Case report

Successful treatment of severe atopic dermatitis and alopecia universalis with upadacitinib in a 29-year-old male patient

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A 29-year-old male patient had severe atopic dermatitis (AD) and alopecia universalis (AU) that could not be controlled by using classic therapy. He started taking upadacitinib and achieved an excellent response for both his AD and AU. Thus, upadacitinib represents a promising therapeutic approach for patients with severe AD and alopecia areata. (J Allergy Clin Immunol Global 2024;3:100269.)

Key words: *Atopic dermatitis, alopecia universalis, upadacitinib, eczema, JAK inhibitor*

Abbreviations used
AA: Alopecia areata
AD: Atopic dermatitis
AU: Alopecia universalis
DLQI: Dermatology Life Quality Index
JAK: Janus kinase
EASI: Eczema Area and Severity Index
SALT: Severity of Alopecia Tool
SCORAD: SCORing Atopic Dermatitis

Atopic dermatitis (AD) is a chronic skin disease marked by intense pruritus, skin barrier defects, and recurrent or permanent inflammatory lesions. It is the most common inflammatory skin condition in children, with a prevalence estimated at 10% to 30%, and it affects 2% to 10% of adults.[1] AD can have a significant impact on the quality of life of patients and their families as a result of loss of sleep hours, school/workday and daily activities, and greater tendency to develop anxiety and depression.[2] It is frequently associated with other atopic diseases, such as asthma, food allergy, rhinitis, and conjunctivitis.[2] Treatments target the inflammatory condition. In general, the first line of treatment includes topicals (ie, emollients, corticosteroids, calcineurin inhibitors, and recently, PDE-4 and Janus kinase [JAK] inhibitors.[3] In more severe cases, phototherapy and systemic immunosuppressors (cyclosporine, methotrexate, azathioprine, and micofenolate mofetil) were widely used before the new advances in therapy using mAbs (dupilumab and tralokinumab) and JAK inhibitors (baricitinib, abrocitinib and upadacitinib).[3] Alopecia areata (AA) is an autoimmune disease that leads to hair loss in a noncicatricial pattern. It can extend from a localized small patch to complete body and scalp hair loss (alopecia universalis [AU]). The lifetime prevalence of AA is around 2% and that of AU is 0.77%.[4] AA has also a significant impact on patients' quality of life owing to its visible nature.[5] AA has been demonstrated to occasionally coexist with AD, and the coincidence of atopy predisposes to a more severe course of the disease.[6] The first systemic treatment for AA, which was approved by the US Food and Drug Administration in June 2022, was baricitinib. Before that, off-label drugs such as corticosteroids, cyclosporine, methotrexate, and minoxidil were the top choices to treat AA.[7]

In 2022, upadacitinib, an oral selective JAK 1 inhibitor, was approved in Brazil for use (at a dose of 15 -30 mg per day) in the treatment of adults and adolescents older than 12 years with moderate-to-severe AD. The available information on upadacitinib's effects in patients with AD and concurrent AA is limited. We report the case of a 29-year-old male patient with long-term severe AD and AU that were successfully treated with upadacitinib.

CASE REPORT

The study was approved by the Albert Einstein Hospital ethics committee (Certificate of Presentation of Ethical Review no. 74319023.4.0000.0071), and the patient signed informed consent. The 29-year-old White male patient with no occupation had had AD since childhood. His AD had worsened since age 14 years. At age 16 years, he was hospitalized for AD for 1 week. He subsequently underwent treatment with methotrexate (20 mg per week) and later with cyclosporine (300 mg per day) for a 1 year each, but both drugs failed to achieve adequate control. Additionally, the patient had a history of mild allergic asthma and chronic rhinosinusitis. At age 17 years, he developed localized AA, with complete hair regrowth after treatment with topical steroids and minoxidil. At age 21 years, he experienced new hair loss, resulting in alopecia of the entire scalp, as well as loss of his facial and body hair (AU). He also developed depression, anxiety, and a fear of leaving his house, requiring 20 to 40 mg of prednisone to do so, because he stated that his AD worsened when he was exposed to heat and sunlight. He had extremely high IgE levels (59,000-77,000 kU/L) for the past year. Complete exome

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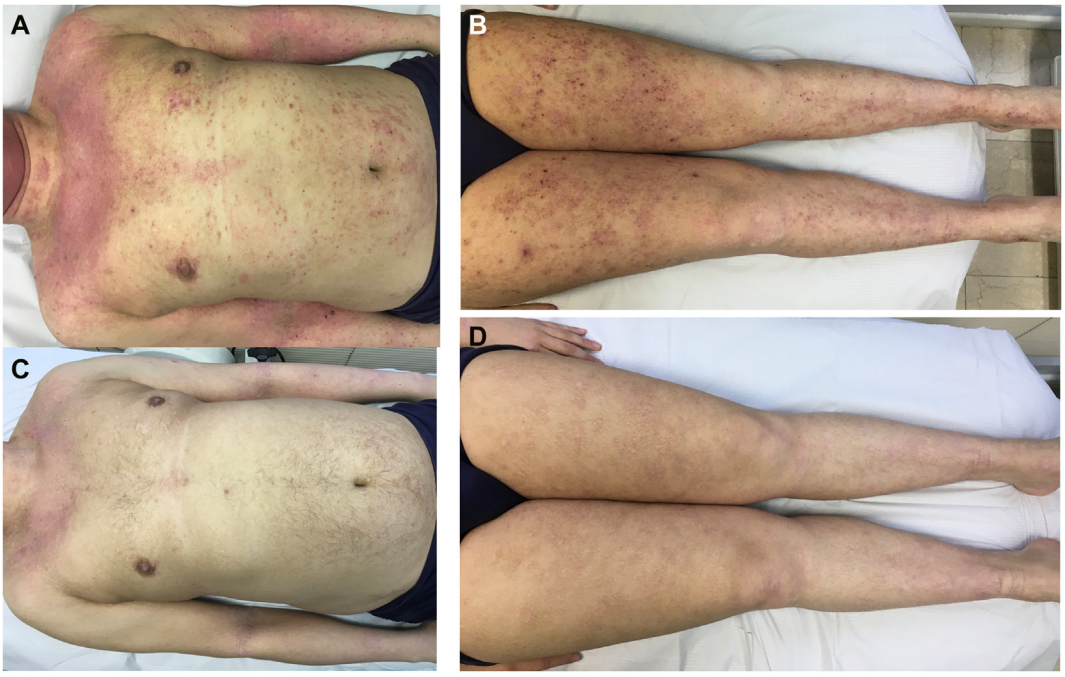

FIG 1. **A** and **B**, AD lesions on anterior patient's body before upadacitinib (SCORAD score, 101.6; EASI, 65.4; and DLQI, 30). **C** and **D**, The same areas after 6 months of treatment (SCORAD score, 18.15; EASI, l3.60; and DLQI, 20).

test performed to investigate hyper-IgE syndrome yielded a negative result. Laboratory tests to evaluate autoimmunity revealed an antinuclear antibody level ANA of 1/80 and speckled pattern; the results of testing for thyroid autoantibodies (TPOAb, TgAb) were negative. Dermatologic examination revealed generalized, extensive, chronic AD plaques, with a SCORing Atopic Dermatitis (SCORAD) score of 101.6, Eczema Area and Severity Index (EASI) of 65.4, and Dermatology Life Quality Index (DLQI) of 30. AA assessment resulted in a Severity Alopecia Tool (SALT) score of 100 and DLQI of 30 (the maximum scores for both). After laboratory investigation, treatment with upadacitinib, 30 mg per day, was started. After 1, 3, and 6 months of treatment, the patient's AD scores were as follows: SCORAD score, 66.8; 55.8, and 18.15, respectively; EASI, 22.8, 23.0, and 3.60, respectively; and DLQI, 15, 23, and 20, respectively. His AU scores were as follows: SALT score, 90.0, 63.6, and 74.4, respectively, and DLQI, 30, 30, and 20, respectively. Fig 1 and Fig E1 (see the Online Repository at www.jaci-global.org) show improvement of the patient's AD, and Fig 2 shows improvement of his AU (as illustrated by the patient's appearance before and after 6 months of treatment with upadacitinib). The control examinations yielded normal results, with the sole adverse drug reaction being folliculitis/acne presenting on the scalp and posterior trunk, manifesting in intermittent flares within the initial month of upadacitinib use. Scalp folliculitis was confined to 2 or 3 isolated spots, resolving spontaneously within days. Conversely, the acneiform lesions on the patient's shoulders and upper and middle back were more pronounced and persistent, although they also resolved without intervention over a few weeks. Opting against localized acne treatment was a strategic decision, as the patient's back remained the primary site of AD severity, with concerns that topical acne therapies could exacerbate the condition. Additionally, the patient reported minimal discomfort from the acne lesions, obviating the need for oral treatments. Notably, the patient's IgE levels remained stable throughout the initial 6 months of upadacitinib therapy but decreased to 48,000 after 9 months.

DISCUSSION

AU is an uncommon condition, especially in association with severe atopic dermatitis, such as in this case report. We could have chosen between JAK inhibitors, such as upadacitinib and baricitinib, and dupilumab (an anti–IL-4/IL-13 mAb), as they were all approved for treatment of severe AD in Brazil. The patient had high levels of IgE and atopic comorbidities; therefore, dupilumab would have been a good choice to target AD in such conditions. On the other hand, we already had information that baricitinib had been approved for treatment of AA in the United States, so, it would have been an interesting choice to target both diseases. However, baricitinib was not accessible to our patient and very expensive for his family to afford. As we had access of 1 year of free samples for evaluation of upadacitinib (another JAK1 inhibitor that is approved in Brazil for moderate-to-severe AD), we made the decision to use it in this case, seeking to control both diseases with the same drug. Nowadays in Brazil, an anti–IL-4/IL-13 (dupilumab), 3 JAK inhibitors (abrocitinib, baricitinb, and upadacitinib), and cyclosporin are approved for moderate-to-severe AD, but there are no approved systemic drugs to treat AA.

According to the recently developed "treat to target" criteria to judge the success of AD treatment,[8] our patient achieved good disease control, reaching the end points of at least a 75% improvement in SCORAD score and at least a 75% improvement in EASI. Regarding AA, a previous study showed

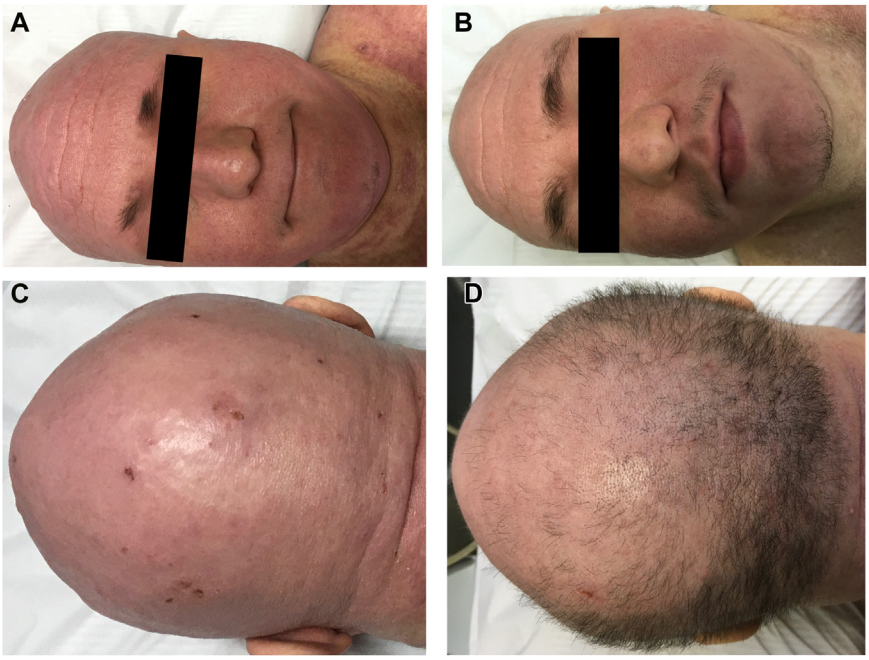

FIG 2. AU on the patient's face (**A**) and scalp (**C**) before upadacitinib (SALT score, 100.0; DLQI, 30). **B** and **D**, The same areas after 6 months of treatment (SALT score, 74.4; DLQI, 20).

variable results and times to elicit a response with upadacitinib.[9] In 1 study, the responder group showed improvement as early as after 4 weeks of treatment, which continued over time, but almost half of the patients (47.1%) were considered nonresponders (SALT score < 50) at week 16, with no further benefit thereafter.[9] At the moment, there is not yet a consensus on treat-to-target in AA, so we considered our patient as having obtained partial control of his AU.

Compared with dupilumab, upadacitinib exhibits a broader spectrum of action within the inflammatory cascade, primarily targeting the type 2 immune response of AD by blocking the interleukins IL-4 and IL-13 while also inhibiting IL-22 and IFN-γ. Notably, the latter cytokine (ie, IFN-γ) has been linked to autoimmune disorders. It is hypothesized that this comprehensive mechanism of action may underlie the observed improvement in both of the patient's conditions.

Upadacitinib may represent a promising therapeutic approach for patients with severe AD and autoimmune conditions such as AA, offering clinical efficacy and enhanced quality of life while maintaining a good safety profile.

DISCLOSURE STATEMENT

Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

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