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CASE REPORT

Dupilumab for recalcitrant prurigo nodularis: Case report

Tratamento de prurigo nodularis recalcitrante com dupilumab: Um caso clínico

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Abstract

Dupilumab is a recombinant fully human monoclonal antibody modulating the signaling of the interleukin (IL)—4 and IL-13 pathways and has been approved for the treatment of moderate/severe atopic dermatitis. We present a case of recalcitrant prurigo nodularis treated off-label with dupilumab.

Keywords: Antibodies. Monoclonal. Humanized. Dupilumab. Prurigo/drug therapy.

Resumo

O dupilumab é um anticorpo monoclonal humano recombinante que inibe a sinalização da interleucina-4 e da interleucina-13 aprovado para o tratamento da dermatite atópica moderada a grave. Apresentamos um caso de prurigo nodular recalcitrante a terapêuticas prévias com resposta ao tratamento *off-label* com dupilumab.

Palavras-chave: Anticorpos monoclonais humanizados. Dupilumabe. Prurigo/quimioterapia.

Case report

Prurigo nodularis (PN) or chronic prurigo of nodular type (CNPG) is a subtype of chronic prurigo defined by the presence of chronic pruritus and multiple localized or generalized pruriginous lesions[1]. The exact pathogenesis of the disease is unknown, although immune and neural dysregulation are indicated in driving the itch-scratch cycle. Research shows that Th2 cytokines related to STAT6 activation, together with some unknown stimuli that activate STAT3, play a main role in the pathogenesis of PN[2]. Dupilumab is a fully human monoclonal antibody targeting the interleukin-4 receptor (IL-4R), blocking IL-4 and IL-13, decreasing the level of Th2 biomarkers[3]. Here, we present a case of recalcitrant PN treated with dupilumab.

A 56-year-old non-atopic woman presented with a 10-years-old history of multiple hyperpigmented papules and nodules, extremely pruritic, involving the trunk and extremities (Fig. 1). The clinical picture was consistent with PN and a punch biopsy from one of the nodules corroborated the diagnosis.

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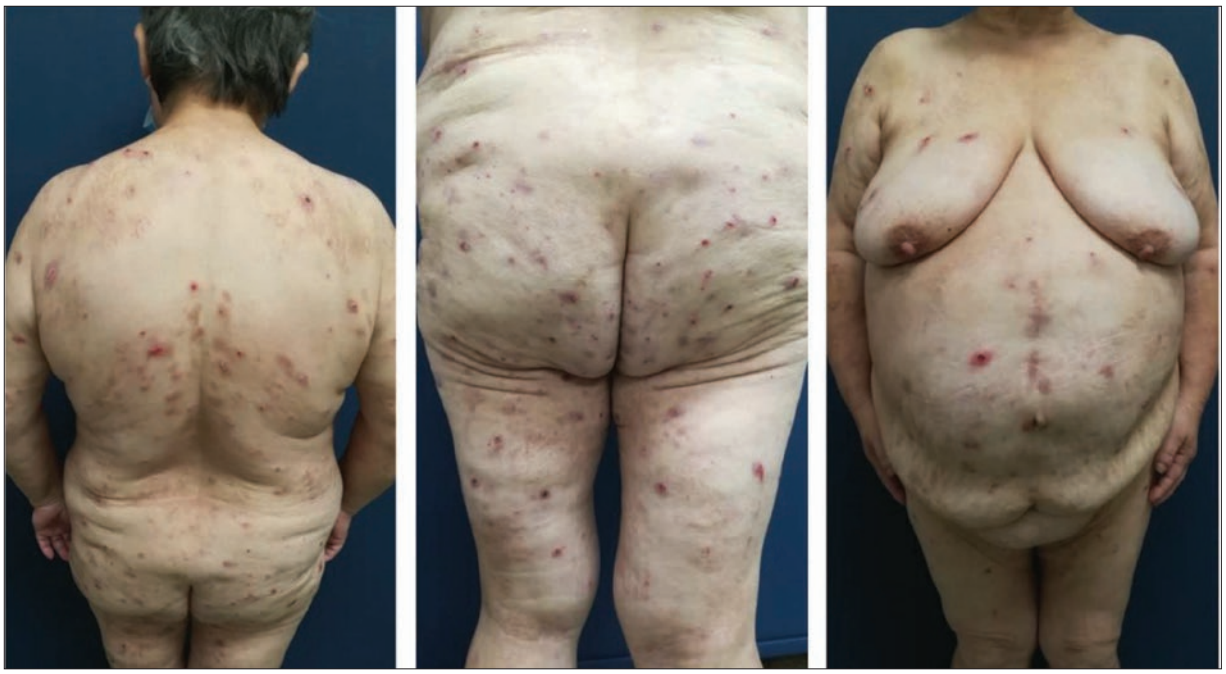

Figure 1. At week 0: Multiple papules and nodules showing lichenification and excoriation.

Her medical history revealed high cardiovascular risk (diabetes mellitus Type 2 - HbA1c >9.5%; obesity - BMI 35.5 kg/m^2; hypertension, and dyslipidemia), chronic kidney disease, and depression. She had no prior history of dermatological complaints.

Cyclosporine (3 mg/kg/day) was used initially and controlled her disease but attempts to wean off this agent because of adverse effects were unsuccessful. The therapeutic course over several years included high-potency topical steroids, oral antihistamines, low-dose naltrexone, and pregabalin all of which failed to control her disease. Dupilumab therapy was subsequently initiated, 600 mg subcutaneous injection at week 0 followed by 300 mg subcutaneous injection every 2 weeks. We performed several evaluations before and during the therapy: the extension of the lesions by the total number of lesions (TNL) score, the patient's itch by a numeric rating scale (NRS) from 0 to 10, the impact on life quality by the dermatology life quality index (DLQI) and blood chemistry. At week 12 (Fig. 2), the patient experienced a significant reduction in the TNL score (from 71 to 15 lesions), pruritus NRS (10-2), DLQI (22-2), and IgE (3253-1452 KU/L) (Fig. 3). The treatment was suspended by week 18 after an acute myocardial infarction submitted later to coronary artery bypass grafting. The discontinuation of the drug led to clinical and symptomatic relapse within 6 weeks (week 24). By week 30, the TNL score, pruritus NRS score, and DLQI increased to 22, 10, and 18, respectively. The patient died 4 months later due to sepsis caused by a surgical wound infection.

Discussion

The treatment of PN is challenging. Treatment typically relies on the use of topical or intralesional steroids and calcineurin inhibitors, though more severe or recalcitrant cases often necessitate the use of neuromodulators such as gabapentin and pregabalin, phototherapy, or systemic immunosuppressives. The few treatment approaches for this condition are often ineffective or related to severe side effects[4,5]. Dupilumab has emerged recently as a therapeutic option for PN. Dupilumab inhibits signaling pathways activated by interleukin (IL)—4 and IL-13, cytokines that seem to be involved in the development and perpetuation of PN[2,3]. Dupilumab was highly effective clinically and symptomatically in our patient, but the relapse occurred after the drug wash-out period. This adds to the growing literature on dupilumab effectively treating PN[6,7]. The preliminary results of PRIME2–a randomized, phase 3, double-blind, and placebo-controlled trial that evaluated the efficacy and safety of dupilumab in 160 adults with PN–are promising. At week 12, 37% of the PN patients treated with dupilumab experienced a reduction in itch compared to 22% of placebo

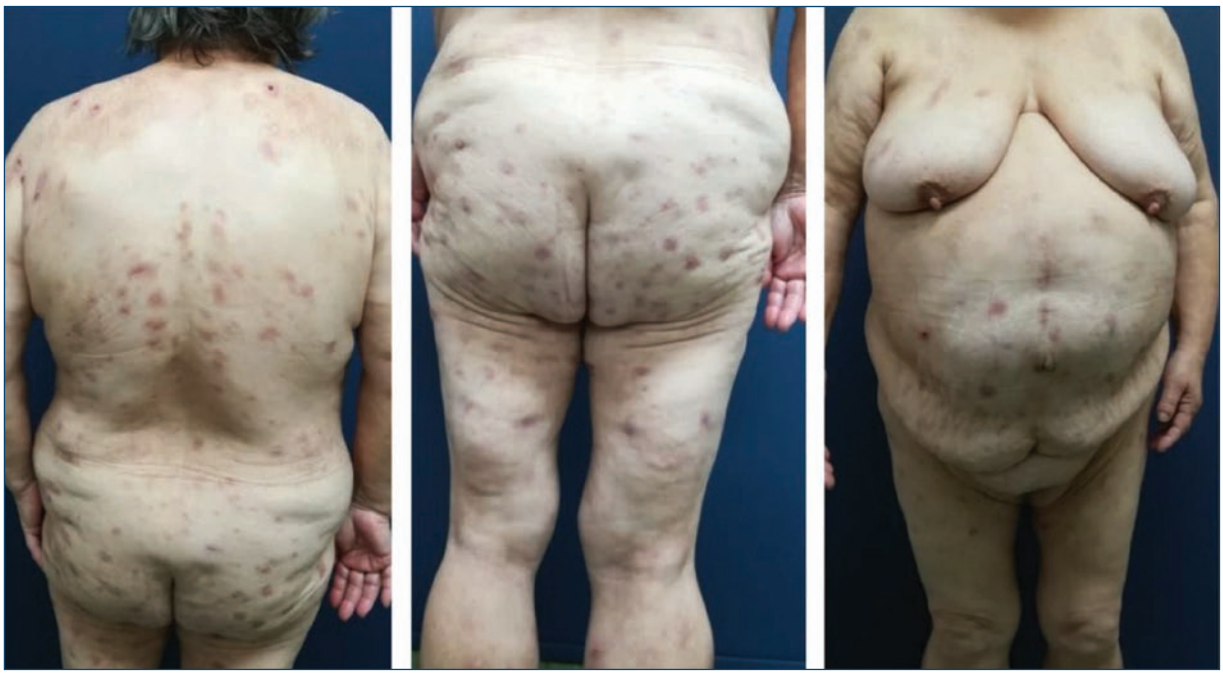

Figure 2. At week 12: The number of active lesions is significantly lower. Hyperpigmentation is seen at the place of previous active lesions.

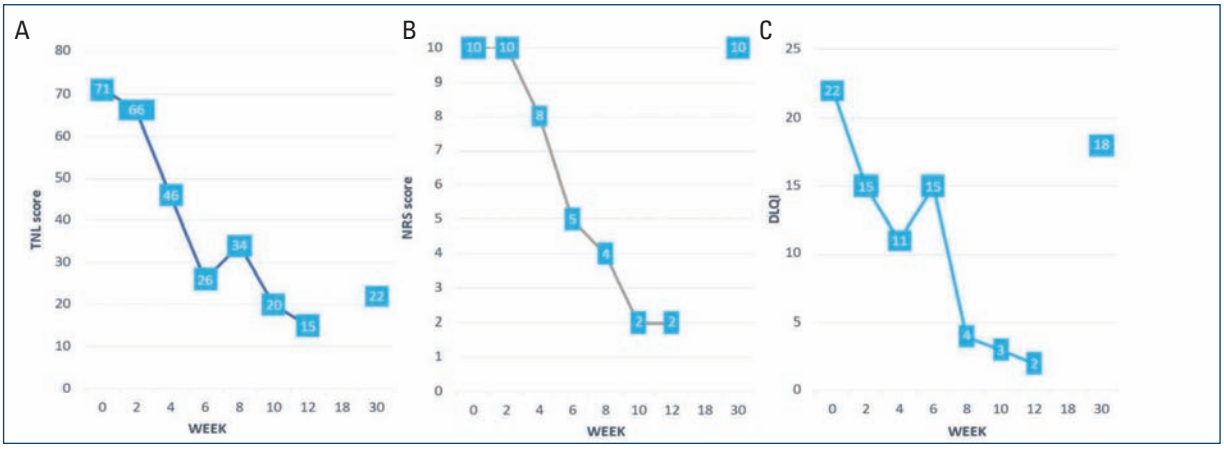

Figure 3. Time course of the clinical parameters including the total number of lesions pruritus and DLQI. **A:** time course of the total number of active lesions (TNL) score. **B:** time course numeric rating scale of pruritus. **C:** time course of DLQI.

patients (p = 0.0216). The difference is even more pronounced at week 24. Nearly, 3 times as many patients treated with dupilumab experience a reduction in itch (58% vs. 20% - p < 0.0001) and achieve clear or almost clear skin (45% vs. 16% p < 0.0001)[8].

The cardiovascular adverse event observed in this patient is not likely to be related to dupilumab, but rather the high cardiovascular risk of this diabetic and obese patient. The long-term safety results from adult with atopic dermatitis suggests a favorable safety profile[9], but the burden of systemic comorbidities in PN often exceeds that of other inflammatory skin disorders (i.e., atopic dermatitis and psoriasis)[10]. The preliminary results of PRIME 2 trial show a similar occurrence of adverse events between dupilumab and placebo groups (57% vs. 51%). The most common was conjunctivitis (6.5% vs. 0%), herpes viral infections (6.5% vs. 0%), and skin infections (5% vs. 9%). In addition, 3% of dupilumab patients and 30% of placebo patients discontinued before week 24[8]. These first results are reassuring, but further studies are needed to assure the long-term safety and efficacy of dupilumab.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Confidentiality of data

The authors declare that they have followed the protocols of their work center on the publication of data from patients.

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