

Significant improvement of refractory cutaneous lesions of lupus erythematosus with the use of anifrolumab: a report of two cases

Melhoria significativa de lesões cutâneas refratárias de lúpus eritematoso com o uso de anifrolumab: relato de dois casos

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Abstract

Anifrolumab, a monoclonal antibody targeting the interferon-1 receptor, is currently approved for the treatment of moderate-to-severe systemic lupus erythematosus, but emerging evidence highlights its potential efficacy in cases with predominant cutaneous involvement. We present two cases illustrating its beneficial impact in refractory cutaneous lupus erythematosus, including both the subacute and chronic subtypes.

Keywords: Cutaneous lupus erythematosus. Discoid lupus erythematosus. Anifrolumab. Subacute cutaneous lupus erythematosus.

Resumo

O anifrolumab, anticorpo monoclonal contra o recetor do IFN-1, encontra-se aprovado para o tratamento do lúpus eritematoso sistémico moderado a grave, mas tem demonstrado evidência crescente de eficácia em doentes com predomínio de envolvimento cutâneo. Apresentamos dois casos ilustrativos do seu impacto benéfico em doentes com lúpus eritematoso cutâneo refratário, incluindo os subtipos subagudo e crónico.

Palavras-chave: Lúpus eritematoso cutâneo. Lúpus eritematoso discóide. Anifrolumab. Lúpus eritematoso cutâneo subagudo.

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Introduction

The therapeutic landscape of cutaneous lupus erythematosus (CLE) remains limited, with hydroxychloroquine and glucocorticoids constituting the only drugs approved by the US food and drug administration (FDA) for this condition¹. Anifrolumab, a monoclonal antibody targeting the type I interferon (IFN)-1 receptor, was approved in 2022 by the European Medicines agency (EMA) for the treatment of moderate-to-severe systemic lupus erythematosus (SLE) in adults who do not respond to standard therapy. Nevertheless, growing evidence indicates its potential role and efficacy in patients with skin involvement²⁻⁴. We present two cases highlighting the efficacy of anifrolumab in lupus patients with predominant cutaneous disease.

Case reports

Case 1

A 51-year-old woman with a 4-year history of lupus erythematosus with hematologic and cutaneous involvement was evaluated in our dermatology outpatient department due to discoid lupus lesions affecting the face, trunk, arms, and hands, along with occasional oral ulcers (Figs. 1A-C). Laboratory tests revealed positivity for antinuclear antibodies (titer > 1:640, speckled pattern), lymphopenia and thrombocytopenia (with lowest values of $870 \times 10^9/L$ and $96 \times 10^9/L$, respectively). The cutaneous lesions were refractory to topical and oral corticosteroids, topical calcineurin inhibitors, hydroxychloroquine, azathioprine, and methotrexate. The patient had a SLE disease activity index 2000 (SLEDAI-2K) score of 6 (lymphopenia, thrombocytopenia, new-onset cutaneous lesions, and oral ulcerations), a cutaneous LE disease area and severity index (CLASI) activity score of 26 (involvement of the face, neck, trunk, arms, and hands, with 19 points for areas of bright-red erythema, 6 points for scaly/hypertrophic lesions, and 1 for mucosal involvement), and CLASI damage score of 8 (due to scarring/dyspigmentation of the face, v-area of the neck, and cervical area/back). Treatment with anifrolumab was initiated (intravenous administration of 300 mg every 4 weeks), leading to marked improvement of the cutaneous lesions after the first dose. In fact, at week 12, only scarring from previous lesions remained, with a CLASI activity score of 0 (Figs. 1D-F). The patient currently completed 9 months of treatment, with a sustained cutaneous and hematological response. The patient reported no treatment-related adverse reactions.

Case 2

A 50-year-old woman diagnosed with SLE at the age of 20, with articular and cutaneous involvement, was followed in our dermatology outpatient department for subacute lupus on the trunk and vasculopathy of the extremities, with severe Raynaud's phenomenon, episodic digital ulcers, and nail dystrophy (Figs. 2A and B). Laboratory tests revealed positivity for antinuclear antibodies (titers of 1:1000 with a homogeneous pattern, and 1:320 with a nucleolar pattern), as well as anti-SSa and anti-dsDNA antibodies. Over the preceding 4 years, she experienced worsening of her cutaneous symptoms, remaining corticosteroid-dependent (10-20 mg of prednisolone daily) and showing no response to antimalarials (chloroquine and hydroxychloroquine), calcium channel blockers, pentoxifylline, mycophenolate mofetil, or azathioprine. The patient maintained a SLEDAI-2K score of 12 (positive anti-dsDNA antibodies, new-onset cutaneous lesions, and periungual infarctions), CLASI activity score of 9 (bright red or violaceous erythema of the v-area of the neck, chest, cervical area, and hands), and CLASI damage score of 1 (due to scarring of the hands). She started treatment with anifrolumab (300 mg/monthly), resulting in complete resolution of trunk lesions and improvement in hand vasculopathy and nail dystrophy after 4 months (Figs. 2C and D). The patient recently completed 18 months of therapy, maintaining gradual improvement in ungual and digital involvement and no treatment-related adverse reactions.

Discussion

CLE is a heterogeneous entity encompassing a wide spectrum of clinical manifestations, with its three main subtypes—acute, subacute, and chronic CLE—implying diagnostic, prognostic, and therapeutic particularities⁵. The therapeutic armamentarium, however, is still insufficient regarding the different forms of the disease, without a significant progress over the past decades. Nevertheless, in recent years, new therapeutic targets emerged, such as interferon-receptor antagonism, JAK/STAT inhibition, plasmacytoid dendritic cell-targeted therapies, cereblon-targeting ligands, and B- and T-cell-targeted therapies¹. In the latter, belimumab, a monoclonal antibody inhibiting B-cell activation, was approved for the treatment of SLE. A meta-analysis of studies of patients with CLE (with or without SLE) demonstrated pooled odds of clinical response at 52 weeks 44% higher in belimumab users compared to non-users⁶, hinting its



Figure 1. A-C: patient's lesions before, D-F: and 6 months after anifrolumab initiation.

potential efficacy in these patients. Furthermore, a phase III trial assessing its efficacy in refractory cutaneous manifestations is currently underway¹. Litifilimab, a monoclonal antibody binding to BDCA2 (a receptor specific to the surface of plasmacytoid dendritic cells), exhibited significant improvements of CLASI activity score in a phase II trial⁷, with other phase II and III trials currently ongoing¹. Deucravacitinib, a tyrosine kinase-2 inhibitor, showed promising results in CLASI activity score reduction in a phase II trial of SLE patients⁸, with an ongoing phase II trial focusing on CLE patients¹. Anifrolumab, on its turn, received approval for the treatment of SLE by the FDA in 2021 and by the EMA in

2022, based on results from the MUSE, TULIP-1, and TULIP-2 trials¹. In the MUSE trial, the percentage of patients with a baseline CLASI activity score of ≥ 10 who had a $\geq 50\%$ reduction at week 52 was greater for anifrolumab (63.0% for 300 mg, $p = 0.013$, and 58.3% for 1,000 mg, $p = 0.077$) in comparison with placebo (30.8%)⁹. In the TULIP-1 trial, this reduction of $\geq 50\%$, but assessed at week 12, was achieved by 42% and 25% of anifrolumab (300 mg) patients and placebo group, respectively, without reaching statistical significance. In addition, in the TULIP-2 trial, the same reduction occurred at week 12 in 49% and 25% of patients receiving anifrolumab and placebo, respectively

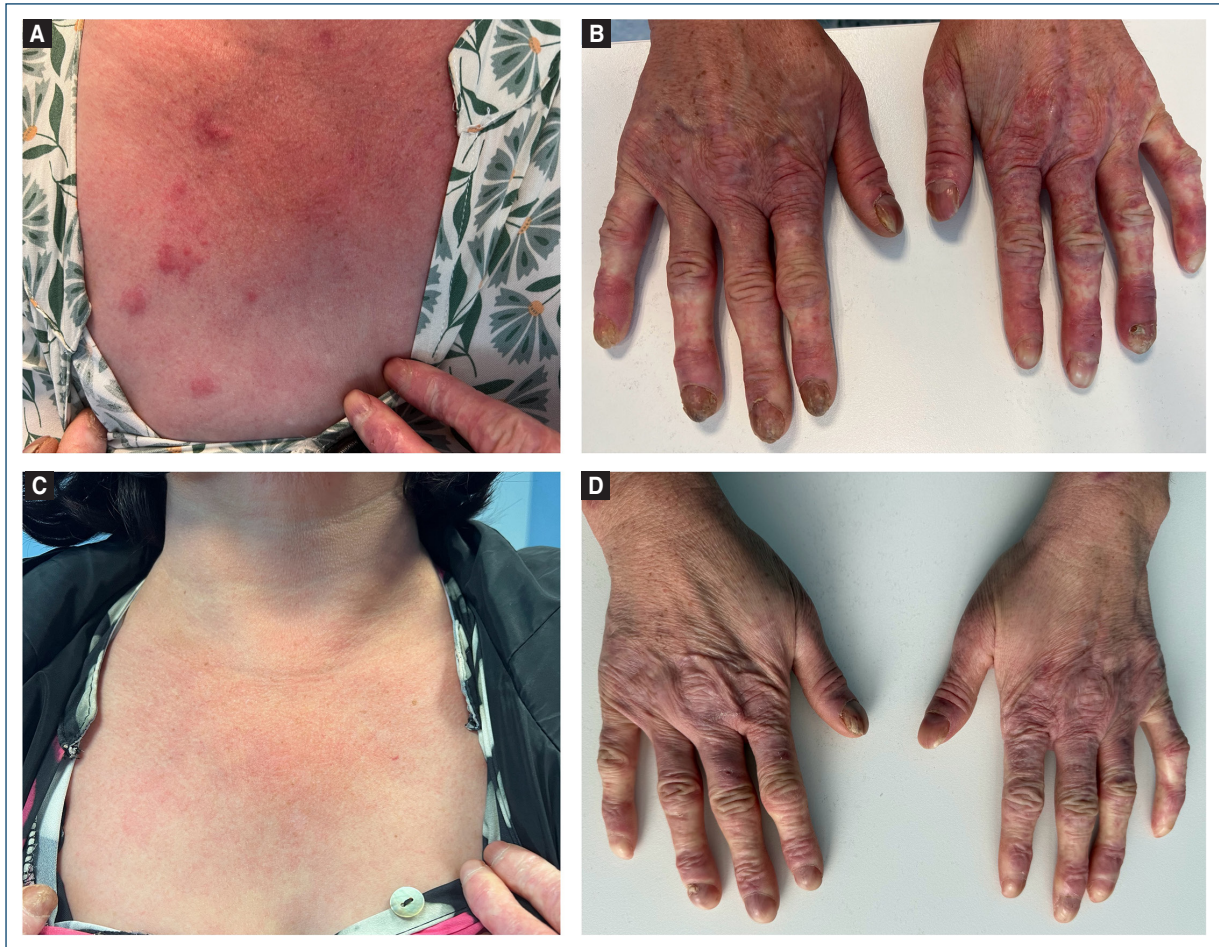


Figure 2. **A** and **B**: patient's lesions before, **C** and **D**: and 12 months after anifrolumab treatment.

($p = 0.04$). A phase III trial is currently being conducted to evaluate the efficacy of anifrolumab in refractory CLE patients (LAVENDER trial)¹. In parallel with clinical trials, many case reports and case series were published reporting the efficacy of anifrolumab in different variants of CLE, ranging from the acute to subacute (including Rowell syndrome), and chronic subtypes (including discoid lupus, lupus *tumidus*, lupus panniculitis, and chilblain lupus), as well as in associated features such as alopecia and mucosal involvement^{3,4,10-12}. Our cases reinforce the beneficial effects of this drug in patients with predominant cutaneous involvement, both in subacute and chronic lupus lesions, with prompt improvement and positive impact on the patient's quality of life, in a field with significant unmet therapeutic needs.

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None.

Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the Institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence.

The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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