

Table 2 Distinctive Characteristics of Acral Syringomas

In men and women in equal proportions
Older (28-70 y)
Exclusively acral sites mentioned (with/without periocular involvement)
Association with tumors

of both lower limbs¹¹; and 1 report described concomitant involvement of the surgical scar of an adenoma of the breast.⁶

Analysis of all published cases of acral syringomas highlights a number of specific features (Table 2). First, the numbers of women and men were very similar (7 women versus 5 men) and the patients were older (between 28 and 70 years) than has usually reported for these tumors. We note that there have been reports of syringomas exclusively in acral areas. Secondly, it is interesting that the lesions were associated with a tumor in 4 of the patients. In 1 patient, they presented concomitantly with a pulmonary carcinoid tumor, the excision of which halted the advance of the syringomas⁷; another patient also had a superficial melanoma and basal cell carcinomas,³ another breast cancer treated with tamoxifen and chemotherapy,¹¹ and finally 1 patient had a tubular adenoma of the breast.⁶

As suggested by other authors, we propose that acral syringomas should be classified as an independent entity in the initial classification of syringomas proposed by Friedman (in fifth place), as they present specific characteristics that differentiate them from other syringomas included in that classification.^{1,4,6} Further series with larger numbers of patients may be able to confirm this hypothesis.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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M. Valdivielso-Ramos,^{a,*} P. de la Cueva,^a M. Gimeno,^b and J.M. Hernanz^a

^aDepartamento de Dermatología, Hospital Infanta Leonor, Madrid, Spain

^bDepartamento de Anatomía Patológica, Hospital Infanta Leonor, Madrid, Spain

*Corresponding author.

E-mail address: mvaldira@yahoo.es
(M. Valdivielso-Ramos).

Sudden Onset of Viral Warts During Treatment With Etanercept

Aparición brusca de verrugas virales durante el tratamiento con etanercept

To the Editor:

Etanercept is a tumor necrosis factor (TNF) antagonist that has been shown to be effective and safe in the treatment of psoriasis.¹⁻³ However, there is some discussion of a possible link with new infections.⁴

We present the case of a 70-year-old woman diagnosed with chronic plaque-type psoriasis resistant to conventional systemic therapy. When the patient first came to the outpatient clinic, she presented numerous plaques on the trunk and limbs (baseline Psoriasis Area and Severity Index [PASI] score of 17.9) and treatment was prescribed with subcutaneous etanercept 50 mg twice weekly. A good response to treatment was seen 3 months later and there was a fall in the PASI score to 1.8; the dosage of etanercept was reduced to 50 mg per week as maintenance therapy. However, the patient reported that, 1 month after starting treatment with etanercept, she developed multiple asymptomatic lesions of sudden onset; this was



Figure 1 Multiple warts on the right arm.



Figure 2 Marked hyperkeratosis, acanthosis, and clubbing of the rete ridges around the borders of the lesions (Hematoxylin-eosin, original magnification $\times 40$).

the first time she had suffered from such lesions. Physical examination revealed numerous skin-colored or slightly hyperpigmented papules measuring 2 to 5 mm in diameter on the face, neck, arms, and legs. Some lesions presented a rough keratotic surface and others a filiform appearance (Figure 1).

Biopsies were taken from 4 different sites on the arms and legs. The histology was similar in all the biopsies: marked hyperkeratosis and acanthosis; parakeratosis on papillomatous papules; dilated blood vessels in the dermal papillae; and clubbing of the rete ridges typical of psoriasis around the borders of the lesions (Figure 2)—all findings characteristic of common and filiform warts. Laboratory tests (hematology, biochemistry, and urine) were all within normal limits. Serology for human immunodeficiency virus (HIV), hepatitis B and C viruses, and tuberculosis were negative. The chest x-ray showed no significant abnormalities.

New warts continued to appear during the treatment with etanercept and were treated by electrocoagulation. Etanercept therapy was suspended when the psoriatic plaques had almost completely cleared, and management was then continued with topical treatment. Further warts continued to appear in the first months after the systemic antipsoriatic treatment was suspended, though at a slower rate. They later stopped appearing completely. No other adverse events were observed during etanercept therapy. Prior to treatment with etanercept, the patient had had no history of viral warts, frequent infections, or other symptoms of immunosuppression.

Clinical trials and our experience have shown etanercept to be safe and well tolerated in the treatment of psoriasis, although we must be aware of possible rare adverse effects. Randomized, multicenter, placebo-controlled studies have detected no increase in the adjusted rates of infection, although some cases of bacterial, mycobacterial, viral, and fungal infections have been reported.⁵ There are few studies in the literature that have investigated the association between viral illnesses and treatment with etanercept.⁶ There are a number of case reports that describe no complications of etanercept therapy in patients with hepatitis C and HIV infection.⁷ However, it is recommended that patients be screened for HIV and hepatitis B and C before starting treatment with etanercept.⁶⁻⁸

There is no known association between etanercept and the risk of infection by human papilloma virus (HPV). However, studies have found that the E6 protein of HPV-16 binds directly to TNF receptor 1 (TNF-R1) and induces apoptosis in host cells^{9,10}; and, etanercept is a fusion protein that acts by inhibiting TNF activity. However, an association between etanercept and warts has only been reported in very rare cases. In one such case, recalcitrant warts were reported in a patient with juvenile rheumatoid arthritis treated with methotrexate and etanercept, and these disappeared a month after treatment was suspended.¹¹ Another report published 2 years later described a patient with psoriasis and psoriatic arthritis who presented a recurrence of perianal condylomata during treatment with etanercept.¹² Also, the Spanish Register of Adverse Events of Biological Treatments in Rheumatic Illnesses (Biobadaser) has only 2 registered cases of infection with HPV in a total listing of 9352 patients.¹³

In our case, the sudden appearance of viral warts in an immunocompetent patient, coinciding chronologically with the initiation of etanercept therapy and disappearing progressively once the drug was suspended, is strongly suggestive of an association between etanercept therapy and warts. Although clinical experience shows this association to be rare, we must be aware of a potential risk during treatment with etanercept, though it must be said that the interruption of therapy was not required in this case.

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- T. Sanz-Sánchez,* E. Daudén, A. González-Arribas, and A. García-Díez
- Servicio de Dermatología, Hospital Universitario de la Princesa, Madrid, Spain*
- *Corresponding author.
E-mail address: tatiana@aevd.es (T. Sanz-Sánchez).

Kaposi Sarcoma Associated With Infliximab Treatment

Sarcoma de Kaposi asociado al tratamiento con infliximab

To the Editor:

Tumor necrosis factor α antagonists alter the inflammatory response, which leads to an increased risk of infections^{1,2} and neoplasms.³ Such neoplasms include Kaposi sarcoma, a tumor of the vascular endothelium described by Moritz Kaposi in 1872.

We describe the case of a patient who developed Kaposi sarcoma following infliximab therapy for corticosteroid-dependent ileal Crohn disease.

The patient was a 61-year-old man referred from the gastrointestinal department for assessment of skin lesions on the right lower leg. He was an ex-smoker of 20 cigars/d and presented bilateral gonarthrosis with left knee replacement, spondyloarthrosis, hiatal hernia, chronic prostatitis, and moderate-to-severe ileal Crohn disease diagnosed in 2005. At the time of the first consultation the patient was receiving treatment with analgesics, mesalazine, budesonide, and azathioprine. Because corticosteroids could not be discontinued, he was classified as corticosteroid-dependent. The chest radiograph, abdominal computed tomography, Mantoux test, antinuclear antibodies, and serology tests (human immunodeficiency virus, hepatitis B and C virus, syphilis, and varicella-zoster virus) were all normal or negative. Following the tests, infliximab therapy was started at 5 mg/kg (500 mg/session) in weeks 0, 2, and 6.

Ten days after the second dose of infliximab, the patient developed lesions consisting of asymptomatic, erythematous-violaceous plaques of different sizes distributed on the dorsum of the foot and the anterior and medial aspects of the distal third of the right leg, and associated with edema of the limb (Figure 1). A biopsy showed proliferation of irregular fine-walled vessels in the superficial dermis and hypodermis and foci of spindle-shaped cells forming small bundles (Figures 2 and 3); immunohistochemistry was positive for human herpesvirus-8 latent nuclear antigen. Kaposi sarcoma was diagnosed.

The work-up showed no visceral involvement and infliximab was therefore discontinued, keeping the skin



Figure 1 Kaposi sarcoma. Asymptomatic erythematous-violaceous plaques distributed over the dorsum of the foot and the right leg. The lesions appeared 10 days after the second dose of infliximab.