen planus, the rare entity of annular atrophic lichen planus, and to discuss a possible beneficial impact of certain TNF-α inhibitors on subtypes of lichen planus.

Key words: inflammation, lichen planus, psoriasis, psoriatic arthritis, tumor necrosis factor-α.

INTRODUCTION

Psoriasis is a chronic inflammatory disease of the skin and joints with a genetic background. Skin lesions are characterized by a high activation of innate immune pathways, a T-helper (Th1/Th17)-driven adaptive immune response with strong expression of pro-inflammatory cytokines (e.g. interleukin [IL]-17, IL-22, tumor necrosis factor [TNF]-α and interferon [IFN]-γ) and hyperproliferation of keratinocytes. Joint involvement may be present in up to one-third of patients as inflammatory arthropathy called psoriatic arthritis (PsA). Early detection and treatment of PsA is necessary to prevent destructive and mutilating courses.

Lichen planus (LP) is characterized by autoreactive CD8+ T cells inducing apoptosis of keratinocytes. Various triggers have been identified, but the exact etiopathology remains unknown. Classical LP is characterized by pruritic polygonal lesions predominantly in flexural areas; however, a variety of clinical subtypes exist. Although the clinical picture is diverse, dermatohistopathology is pathognomonic in all variants. Annular LP is a less pruritic subtype with a male predominance that shows a typical round configuration with slightly elevated margins and an optional central atrophy; typically, intertriginous areas are affected.

Nail involvement may be present both in psoriasis and LP and is described to be indicative of PsA in psoriatic patients as it is caused by inflammation of the enthesis of the distal interphalangeal joints.

While antagonists of TNF-α such as etanercept (ETN) are well established both in therapy of psoriasis vulgaris (PV) and PsA, in LP, other agents are favored for treatment, especially corticosteroids. Interestingly, there are numerous reports of TNF-α inhibitor-induced LP, opposed to a few reports of successful therapy of LP itself with the same drugs. Here, we present a rare case of comorbid psoriasis with arthritic involvement and annular atrophic LP which both responded well to therapy with ETN.

CASE REPORT

A 52-year-old male patient, who gave his written consent for the publication of his case and photographs, was referred to our department in November 2015. He had noticed multiple, asymptomatic, progressive, annular-shaped, red-violaceous plaques located bilaterally at the flank and the groin for 3 months. The size of the lesions ranged from 0.5–3 cm, most of them showing an atrophic center. The oral and genital mucosa was not involved; the anal cleft was erosive (Fig. 1).

The patient had a 20-year history of PsA and had been treated intermittently by various rheumatologists with methotrexate, leflunomide and sulfasalazine without achieving disease control. Lately, the patient was dependent on therapy with prednisolone 5 mg/day and frequent use of non-steroidal anti-inflammatory drugs; he had received no new medication in the last months. The nails had been dystrophic for at least 10 years; however, psoriatic skin lesions had always been...
minimal. Physical examination revealed pitting, nail plate crumbling and leukonychia on all nails (Fig. 1).

Laboratory investigations showed normal blood count, glucose, renal and liver function and absence of rheumatoid factor and anti-citrullinated protein antibody. Chronic infections (hepatitis B/C, tuberculosis) were excluded.

Chest X-ray and ultrasonography of the abdomen showed no pathology except hepatic steatosis.

A skin biopsy of an untreated macule of the submammary region showed a sparse lymphocytic infiltrate along the basal membrane and melanophages in the center. An active edge of the same lesion showed prominent orthohyperkeratosis and acanthosis over a pronounced interface dermatitis with formation of colloid bodies; hence, annular atrophic LP could be diagnosed. Immunohistochemistry (IHC) including CD3, CD1a and S100 was used to better characterize differences between the inactive center and the active ring edge of the lesion. T cells and Langerhans cells (LC) accumulated in the peripheral area and appeared partly depleted in the atrophic center (Fig. 2).

X rays of the spine revealed advanced osteochondrosis with partly ankylosing spondylitis. X rays of the acral regions showed advanced osteopenia as well as osteophytes and erosive lesions in proximity to the joints, consistent with PsA (Fig. 1).

After failure of the above-mentioned disease modifying anti-rheumatic drugs (DMARDs), a TNF-α-directed therapy was proposed. Upon completion of immunizations, we initiated an s.c. therapy with ETN 50 mg once weekly which has been continued until now. Simultaneously, potent topical corticosteroid
Figure 2. Histopathology and immunohistochemistry of a representative lesion of the submammary region in December 2015. (a–d) The active edge of the lesion displayed acanthosis with hypergranulosis and vacuolar degeneration of the basal membrane caused by a dense lymphocytic infiltrate at the dermoepidermal junction. (b) Detail of a colloid body. In immunohistochemistry, an abundance of T cells and dermal Langerhans cells is obvious. (e–h) The center of the lesion merely displayed a sparse inflammatory infiltrate but numerous melanophages. T cells and Langerhans cells are still present but markedly reduced. (a,b,e,f) Hematoxylin–eosin, original magnifications: (a,e) ×20, (b,f) ×40, (c,g) CD3, ×20, (d,h) CD1A, ×20.
Annular LP comprises only approximately 5–10% of all LP cases. Proposed mechanisms in the formation of lesions include a convergence of multiple papules in a ring shape or a central involution of lichenoid plaques yielding an elevated border. This process may be a result of initial recruitment and central involution of lichenoid plaques yielding an elevated border; cytokine release by keratinocytes or inflammatory cells may give rise to a negative loop resulting in sequential inflammation.7

Differential diagnoses must be considered (Table 1). Lichenoid drug eruption could be excluded in the absence of a plausible trigger in the patient’s history. The general criteria of drug eruptions such as papillary edema, abundance of leukocytes in dermal vessels and presence of eosinophils must be recognized. IHC further aids to highlight the differences between the composition of the inflammatory infiltrate and the cell numbers of the active ring edge and the center of a lesion (Fig. 2). Previous authors described that TNF-α may play a central role in formation of annular lesions as only the ring edge showed increased expression.8 The positive therapeutic response to treatment with ETN in this case is in line with this finding. However, the parallel use of potent TCS may be partially responsible for the amelioration of the lesions as oral LP lesions showed sustained decrease of TNF-α expression upon treatment with TCS in another study.9 So far, there are few reports about a beneficial effect of TNF-α inhibitors in the treatment of LP opposed to a greater number of TNF-α inhibitor-induced LP-like lesions. A study of the effects on cytokine expression between the best-established TNF-α-directed drugs adalimumab, infliximab and ETN implies that among the group the latter shows a diverging effect on antigen-induced IFN-γ levels.10 More detailed knowledge about the pathogenesis of distinct clinical subtypes of LP and their response to different TNF-α inhibitors is warranted. Because the patient had used TCS before ETN treatment without achieving improvement, we feel that the therapeutic intervention of TNF-α blockade is accountable for amelioration of skin lesions.

Another interesting observation in our patient is the concomitant existence of psoriatic skin lesions (nails, anal cleft) and LP skin lesions (axillary region, groin). Overall, considering the frequency of both diseases, this is a rare finding. Common features include multigenetic predisposition, isomorphic response and parainfectious exacerbations. Subtypes of T cells

| Table 1. Synopsis of an excerpt of clinical subtypes of lichen planus in relation to this case report |
|---------------------------------------------------------------|
| Subtype | Morphology and distribution | Sequence | Predisposing factors | Differential diagnoses |
| Classical LP | Pruritic purple polygonal planar papules and plaques | Unknown antigen triggers | 95% of cases occur in adulthood | Lichenoid drug eruption |
| | Symmetrical distribution in flexural areas | T-cell-mediated anti-epithelial reaction | No sexual predisposition | Lichenoid MF |
| | Face generally spared | Mostly self-limiting course | Viral infections | Lichen nitidus |
| | | (months to years) | | Viral exanthema |
| Oral LP | Clinical subtypes (reticular, erosive, papular, plaque-like) | Untreated: chronic course | Mechanical trauma/irritation | Syphilis |
| | show varying appearance on oral mucosa; characteristic Wickham striae are facultative | Erosive subtypes may lead to severe ulcers and malignant transformation | Female predominance | Candidiasis |
| | Buccal area and dorsal tongue | | Noxious agents (e.g. tobacco) | Leukoplakia |
| | most commonly affected | | | Chronic ulcerative stomatitis |
| Annular LP | Red-purple macules or plaques of 2–8 cm diameter with central atrophy or raised borders | Convergence of multiple papules to a ring structure or expansion of a macule with central atrophy | Middle aged adults | Granuloma annulare |
| | Genital and intertriginous areas (axillae, groin folds), rarely extremities and trunk | Chronic, (mostlly) asymptomatic course, atrophic residues occur as annular atrophic LP | Male predominance | Tinea corporis |
| | Wickham striae | | Race (dark skin) | Anular subtype of SCLE |
| Annular atrophic LP | Residual end-point of annular LP | Chronic, (mostly) asymptomatic course | Long-term use of high-potency topical corticosteroids | Porokeratosis |
| | Distribution identical to annular LP | | | Lichen sclerosus |

Modified according to Weston and Payette. LP, lichen planus; MF, mycosis fungoides; MMP, mucous membrane pemphigoid; SCLE, subacute cutaneous lupus erythematosus.
Some authors speculated about an underlying imbalance of TNF-α and IFN-γ as a result of an antigenic stimulus that caused superimposed linear LP lesions in a psoriatic patient. Local production of IFN-γ was assigned to an improvement of psoriasis during development of LP in another case report. Apart from well-described T-cellular inflammatory mechanisms in psoriasis, high activation of innate immune pathways may lead to enhanced epidermal antigen release which could pave the way to an anti-epithelial reaction and development of other inflammatory skin diseases. Underreporting may be the main reason for the sparse availability of published work on concomitant PV and LP.

The prolonged inconsequent treatment of PsA prior to the first visit of our patient had led to significant mutilations of the fingers. This underlines the urgency for early detection and treatment of PsA. For patients whose disease activity cannot be controlled with conventional DMARDs, biologics like TNF-α- or IL-17-directed therapies must be considered. Tofacitinib, an oral Janus kinase 1/3 inhibitor, is another option for treatment of PsA.

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