

THERAPEUTIC HOTLINE: LETTER

Eczematous reaction to ixekizumab successfully treated with dupilumab

Biological drugs can induce paradoxical reactions through the blockade of immunological targets as a result of a cytokine imbalance (Munera-Campos, Balleca, Richarz, Ferrandiz, & Carrascosa, 2019). We have recently described the possible occurrence of eczematous eruption (EE) during anti-interleukin (IL)-17 treatment of psoriasis (Napolitano et al., 2019) as well as psoriasiform eruption during dupilumab therapy for adult atopic dermatitis (AD) (Napolitano, Scalvenzi, Fabbrocini, Cinelli, & Patruno, 2019). Herein we report an EE (AD-like) in a psoriasis patient receiving anti-IL-17 (ixekizumab) treatment completely cured with dupilumab.

A 62-year-old man with psoriasis presented with a 2-month history of a diffuse pruritic rash. The patient had personal history of AD in childhood with remission during adolescence. He was affected by psoriasis since the age of 25 years. Previous psoriasis therapies included phototherapy, methotrexate, adalimumab, and etanercept without consistent improvement. Cyclosporine, even if effective, was discontinued after 5 months due to the onset of hypertension and moderate renal failure. The patient was then treated with ixekizumab (5 months before the onset of the pruritic rash) achieving an almost complete response

(PASI decreased from 14.8 at baseline to 0.8 after 20 weeks). Physical examination revealed diffuse erythematous papules, excoriation, and serous exudation, especially on the trunk and upper and lower limbs (Figure 1). Blood test results were within the normal range except for immunoglobulin E (1,400 kU/L, normal value <140). Spongiosis, edema in upper dermis, and perivascular lymphocytic infiltrate were identified through skin biopsy sent for histological examination. Despite oral prednisone therapy (0.5 mg/kg) and discontinuation of ixekizumab, clinical manifestations and itching persisted over time. Based on the clinical and medical history and histological examination, AD-like eruption was diagnosed and a treatment with dupilumab (600 mg induction dose and then 300 mg every 2 weeks) was started, with improvement within 2 weeks and complete clearance sustained up to 22 weeks follow-up (Figure 2). Biological therapies induce changes in the cytokine expression which may direct cutaneous immune response to an eczematous phenotype in predisposed individuals. Psoriasis and AD are characterized by an imbalance in the T helper (Th)1/Th2 immune response, with Th1 being more prominent in psoriasis and Th2 in AD. Probably, during biologic therapies, when the Th1 response is blocked or decreased, the Th2 balance will in



FIGURE 1 Eczematous eruption under ixekizumab treatment



FIGURE 2 Eczematous eruption resolution with dupilumab

turn increase, and vice versa. Anti-IL-17 drugs may shift the immune response from a Th1/Th17 pathway to the Th2 pathway, thus explaining the probable reason why AD reappeared. Recently, Burlando et al. observed a case of atopic-like dermatitis occurring after secukinumab injection (Burlando, Cozzani, Russo, & Parodi, 2019). To our knowledge, this is the first report of recurrence of AD in a patient treated with anti-IL-17 successfully cured with dupilumab, a fully human monoclonal antibody specifically preventing the signaling of IL-4 and IL-13 by inhibiting the IL-4 receptor alpha subunit (Napolitano, Scalvenzi, et al., 2019). This drug has been evaluated for diseases that are implicated by Th2 pathways predominant with IL-4 and IL-13 such as moderate-to-severe AD, asthma, and chronic sinusitis and showed to be effective in terms of clinical outcome and patient-reported symptoms of anxiety and health-related quality of life (Le Floch et al., 2019). Further studies are needed to clarify the pathophysiology and treatment of EE or AD-like eruptions under anti-IL-17. In this context, dupilumab appears like a valuable and efficacious treatment.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

Maddalena Napolitano¹

Lucia Gallo²

Cataldo Patruno³

Gabriella Fabbrocini²

Matteo Megna²

¹Department of Medicine and Health Sciences "Vincenzo Tiberio",
University of Molise, Campobasso, Italy

²Section of Dermatology, Department of Clinical Medicine and Surgery,
University of Naples Federico II, Naples, Italy

³Department of Health Sciences, University Magna Graecia of Catanzaro,
Catanzaro, Italy

Correspondence

Maddalena Napolitano, Department of Medicine and Health Sciences
"Vincenzo Tiberio", University of Molise, Campobasso, Italy.
Email: maddy.napolitano@gmail.com

DOI 10.1111/dth.13218

ORCID

Maddalena Napolitano <https://orcid.org/0000-0003-3309-8190>

Gabriella Fabbrocini <https://orcid.org/0000-0002-0064-1874>

Matteo Megna <https://orcid.org/0000-0003-1803-2046>

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