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Esomeprazole-Induced Subacute Cutaneous Lupus Erythematosus[☆]

Lupus eritematoso cutáneo subagudo inducido por esomeprazol

To the Editor:

We report the case of a 74-year-old woman with a history of hypertension, diabetes mellitus, dyslipidemia, spondyloarthritis, and idiopathic thrombocytopenic purpura for which she had undergone splenectomy 5 years previously. She was being followed up by her rheumatologist for joint pain of inflammatory origin with low titers of rheumatoid factor and was taking lorazepam, ranitidine, domperidone, indapamide, AM3, and ursodeoxycholic acid. She attended our clinic with a pruritic disorder that had begun a week earlier and took the form of well-defined discretely desquamative erythematous papules on her back and, to a lesser extent, on her chest, thighs, and proximal upper arms. She had no blisters or mucosal lesions. These signs first appeared during winter, and the patient reported no previous sun exposure. Of interest, she reported starting esomeprazole and a vitamin complex (B₁, B₆, and B₁₂) 3 weeks before the lesions first appeared. A biopsy specimen of one of the lesions was obtained, and the patient was prescribed mometasone cream twice daily. Esomeprazole and the vitamin supplement were withdrawn.

At 3 weeks, the lesions had progressed to confluent annular erythematous-violaceous plaques on the above-mentioned sites (fig. 1). The biopsy revealed hyperkeratosis in the epidermis, epidermal atrophy, degeneration of the basal layer, lymphocytic exocytosis, spongiosis, and occasional necrotic keratinocytes. A superficial perivascular lymphohistiocytic inflammatory infiltrate was observed in the dermis (fig. 2). Based on clinical and microscopy findings, the patient was diagnosed with subacute cutaneous lupus erythematosus (SCLE).

The results of a complete blood count and routine biochemistry were unremarkable. The immunology workup revealed positive titers for antinuclear antibody (1/160), anti-SSA/Ro antibody, and anti-SSB/La antibody. These results had also been positive in laboratory studies performed 2 years previously in the rheumatology department.

Based on a suspected diagnosis of SCLE induced or exacerbated by esomeprazole, treatment with a topical corticosteroid was continued and the culprit medication was withdrawn. The lesions had completely resolved 8 weeks after the interruption of esomeprazole.

SCLE is a well-defined subtype of lupus erythematosus characterized by annular or psoriasiform lesions, limited systemic involvement, and the presence of circulating anti-SSA/Ro antibody.¹⁻³ An association has been described between SCLE and various drugs, including thiazides, statins, calcium channel antagonists, phenytoin, griseofulvin, tumor necrosis factor antagonists, terbinafine,¹⁻⁵ and, recently, proton pump inhibitors such as omeprazole, lansoprazole, and pantoprazole.⁶⁻⁸ Esomeprazole is the S enantiomer of omeprazole and is used to treat gastroesophageal reflux disease. It came onto the market in Spain in 2002.⁹

Unlike drug-induced systemic lupus erythematosus, which usually involves positive antihistone antibody titers, drug-induced SCLE is generally associated with positive anti-SSA/Ro antibody titers, but not with positive antihistone antibody titers. In some cases, these titers become negative once the culprit agent is withdrawn.⁷

In the case we present, it is striking that anti-SSA/Ro and anti-SSB/La antibody titers were previously positive and that this finding was maintained after onset of the skin symptoms. Four of the 8 previously reported cases of SCLE induced by proton pump inhibitors presented positive antinuclear antibody titers before the onset of cutaneous symptoms; however, it is unknown whether anti-SSA/Ro or anti-SSB/La antibody titers were positive. No analytical results were available for the remaining 4 patients (Table 1).⁶⁻⁸ These findings point to a predisposition to SCLE, which was triggered by proton pump inhibitors. The pathogenic mechanism responsible for the formation of antibodies is unknown. It has been postulated that binding of the drug to proteins could trigger the immune response through a hapten-type mechanism, leading to formation of antibodies.³

The suspect medication must be withdrawn in order to achieve resolution of the symptoms; topical or oral corticosteroids can be used as adjuvant therapy to speed up recovery. Without withdrawal of the medication, cure is not possible, as shown in previous cases where lesions persisted despite treatment with oral corticosteroids or hydroxychloroquine.⁶

Our patient was taking a vitamin complex concomitantly with esomeprazole; however, this medication seems a highly unlikely culprit, since there have been no previous reports

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Figure 1 Confluent, ring-shaped erythematous-violaceous plaques on the back.

of cases of lupus erythematosus caused by this agent. Nor can we rule out an episode of idiopathic SCLÉ, although the apparently clear temporal relationship with the medication and the absence of previous sun exposure and of other characteristic symptoms do not seem to support this possibility as a first option.

To conclude, we present the first case of SCLÉ induced by esomeprazole. Similarly, we observed positive anti-SSA/Ro and anti-SSB/La antibody titers before the onset of symptoms, suggesting the need for individual predisposition before the condition can develop.

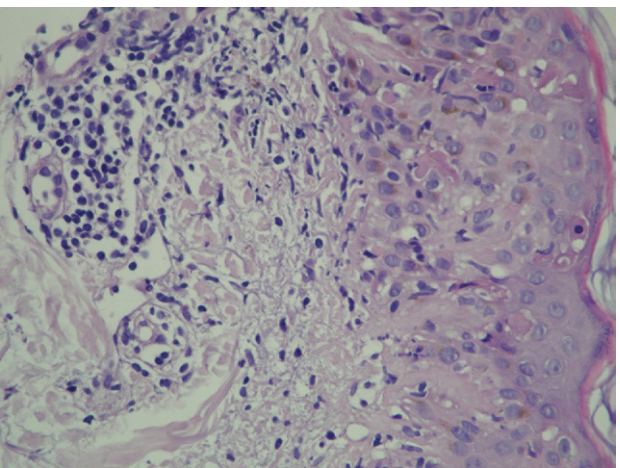


Figure 2 Hyperkeratosis, vacuolar degeneration of the basal layer, discrete lymphocytic exocytosis, and presence of necrotic keratinocytes. Note the superficial perivascular inflammatory infiltrate in the dermis (hematoxylin-eosin, original magnification $\times 20$).

Table 1 Previous Cases and Characteristics of Patients With Subacute Cutaneous Lupus Erythematosus Induced by Proton Pump Inhibitors.

Author	Sex	Age	Medication	Latency	Previous Serology Results	Serology During Symptoms	Outcome After Withdrawal
Bracke et al ⁷ (2005)	Woman	69	Lansoprazole	3 mo	NA	ANA+, SSA+, histone–	Resolution in 3 wk
Bracke et al ⁷ (2005)	Woman	63	Lansoprazole	3 mo	NA	ANA+, SSA+, RF+	Resolution in 1 mo
Dam et al ⁶ (2008)	Woman	61	Lansoprazole	3 wk	ANA+, dsDNA–	ANA+, SSA+, SSB–, dsDNA–, histone–, RF+	Resolution in 12 wk
Dam et al ⁶ (2008)	Woman	50	Omeprazole	7 wk	ANA+, dsDNA+	ANA+, dsDNA–, histone–	Resolution in 4 wk
Dam et al ⁶ (2008)	Woman	51	Pantoprazole	4-8 wk	ANA+, dsDNA–	ANA+, SSA–, SSB–, dsDNA–, RF+	Active until death in 2001 (not withdrawn)
Dam et al ⁶ (2008)	Woman	57	Lansoprazole	4 wk	NA	ANA+, SSA+, SSB–, dsDNA+, histone–, RF+	Active until death in 2000 (not withdrawn)
Dam et al ⁶ (2008)	Woman	63	Pantoprazole	3 d	ANA+	ANA–, SSA+, SSB–, histone–	Resolution in 4 wk
Mankia et al ⁶ (2010)	Woman	60	Omeprazole	4 mo	NA	ANA+, SSA+, SSB–, dsDNA+, histone–	Resolution in 1 mo
Present case	Woman	74	Esomeprazole	2 wk	ANA+, SSA+, SSB+, RF+	ANA+, SSA+, SSB+	Resolution in 8 wk

Abbreviations

ANA antinuclear antibody; dsDNA double-stranded anti-DNA antibody; histone antihistone antibody; NA not available; RF rheumatoid factor; SSA anti-Ro/SSA antibody; SSB anti-La/SSB antibody.

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Posttraumatic Eosinophilic Fasciitis: Diagnostic Usefulness of Magnetic Resonance Imaging[☆]

Fascitis eosinofílica asociada a traumatismo: utilidad diagnóstica de la resonancia magnética

To the Editor:

Eosinophilic fasciitis is a rare scleroderma-like disorder that mainly affects the muscle fascia. It usually occurs in adults between the ages of 20 years and 70 years.¹

We present the case of a 54-year-old patient with no past medical history of interest, who came to the clinic because of a rapidly progressive induration of the limbs, abdomen and lower back 1 month after an accidental fall (Fig. 1A). The condition had started as edema and erythema of the lower limbs, spreading to other areas, with the subsequent appearance of induration. The diagnoses considered were eosinophilic fasciitis, scleroderma, scleredema, and scleromyxedema. The patient did not present Raynaud phenomenon, dysphagia, or sclerodactyly.

Complete blood count showed a raised white cell count with marked eosinophilia ($3.10 \times 10^3/\mu\text{L}$, 22%). Other laboratory tests, including the erythrocyte sedimentation rate, antinuclear antibodies and rheumatoid factor, were normal or negative.

Histopathology of a deep biopsy of the forearm showed interlobular septal thickening and an inflammatory infiltrate with numerous eosinophils affecting the septa and adjacent subcutaneous tissue, which was moderately edematous

(Fig. 2). There were no changes of note in the epidermis and dermis; the muscle fascia could not be assessed. Magnetic resonance imaging (MRI) of the lower limbs showed thickening of the muscle fascia with signal hyperintensity on short TI inversion recovery sequences, indicating inflammation (Fig. 3).

The patient was diagnosed with eosinophilic fasciitis on the basis of the peripheral eosinophilia, histological findings, and the fasciitis observed on MRI. Treatment was initiated with oral prednisone at a dose of 1 mg/kg/d and hydroxychloroquine, with the subsequent addition of methotrexate to reduce the necessary dose of corticosteroids. The clinical course was favorable, with blood parameters returning to normal at 2 months and disappearance of the induration after 12 months of treatment (Fig. 1B).

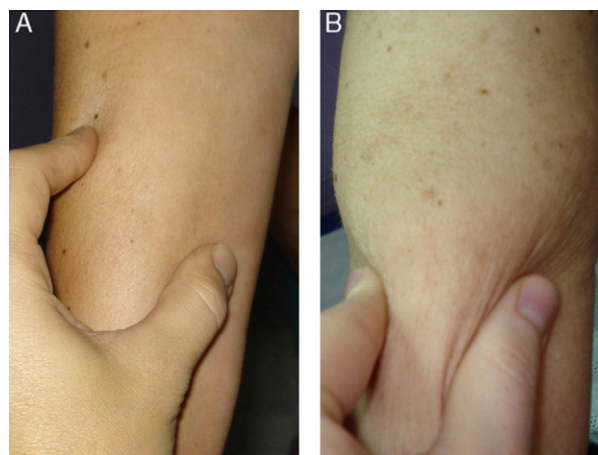


Figure 1 Photograph of the forearm. A, Pinching the skin is difficult due to induration. B, There is a decrease in induration after 12 months of treatment.

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