Dupilumab Treatment in Two Patients with Cutaneous T-cell Lymphomas

Ingrid LAZARIDOU[1], Caroline RAM-WOLFF[1], Jean-David BOUAZIZ[1], Edouard BEGON[2], Maxime BATTISTELLA[1,3], Jacqueline RIVET[3], Marie JACHIET[1], Martine BAGOT[1#]* and Adèle DE MASSON[1#]

[1]Department of Dermatology and [3]Department of Pathology, Saint-Louis Hospital, APHP, University of Paris, 1 avenue Claude Vellefaux, FR-75010 Paris, and [2]Department of Dermatology, Pontoise Hospital, Pontoise, France. E-mail: martine.bagot@aphp.fr

[#]These authors share last authorship.

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Dupilumab is an interleukin 4/13 blocker approved for the treatment of atopic dermatitis (AD), asthma and chronic rhinosinusitis with nasal polyps (1). In AD, dupilumab treatment significantly improves pruritus (2). Treatment with dupilumab has been associated with transient improvement followed by disease progression in 7 patients with cutaneous T-cell lymphomas (CTCL) (3). We report here 2 patients with epidermotropic CTCL who were treated with dupilumab for refractory pruritus.

CASE REPORTS

Case 1. The first case was a 37-year-old woman, with a 19-year history of pruritic dermatosis of the trunk, who presented to our clinic with worsening disease symptoms. Physical examination revealed arcuate, finely scaly erythematous patches affecting 70% of the body surface area. The disease, diagnosed as eczema, had not responded to several lines of treatment, including psoralen plus ultraviolet A (PUVA), topical tacrolimus, topical corticosteroids, and methotrexate. Skin biopsy showed a thickened epidermis with surface parakeratosis, discrete spongiosis, and a mononuclear infiltrate of the superficial dermis, consistent with eczema. Treatment with oral ciclosporin (5 mg/kg/day), induced a partial remission after 3 months of treatment followed by a subsequent relapse and introduction of dupilumab (600 mg/2 weeks). After 2 months of treatment with dupilumab there was no clinical response. The patient had intense pruritus, skin plaques and palmoplantar keratosis. Skin biopsy revealed an atypical dermal infiltrate of medium $CD3^+CD4^+$ lymphocytes with strong expression of PD1 and no expression of CD30. Blood immunophenotyping showed an aberrant $CD4^+$ T-cell population with CD7 loss, aberrant expression of KIR3DL2 (2,738/mm^3) and a CD4/CD8 ratio of 22. The same massive T-cell clone was found in her peripheral blood and in the skin, consistent with Sézary syndrome (SS). The patient was treated with mogamulizumab and is now in partial remission after 4 months of follow-up.

Case 2. The second case was a 55-year-old man with a past history of AD. The patient was referred to our centre for excoriated patches of the neck, trunk, inguinal folds, and the retroauricular region (**Fig. 1**A). A biopsy of lesional skin showed a hyperplastic, acanthotic, papillomatous epidermis, a thin parakeratotic stratum corneum and spongiosis, consistent with AD. A second lesional biopsy revealed atypical lymphocytic infiltrates within the dermis and prominent epidermotropism with a $CD3^+$, $CD4^+$ (90%) immunophenotype and complete loss of CD7, consistent with mycosis fungoides (MF). The same clonal T-cell receptor (TCR) pattern was found by high throughput sequencing in 2 different skin biopsies. Tumour cell frequency was 1.3%. He had severe pruritus and a Dermatology Life Quality Index (DLQI) of 22/30. Because of his previous history of AD, dupilumab treatment was initiated resulting in an improvement in his pruritus and partial remission of MF (Fig. 1B) after 4 months of follow-up.

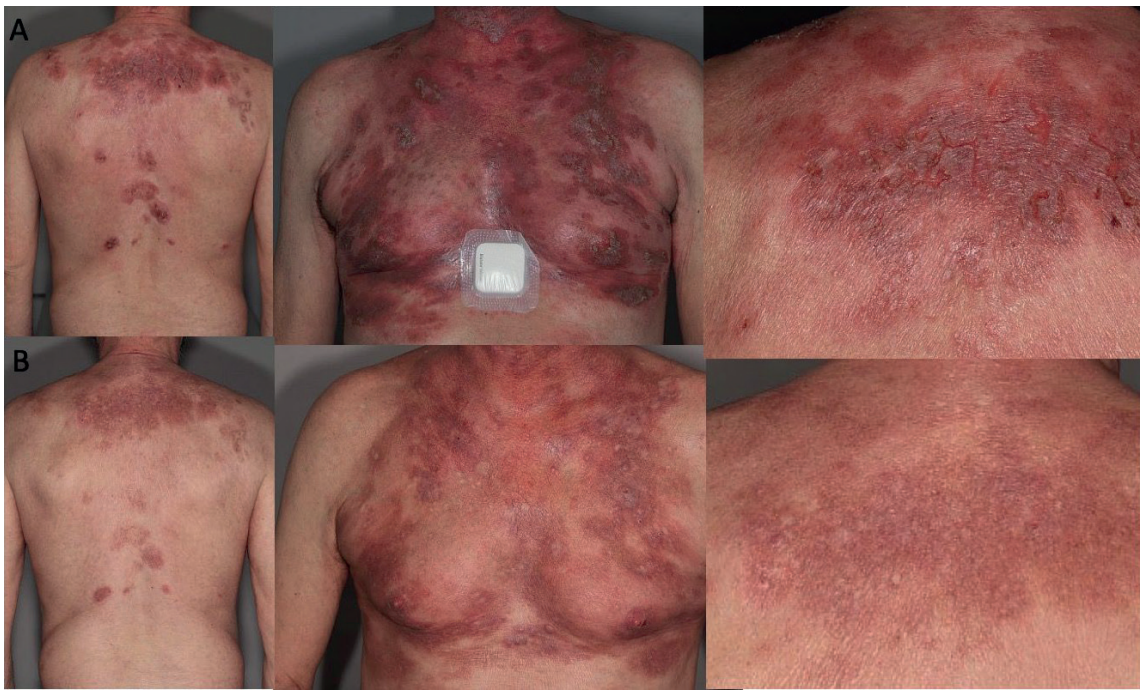

Fig. 1. Case 2: Clinical photographs of mycosis fungoides lesions (A) before and (B) after 1 month of dupilumab treatment.

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DISCUSSION

Pruritus severely impacts quality of life in patients with CTCL (4). Treatment of CTCL-associated pruritus remains challenging. By blocking the Th2 key cytokines IL4 and IL13, dupilumab inhibits the Th2 pathway. A Th2 cytokine shift has been observed in the microenvironment of MF and SS during disease progression (5). These 2 cases highlight the various responses of CTCL to dupilumab. Dupilumab was initiated in case 1 in order to treat refractory pruritic symptoms of presumed AD, but the diagnosis was SS and the clinical response was minimal. In case 2, dupilumab was efficient in relieving the symptoms of MF, although the follow-up is still short. A previous case showed clinical improvement in an MF patient (3), but another reported dupilumab inefficacy in an MF patient misdiagnosed as AD (6). Dupilumab may help to relieve pruritus in patients with MF, but they should be closely and carefully monitored, and further long-term data are needed.

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The authors have no conflicts of interest to declare.

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