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LETTER

Cutaneous lupus erythematosus induced by adalimumab: A case report

Dear Editor

The relatively recent onset of a wide variety of biological therapies has brought enormous advantages in the treatment of multiple autoimmune diseases. Currently, anti-tumor necrosis factor-α drugs (anti-TNFα) are the most widely used biologic agents worldwide, and despite being very safe treatments, they are not exempt from producing adverse reactions that could limit their use.

We present the case of a 15-year-old male patient with clinical history of recalcitrant uveitis, with poor response to oral corticosteroids. Four months after initiating treatment with methotrexate and an anti-TNFα drug (Adalimumab), the patient developed infiltrated erythematous plaques on both cheeks, which were exacerbated by sunlight exposure (Figure 1A,B). Evaluation in the dermatology office included antinuclear antibodies (ANA), extractable nuclear antigens

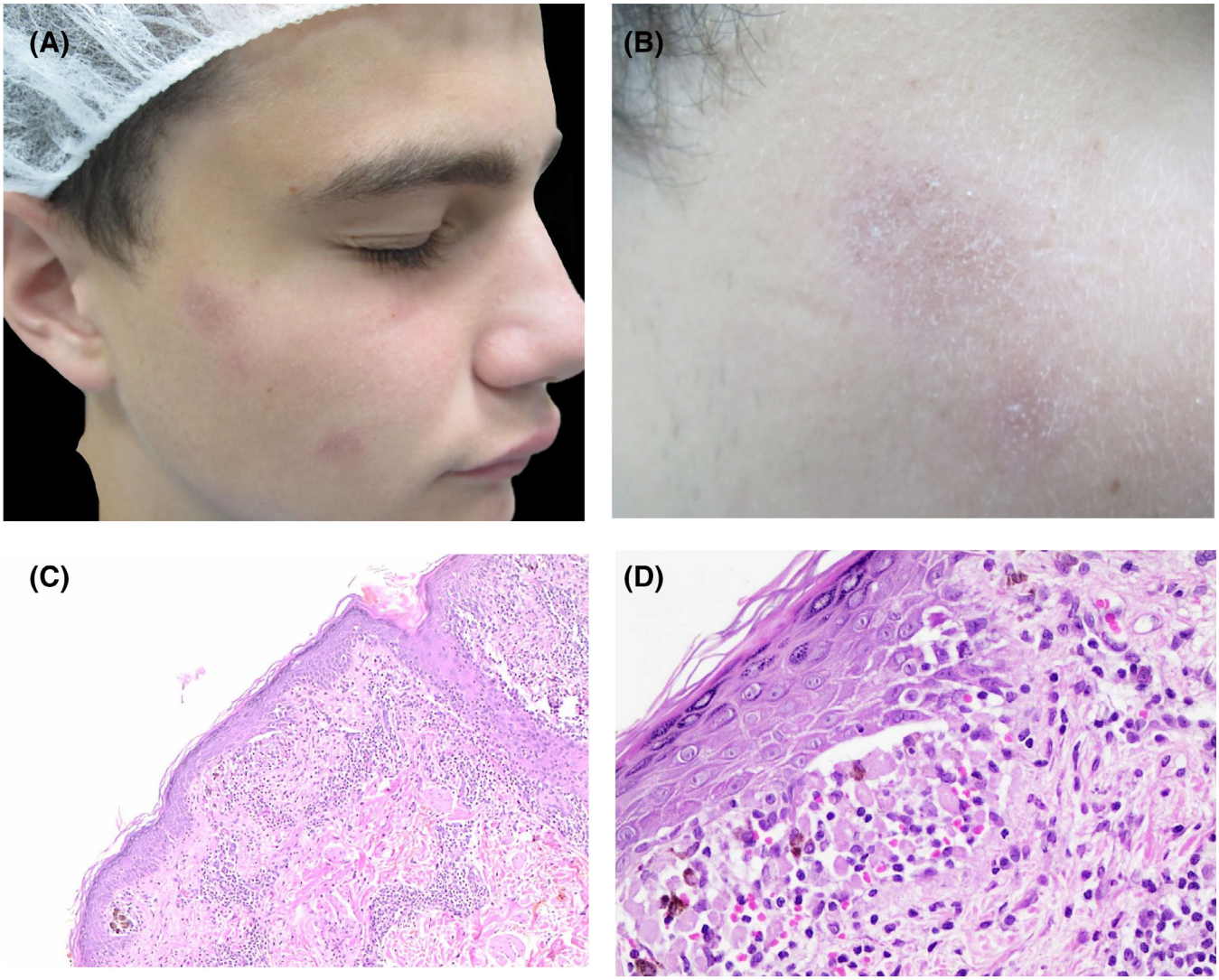

FIGURE 1 A, Erythematous infiltrated plaques appear on right cheek. B, Close up of the erythematous plaque. C, Vacuolar and lichenoid interface dermatitis, superficial, and deep perifollicular lymphoplasmacytic infiltrate (HE ×4). D, Melanophagos and abundant apoptotic bodies (HE ×10)

antibodies (ENA), and anti-double stranded DNA antibodies (Anti-DNA_{ds}), which were normal. Skin biopsy revealed vacuolar and lichenoid interface dermatitis, superficial and deep perifollicular lymphoplasmacytic infiltrate, and mild dermal mucin, suggesting the diagnosis of cutaneous lupus erythematosus (Figure 1C). It was also noticed the presence of abundant apoptotic bodies, what was suggestive of an adverse drug reaction (Figure 1D). Due to the absence of proven systemic disease both clinically and in the laboratory assessment, and the need to maintain the treatment for recalcitrant uveitis, topical treatment was chosen based in topical tacrolimus ointment and photoprotection, with rapid improvement of the lesions during 12-month follow-up.

Within the most frequent side effects of anti-TNFα drugs are site injection reactions, infusion reactions, skin infections, and systemic infections.[1] However, several cases have been reported in the literature presenting an increasing number of autoimmune mediated reactions such as cutaneous vasculitis, erythema multiforme, annular granuloma, palmoplantar pustulosis, lichen planus, SSJ/NET, and anti-TNFα-induced lupus-like syndromes (ATILS).

ATILS may present as an asymptomatic elevation of lupus-related antibodies, a clinically evident systemic lupus-like reaction, or a cutaneous lupus-like reaction without systemic involvement. Pathogenesis have been related with an increased Th2 immune response, inhibition of cytotoxic T lymphocytes, and induction of lupus-related autoantibodies.[2,3] The prevalence of positive ANA ranges between 23% and 57%, and the prevalence of anti-DNA ranges between 9% and 33%. However, ANA seroconversion with Adalimumab is uncommon compared to infliximab (16% vs 53%), and concomitant treatment with methotrexate have been related with a suppression of the induction of lupus-related autoantibodies.[4-6] Moreover, the possibility to trigger a symptomatic lupus-like reaction in patients treated with Adalimumab is very low (<1%), and the risk of an specific skin-limited lupus-like reaction is even less likely.[7]

There are currently no evidence-based clinical guidelines for the prevention and management of ATILS, however, available recommendations usually encourage the withdrawal of the anti-TNFα drug, which may lead to complete remission in up to 94% of patients.[8] Despite the above, conservative treatments are a feasible alternative in mild skin-limited ATILS, that allows the benefits for the underlying disease to be maintained without considerable risks to the patients. Topical corticosteroids, topical tacrolimus ointment and intralesional corticosteroids have shown favorable effects with persistent remission of skin symptoms.[2,3,8] In these cases, close monitoring of cutaneous and systemic symptoms and laboratory follow-up should be considered.[2,3]

Anti-TNFα agents have been associated with an increased number of autoimmune reactions, and their increased availability may rise adverse reactions. Although systemic lupus-like reactions are a known side effect, the isolated skin-limited form is less frequent. Here, we highlight the possibility to maintain the Anti-TNFα treatment in these mild cases, which along with additional conservative treatments may lead to complete remission of the lesions, without losing the benefits of the therapy.

Informed consent has been obtained for the publication of images.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Ruben Gonzalez-Cuevas, Leonado Peruilh-Bagolini, Fernando Valenzuela, and Pablo Vargas-Mora: have made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; Leonado Peruilh-Bagolini, Fernando Valenzuela, and Pablo Vargas-Mora have been involved in drafting the manuscript or revising it critically for important intellectual content; and Ruben Gonzalez-Cuevas, Fernando Valenzuela, and Pablo Vargas-Mora: given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content; and Ruben Gonzalez-Cuevas, Fernando Valenzuela: agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ETHICS STATEMENT

All authors have reviewed and approved this publication. All ethical standards requested by the journal have been met. The brightness of some images has been adjusted and within Figure 1, some objects have been removed from the background, following the ethical considerations of the journal.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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