

Exacerbation of generalized plaque psoriasis after tuberculin test

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Abstract

Koebner phenomenon, also known as isomorphic response, is the appearance of active skin lesions in sites of epidermal injury. This manifestation is characteristic of different dermatological diseases, such as lichen planus, vitiligo and psoriasis. We present the case of a psoriatic patient who experienced Koebner phenomenon after Mantoux test, followed by eruption of generalized plaque psoriasis.

Introduction

Biologic drugs have revolutionized the treatment of moderate to severe psoriasis, with a well-known increased risk of tuberculosis (TB) reactivation. In order to avoid this risk, screening for latent tuberculosis infection (LTBI) is essential to prevent the risk of active TB. Despite several disadvantages, tuberculin skin test (TST) still represents one of the most useful tools for LTBI detection. In this paper, we report the case of a 61-year-old female who experienced a severe relapse of psoriasis after Mantoux test.

Case report

A 61-year-old female presented with a 7-year history of severe arthropathic plaque psoriasis. The patient was also affected by mild hypercholesterolaemia. In the last years, she has been treated with different therapies including UVB-narrowband phototherapy, methotrexate, cyclosporine and etanercept. Cyclosporine revealed to be the best effective approach for the patient, but it was discontinued for arterial hypertension onset, while etanercept has revealed ineffective in a 3-months treatment course. Her past medical history included also an episode pneumococcal pneumonia occurred several years before, successfully treated

with antibiotic therapy. At the time of visit, the patient showed several well-defined plaques, characterized by mild infiltration, moderate erythema and scaling, involving trunk and principally extensor surfaces of limbs, with a Psoriasis Area Severity Index (PASI) score of 18.2. Since the patient had previously shown to be unresponsive to TNF- α -inhibitors, we considered ustekinumab in accordance with rheumatologists. Before starting treatment, we collected personal history, physical examination, and laboratory tests. On infectious diseases specialist's indication, screening for HIV, TB and viral hepatitis were also performed. A chest radiograph showed calcifications and scarring consistent with previous infection, while Mantoux test (MT) performed on her left forearm revealed a negative reaction. Other investigations were all within normal limit, including Quantiferon-TB Gold test. After four days, the patient developed a psoriatic plaque at the site of injection, while a severe worsening of psoriasis was observed, with comparison of new lesions and enlargement of the pre-existing ones with a PASI score of 28 (Figure 1).

The lesions were deeply infiltrated and mildly scaly. A skin biopsy showed confluent areas of epidermal hyperplasia with parakeratosis, moderate inflammatory infiltrate in the upper dermis with scattered eosinophils and dilated small vessels in the papillary dermis. Histopathological data confirmed the clinical diagnosis of generalized plaque psoriasis. Patient started topical treatment with calcipotriol and betamethasone ointment, in addition to systemic ustekinumab (45 mg every three months) which revealed effective in reducing psoriatic lesions with PASI score of 3.2 at the successive 3 months follow-up.

Discussion and conclusions

The MT is a screening tool for LTBI, consisting in subdermal injection of purified proteins derivative (PPD), obtained from stains of *M. tuberculosis*. This screening test is commonly performed to exclude LTBI in patients eligible for immunosuppressive treatment, while it is not reliable for patients already in treatment with anti-TNF drugs,^{1,2} since TNF is a key-cytokine in tuberculin-hypersensitivity reaction development and its inhibition can lead to false-negative results. IGRA (interferon-release assay) is a test measuring specific Tcell-based responses to *M. tuberculosis*-specific antigens including ESAT-6, CFP-10 and can be used in addition to MT or in alternative to it.³ Since MT produces a epi-

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dermal rupture, a Koebner phenomenon, or isomorphic response, can be induced. Indeed, psoriatic patients develop active skin lesions at sites of skin injury, even if previously unaffected. Skin injuries may be represented by trauma, infective or inflammatory diseases, sunburn, or medicaments.⁴ In literature, we found few other cases of Koebner phenomenon in which a psoriatic plaque developed after MT in the site of injection of.⁵⁻⁷ One of the patients reported was previously unaffected by psoriasis. In these cases, the lesions appeared within 3 days from the injection, a latency similar to

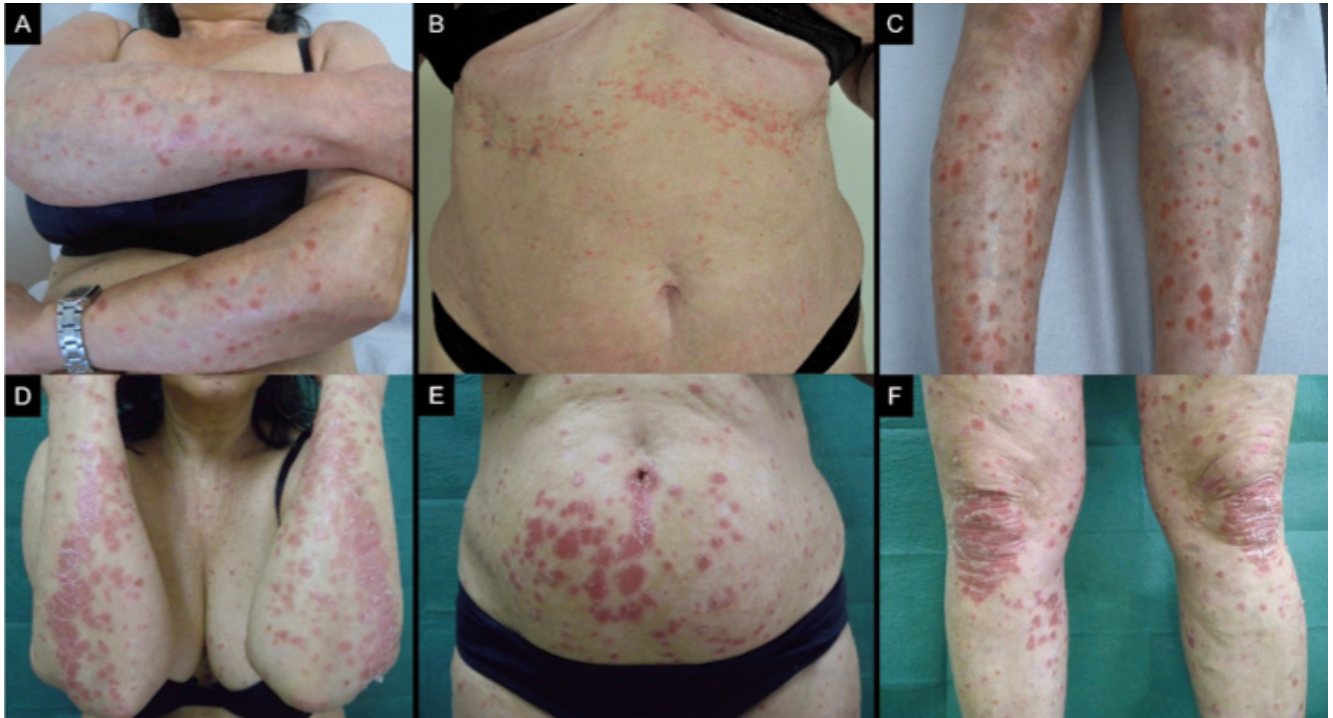


Figure 1. A-C) small erythematous scaly lesions on arms, elbows, abdomen and legs before the Mantoux test. D-F) Pictures taken one week after the tuberculin test show enlargement of pre-existent lesions and appearance of new larger erythematous, scaly plaques in sites not previously involved.

the one of the patients described in our case. However, this phenomenon may happen more frequently than reported in literature, according to a study in which PPD seems to be more effective in inducing koebnerization than injury alone.⁸ On the contrary, other works showed opposite findings,⁹ so this aspect is not fully understood. Concerning the physiopathology, some Authors suggested that the upregulation of pro-inflammatory cytokines (such as interferon- α and TNF- α) following epidermal injury could lead to inflammatory infiltration in the site of tuberculin injection and activate pathogenic processes involved in the development of psoriatic plaque in pre-disposed patients. The Koebner phenomenon would not explain the appearance of generalized lesions few days after the tuberculin test. The causal relationship between PPD injection and exacerbation of psoriasis was suspected on the basis of the compatible timing, while a spontaneous worsening of the disease could not be excluded considering the unpredictability of psoriasis course. Similar reports are scarce in literature: a case of generalized pustular psoriasis occurred after MT with a latency of 72 hours.¹⁰ The timing is comparable to the relapse experienced by our patient, but this is still not sufficient to define a clear causality link. Tubercular antigens showed

in vitro the capability to stimulate activation and proliferation of T-lymphocytes collected from inflammatory synovitis of patients with rheumatoid arthritis and psoriatic arthritis. Response to mycobacterial antigen may be secondary to cross-reactivity due to homology with human inflammatory proteins.¹¹ A similar process may be responsible for the enhancement of inflammatory cutaneous response, leading to the worsening of disease in psoriatic patients. Conversely, peripheral mononuclear cells of psoriasis patients showed *in vitro* decreased responsiveness to mycobacterial antigens, compared to healthy controls.¹² To date, the pathophysiology of this mechanism is still far from being fully comprehended. However, this seems to be an occurrence that, although rare, should be considered in the management of psoriasis.

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