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Hair regrowth and dissemination of molluscum contagiosum: two unexpected effects with dupilumab

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To the editor,

Dupilumab is an interleukin (IL)-4 receptor alpha antagonist that was approved by the US Food and Drug Administration in April 2017 for the treatment of adult patients with moderate-to-severe atopic dermatitis (AD) not adequately controlled with topical therapies (1). Dupilumab is a fully human monoclonal antibody that binds to the alpha subunit of the IL-4 receptor and inhibits

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downstream signaling of IL-4 and IL-13, thus inhibiting the helper T cell, type 2 (TH2) pathway activation and cytokines that play a key role in atopic diseases (1).

Dupilumab has been associated with adverse reactions including injection-site reactions, conjunctivitis, blepharitis, oral herpes, keratitis. To our knowledge, molluscum contagiosum (MC) extension has never been described.

We report herein the first known case of both disseminated MC and hair regrowth in a patient with alopecia totalis during a treatment with dupilumab.

A 47 year-old man presented with a severe AD since childhood and persistent alopecia areata totalis evolving for five years (figure 1a). Topical treatments, ciclosporin and methotrexate were ineffective or poorly tolerated. The patient also developed disseminated papules diagnosed as MC based on both typical clinical appearances and pathological findings, such as budlike proliferation of the epidermis and molluscum bodies.

Laboratory examinations showed only a mild lymphopenia (900/mm^3 with 554 CD4 /mm^3) without other infections, including HIV. Hyper IgE syndrome was ruled out with no underlying gene defects such as in DOCK8 and STAT3.

MC were treated with cidofovir without any success. In front of the inefficiency of systemic treatments for AD, dupilumab was initiated. After 8 weeks of treatment, the patient experienced a dramatic hair regrowth (figure 1b) as well as a good response on AD. However, MC multiplied in size and number (figure 2) with stable CD4 count, which pushed to stop dupilumab treatment. Six months after stopping dupilumab, a partial regression of MC was reported, without any relapse of alopecia areata.

To the best of our knowledge, this report is the first case of dissemination of MC in a patient with dupilumab. Until now, hair regrowth in patients with alopecia areara were rarely published. Another case of hair regrowth with dupilumab was described by Penzi et al. recently. The authors suggested that dupilumab's antagonism of the TH2 pathway could explain its effects in both atopic dermatitis and alopecia totalis (2).

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In patients with AD, MC eruption can be widespread and prolonged, since the alterations of the epidermal barrier lead to increased susceptibility to viral skin infection (3), as well as pruritus leading to scratching and auto-inoculation, and long-term treatments with topical anti-inflammatory agents that induce local immunodeficiency. Giant MC are common among HIV-positive patients and patients on immunosuppressive therapy, such as transplant recipients (4), suggesting that the immune system of an individual is important in controlling the size and spread of MC lesions. In our case, the skin lesions multiplied despite the lack of immunodeficiency aggravation. Immunodeficiency, especially a lack of type I interferons (IFN), has been demonstrated to cause an extensive infection of MC virus, the causative agent of MC (5). Cases of MC have also been reported in patients receiving immunosuppressive drugs such as methotrexate, tumor necrosis factor alpha inhibitors and more recently ruxolitinib, a Janus kinase 1 and 2 inhibitor (6). Kinoshita and al suggested that MC dissemination may be mediated by the decreased number of type I IFN-producing plasmacytoid dendritic cells and inhibition of JAK–STAT signal transduction pathway by ruxolitinib. Dupilumab is a human monoclonal antibody targeting the a-subunit of the interleukin (IL)-4 receptor, shared by the Th2-related cytokines IL-4 and IL-13. Disseminated MC with dupilumab suggested that Th2-related cytokines would be also important for the clearance of MC lesions. In our patient, the rapid regression of the lesions on withdrawal of dupilumab strongly suggests a relationship between the drug intake and the extension of MC.

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Figure 1: 1a: alopecia areata totalis et 1b : Hair regrowth after 8-week dupilumab treatment

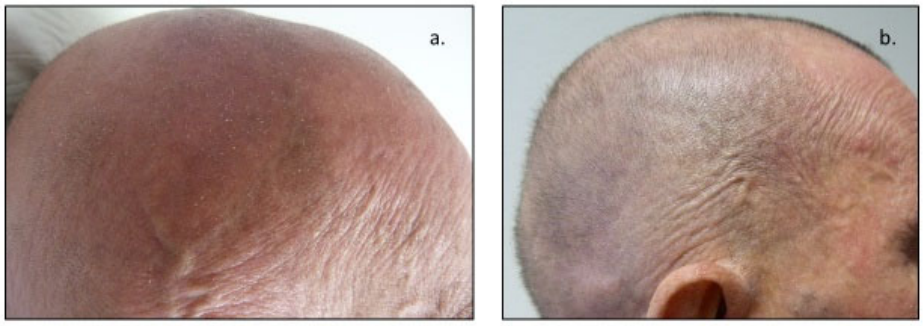
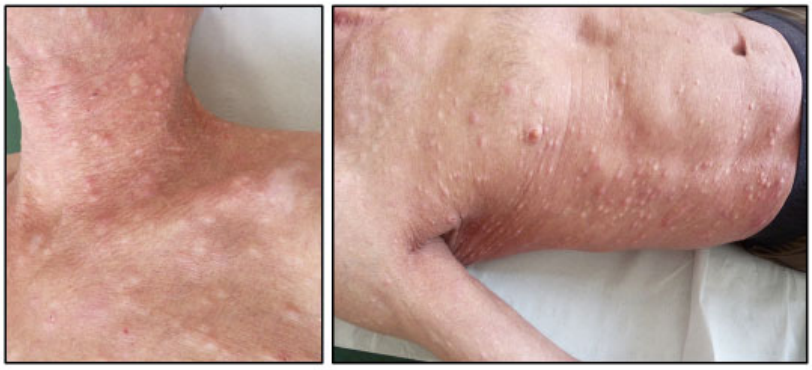


Figure 2 : disseminated molluscum contagiosum



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