At the same time, new cases of AA have become more frequent in patients undergoing treatment with anti-TNF-α and other biologic therapies. Cases of AA induced by etanercept, infliximab, and adalimumab are being reported. García Bartels et al[6] were the first to describe adalimumab-induced AA; the patient was a 23-year-old woman who developed AA universalis 2 months after starting treatment. Seven patients have since been described; only 2 had a past history of AA and 3 developed the universalis form.[1,6–10] The amount of time from starting treatment with anti-TNF-α to the appearance of AA ranged between 2 months and 2 years. In cases in which adalimumab was withdrawn, no new hair growth occurred in any of the patients studied. Similarly, hair did not regrow on our patient's plaques.

The mechanism by which TNF-α inhibition induces AA is unknown. In 2005, De Bandt et al[11] hypothesized, on the basis of 22 cases of anti-TNF-α-induced systemic lupus erythematosus in France, that TNF-α initiates the spread of suppressed $CD4^+$ regulatory T lymphocytes that are responsible for maintaining immunological tolerance and preventing autoimmunity. Thus, both AA and other autoimmune processes induced by anti-TNF-α may develop through the inhibition of regulatory T cells. However, whereas all patients with lupus went into remission after the withdrawal of anti-TNF-α, patients with AA do not usually respond.

In this new case of AA associated with adalimumab treatment, the possibility of coincidence cannot be ruled out; however, earlier reports of AA in patients treated with adalimumab and the implication of anti-TNF-α medications in inducing other autoimmune disorders suggests an association between hair loss and the use of this TNF inhibitor.

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J. Neila,* A. Carrizosa, C. Ceballos, F.M. Camacho

Departamento de Dermatología Médico Quirúrgica, Hospital Universitario Virgen Macarena, Sevilla, Spain

* Corresponding author.
E-mail address: drneils@hotmail.com (J. Neila).

Episode of Pustular Psoriasis After a Tuberculin Test in a Patient With Plaque Psoriasis on Treatment With Etanercept☆

Brote de psoriasis pustulosa después de la prueba de la tuberculina en un paciente con psoriasis en placas en tratamiento con etanercept

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To the Editor:

Despite the efficacy of tumor necrosis factor (TNF) α inhibitors in the management of moderate to severe psoriasis, some adverse effects associated with psoriasis have been reported in patients undergoing treatment with these biologic agents. The most frequently described effects are new-onset psoriasis in patients with no history of the disease and exacerbation or modification of the morphology of a previously diagnosed psoriasis. A large percentage of new-onset psoriasis is in the form of pustular psoriasis, mainly affecting the palms and soles,[1,2] whereas guttate psoriasis is more common in patients with a prior history of the disease.[3,4] We describe a patient with plaque psoriasis that was being treated with etanercept, who presented an exacerbation due to a change in the morphology of the disease to

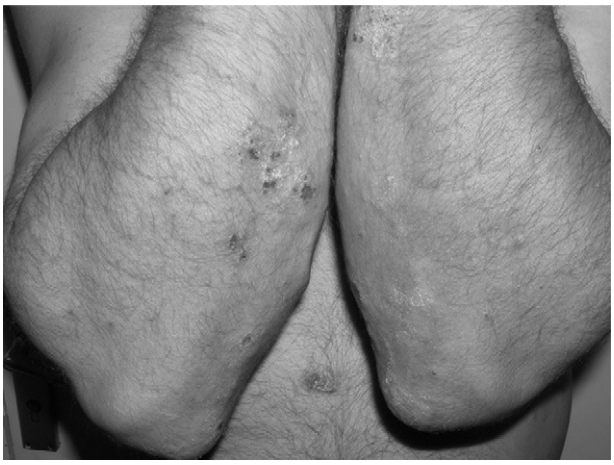

Figure 1 Pustules on the residual psoriasis plaques.

generalized pustular psoriasis, immediately after undergoing a purified protein derivative (PPD) tuberculin skin test, suggesting an association between the two events.

The patient was a 49-year-old man with a 29-year history of plaque psoriasis, which had previously been treated with topical corticosteroids; he had undergone 2 years of treatment with acitretin until the therapy was stopped due to dyslipemia. In 2005, with a psoriasis area and severity (PASI) score of 19.8, the patient began treatment with etanercept (25 mg twice a week), with an excellent response in the first year. Four months after stopping treatment, the patient suffered a relapse (PASI score, 22) and it was therefore decided to reinstate treatment with etanercept at a dosage of 50 mg twice a week for the first 12 weeks, with a subsequent maintenance dosage of 25 mg twice a week. The patient's condition was adequately controlled during the initial 3 years of treatment, with a mean PASI score of 3. However, 24 hours after undergoing the routine annual PPD test, pustules developed on the residual psoriasis plaques (Fig. 1); 48 hours later, the rash had evolved into generalized pustular psoriasis, mainly involving the extremities (Fig. 2). Bacterial cultures were negative and histology was compatible with a diagnosis of pustular psoriasis. Treatment

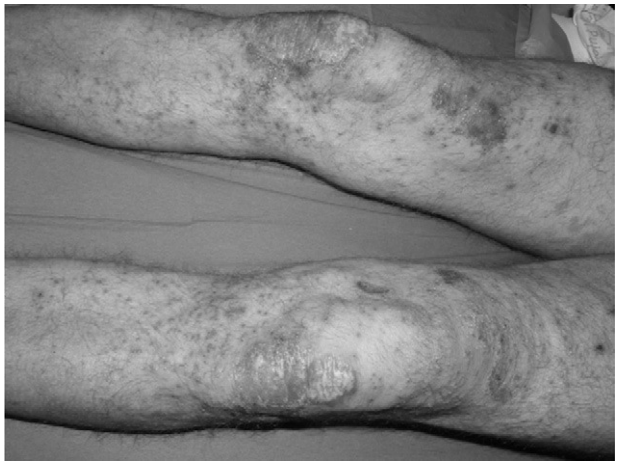

Figure 2 Episode of generalized pustular psoriasis 72 hours after performance of the tuberculin skin test.

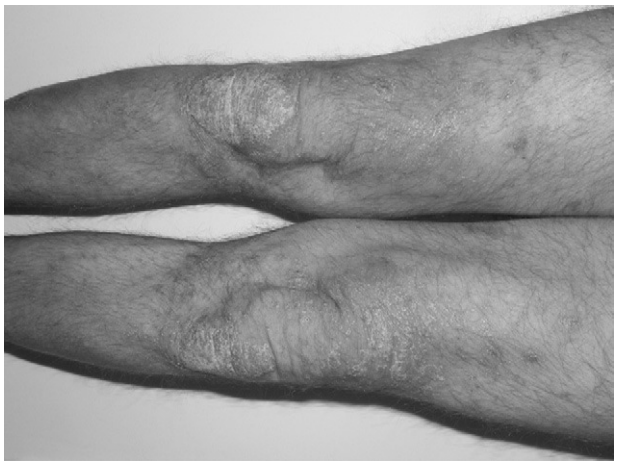

Figure 3 Improvement of the lesions after 2 weeks of treatment with ciclosporin.

with etanercept was suspended due to a suspected paradoxical reaction with the drug, and the patient was started on ciclosporin (4 mg/kg/d). The episode was brought under control after 2 weeks (Fig. 3). Treatment was then started with ustekinumab, while the dosage of ciclosporin was gradually reduced.

Psoriasis may be paradoxically exacerbated or induced by the 3 available anti-TNF agents.[2,5] However, etanercept is more usually associated with exacerbations of previously existing psoriasis, whereas monoclonal antibodies (infliximab and adalimumab) mainly induce an initial outbreak of psoriasis.[6] The mechanisms that cause these paradoxical effects are unknown. No trigger factors have been identified in pustular psoriasis of the palms and soles and a potential causal role of TNF-α inhibitors has been suggested. Generalized pustular psoriasis has been associated with factors such as pregnancy, infections, severe skin irritation caused by topical medication, and some drugs (lithium, salicylates, indomethacin, and various β-blockers). On the other hand, generalized pustular rashes in patients with stable plaque psoriasis have been linked to ultraviolet light, infections, and allergic contact dermatitis,[7,8] but have not been reported in the literature in patients with psoriasis being treated with anti-TNF-α agents. In our patient, the acute outbreak only 24 hours after performing the PPD skin test and the continuous blanching achieved in the previous 3 years of treatment with etanercept suggests a synergistic effect of the combination of the biologic agent and the diagnostic test. Generalized pustular psoriasis as a complication of PPD is not reported in the literature, but a case has been described of a patient with a history of plaque psoriasis, who was receiving no systemic treatment when the tuberculin skin test was performed; the patient presented a pustular exacerbation of the psoriasis after the skin test was performed.[9] The pustular episode in our patient could also be considered as an atypical presentation of acute exanthematous pustulosis due to the tuberculin skin test. However, the histology findings and the coexistence of some typical plaque psoriasis lesions with the pustular rash make this option unlikely. Thus, although the chronologic course is compatible with a direct causal link between the PPD skin

test and the episode, the explanation for this phenomenon continues to be a subject of speculation. The tuberculin test may have acted as a traumatic or infectious trigger that activated the patient's innate immunity, thus increasing TNF-α production by the plasmacytoid dendritic cells and stimulating local activation and proliferation of pathogenic T cells, thereby leading to the episode. Because treatment with the same agent (or an agent of the same family)[5] could have caused the episode to persist, it was decided to change to a treatment with a different mechanism of action; the lesions were brought under control in a few days. In conclusion, our case extends the tuberculin-related complications that may be seen in patients with psoriasis who are undergoing treatment with etanercept.

Conflicts of Interest

Dr. Carlos Ferrándiz and Dr. José Manuel Carrascosa have received fees as consultants and/or speakers sponsored by Wyeth, Abbot, Schering-Plough, and Janssen-Cilag.

The other authors declare that they have no conflicts of interest.

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R.M. Guinovart,* C. Ferrándiz, I. Bielsa, J.M. Carrascosa

Servicio de Dermatología, Hospital Universitari Germans Trias i Pujol, Badalona, Universitat Autònoma de Barcelona, Badalona, Barcelona

* Corresponding author.
E-mail address: rosa_guinovart@hotmail.com
(R.M. Guinovart).

Flagellate Dermatitis After Eating Shiitake Mushrooms☆

Dermatitis flagelada tras la ingesta de setas del género Shiitake

To the editor:

The shiitake mushroom (*Lentinus edodes*), commonly eaten in China and Japan, is the second most widely consumed mushroom species worldwide and it is also becoming increasingly available in Western markets.[1,2] In Japan, the shiitake mushroom is used as an antihypertensive or lipid-lowering agent and as adjuvant therapy against colorectal or gastric cancer because of the beneficial properties of its polysaccharide lentinan.[1–4]

Flagellate dermatitis caused by the consumption of undercooked or raw shiitake mushrooms usually occurs 48-72 hours after ingestion. It presents as papular, petechial, or vesicular lesions in a crisscrossed, linear pattern, primarily on the trunk, upper limbs, neck, and face, accompanied by marked pruritus.[1–4]

Several authors have reported other adverse reactions to shiitake mushrooms, including allergic contact dermatitis, phototoxicity, contact urticaria, allergic asthma, and isolated cases of chronic hypersensitivity pneumonitis induced by shiitake spores.[5–7]

We present the case of a 79-year-old woman who visited our unit for an emergency examination of a very itchy rash 72 hours after onset. The only relevant medical history was that the patient was being monitored for chronic cutaneous lupus. The lesions had not responded to an intramuscular corticosteroid injection administered 24 hours earlier.

The patient reported eating grilled mushrooms 72 hours prior to the appearance of the lesions. She had not taken any medication prior to the onset of the cutaneous symptoms, and presented no fever, joint pain, or other systemic symptoms.

Physical examination revealed multiple crisscrossing linear erythematous lesions composed of petechiae that did not blanch with pressure. The lesions were located primarily on the trunk, neckline, and proximal areas of the upper and lower limbs (Fig. 1). There was no mucosal involvement.

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