Clinical Letter

Effective treatment of atopic dermatitis with dupilumab in an HIV-positive patient

Dear Editors,

Dupilumab was approved for the treatment of patients with atopic dermatitis at the end of 2017 [1]. The drug inhibits Th2-mediated immune responses by binding to the interleukin (IL)-4Rα subunit of the IL-4 and IL-13 receptors. In the pivotal studies, 38 % of patients treated with dupilumab achieved an IGA (Investigator’s Global Assessment) score of 0 or 1, whereas only 10 % did so in the placebo group [2]. Type 2 immune responses play a pathogenetic role not only in atopic disorders but also in chronic infections. For example, IL-4 serum levels have been shown to be elevated in HIV-positive individuals not undergoing treatment [3]. Given that HIV-positive patients were excluded from previous clinical studies of dupilumab, it is as yet unclear in this patient group whether and to what extent dupilumab (1) is effective against atopic dermatitis, (2) has an impact on the HIV infection and (3) interacts with antiretroviral drugs.

We report the case of a 54-year-old man with a history of atopic dermatitis since childhood. He had a body mass index of 29.8 but was otherwise in good health. His past medical history also included allergic bronchial asthma and perennial allergic rhinoconjunctivitis, with seasonal deterioration in the spring and summer (total IgE: 8,264 kU/L; specific IgE to SX1 [screening for inhalant allergy]: 88.4 kU/L). While this deterioration did not coincide with atopic dermatitis flares, the patient reported that increased perspiration did exacerbate his skin condition. In 2015, he had been diagnosed with HIV; at the time of presentation, he was being treated with the integrase inhibitor dolutegravir and the nucleoside reverse transcriptase inhibitors emtricitabine and tenofovir. On this regimen, he showed a substantial reduction in the amount of topical corticosteroids required. Both the number of T helper cells (Figure 2a) and the viral load remained largely unchanged 4, 8 and 24 weeks after treatment initiation; so did the serum levels of tumour necrosis factor (TNFα) prior to and during dupilumab treatment, and levels remained within normal limits throughout (Figure 2b). During treatment, the patient experienced an increase in body hair, a side effect that has previously been reported [6]. There were no other adverse effects.

At initial presentation, the patient showed erythroderma, generalized scaling and significant lichenification of the entire skin. In addition, he reported a 20-year history of alopecia areata totalis, a condition commonly described in association with atopic dermatitis [4]. Given the marked severity of his atopic dermatitis and given the presence of relative contraindications for reintroducing cyclosporine (arterial hypertension, prior treatment discontinuation due to recurrent infections), the patient was started on dupilumab, after being properly informed about possible adverse effects and infections associated with this drug. Prior to treatment initiation, the total number of CD4 cells was 603/μL and the CD4/CD8 ratio was 4.25. The SCORAD (SCORing Atopic Dermatitis) score was 42.2 prior to treatment and 27.2 after 24 weeks. The Dermatology Life Quality Index (DLQI) decreased from 13 points prior to treatment to two points after 24 weeks (Figure 1). This was accompanied by a substantial reduction in the amount of topical corticosteroids required. Both the number of T helper cells (Figure 2a) and the viral load remained largely unchanged 4, 8 and 24 weeks after treatment initiation; so did the serum levels of dolutegravir. In addition, this was the first time in such a constellation that we measured serum levels of IL-1β, IL-6 and TNFα prior to and over the course of treatment. These cytokines play a significant role in the immune control of viral infections and may therefore be early markers for any potential impact dupilumab might have on HIV infection [5]. There were no significant variations in these cytokines prior to and during dupilumab treatment, and levels remained within normal limits throughout (Figure 2b). During treatment, the patient experienced an increase in body hair, a side effect that has previously been reported [6]. There were no other adverse effects.

In summary, in the present case treatment with dupilumab resulted in (1) significant improvement in atopic...
dermatitis, (2) no reactivation of HIV infection or shifts in T cell subpopulations and cytokine levels in peripheral blood, and (3) no changes in serum dolutegravir levels. Thus, at the time this case report was written (six months after treatment initiation), dupilumab had been well tolerated by our patient and proven to be beneficial.

The positive effects of dupilumab were not entirely unexpected, given the available experimental data and study observations on the impact of IL-4 and IL-13 in patients with HIV [7]. Interleukin-4 has been shown to upregulate the expression of HIV co-receptors (CXCR-4 and DC-SIGN) on CD4+ T cells and to stimulate intracellular HIV production [8]. Consequently, elevated IL-4 levels may be associated with more rapid disease progression. In addition, synergistic mechanisms – primarily caused by elevated Th2 cytokine (IL-4, IL-5, IL-13) levels – may lead to insufficient immune control of HIV [4]. In keeping with these reports, it has been demonstrated that elevated serum IL-4 levels in treatment-naive HIV patients normalize over the course of 6–12 months after initiation of HAART [8]. In this context, it has been suggested that IL-4/13 blockade might play an important role in the development of a vaccine against HIV [9]. Given the aforementioned data and following a careful risk/benefit assessment and informed consent, we considered systemic therapy with dupilumab to be warranted in the present case. In a recently published case series of four patients [10] and in one other case report [11], dupilumab was likewise shown to be well tolerated by HIV-positive individuals; however, detailed monitoring of immunological markers was not performed in these cases. Nevertheless, longer observation periods and larger patient populations are needed in order to be able to draw more reliable conclusions as to the safety of dupilumab in patients with HIV.

Conflict of interest
None.

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