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CASE STUDY

Immediate exacerbation of atopic dermatitis after switching from upadacitinib to dupilumab: A report of two cases

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Abstract

Janus kinase (JAK) inhibitors are efficacious for atopic dermatitis (AD). However, some patients receiving JAK inhibitors develop acne, especially younger patients, or herpes zoster, especially elderly patients, and desire to switch to dupilumab. We experienced two patients with immediate exacerbation of AD after switching from upadacitinib to dupilumab, and herein report these cases. This phenomenon is attributed to the difference in elimination half-life of the two drugs and a slower onset of efficacy of dupilumab than upadacitinib. When switching from a JAK inhibitor to dupilumab, short-term concomitant use, intensifying topical treatment, and/or rescue with cyclosporine should be considered.

KEYWORDS
atopic dermatitis, biologics, dupilumab, Janus kinase, upadacitinib

1 | INTRODUCTION

Dupilumab demonstrated effectiveness for atopic dermatitis (AD),[1,2] but real-world evidence in patients receiving dupilumab raised the issues of refractory or newly developed facial redness.[3] Certain patients are refractory to dupilumab. In those patients, switching to upadacitinib can be considered based on superior efficacy to dupilumab[4] and reports of cases with refractory facial redness while receiving dupilumab successfully treated with upadacitinib.[5] Meanwhile, some patients receiving upadacitinib develop acne, especially younger patients,[6] or herpes zoster, especially elderly patients,[7] and desire to switch to dupilumab. We experienced two patients with immediate exacerbation of AD after switching from upadacitinib to dupilumab.

2 | CASE 1

A 50-year-old male with a history of AD since childhood had been treated with topical corticosteroid, delgocitinib, and phototherapy. Due to their ineffectiveness, he was referred to our department. He presented with erythema and lichenification with slight scales on his entire body (Figure 1A). They were severe, especially on his face. His eczema area and severity index (EASI) score was 26.5 and that of the head and neck was 4.0. The affected body surface area (BSA) was 65%. The visual analog scale (VAS) score of pruritus was 100/100 mm. He received dupilumab every other week in addition to topical treatment. In 12 months, he showed significant improvement in skin manifestations (EASI, 6.0; EASI of the head and neck, 1.8; affected BSA, 20%; VAS score of pruritus, 11 mm;

Figure 1B). Due to dissatisfaction with residual eruption on his face, he switched the treatment from dupilumab to 30 mg/day of upadacitinib, which induced further amelioration (EASI, 3.4; EASI of the head and neck, 1.0; affected BSA, 15%; VAS score of pruritus, 3 mm; at 12 weeks; Figure 1C). Then, he wanted to change his treatment back to dupilumab because he feared the risks of adverse events of upadacitinib, especially herpes zoster. Therefore, upadacitinib was discontinued 12 weeks after its initiation, and dupilumab was re-initiated. Immediately thereafter, his AD symptoms worsened (EASI, 22.6; EASI of the head and neck, 4.0; affected BSA, 60%; at 2 weeks; Figure 1D). He was treated with 150 mg/day of cyclosporine in addition to dupilumab and intensive topical treatment, which induced improvement. The additional treatment with cyclosporine was withdrawn 1 month after the re-initiation of dupilumab.

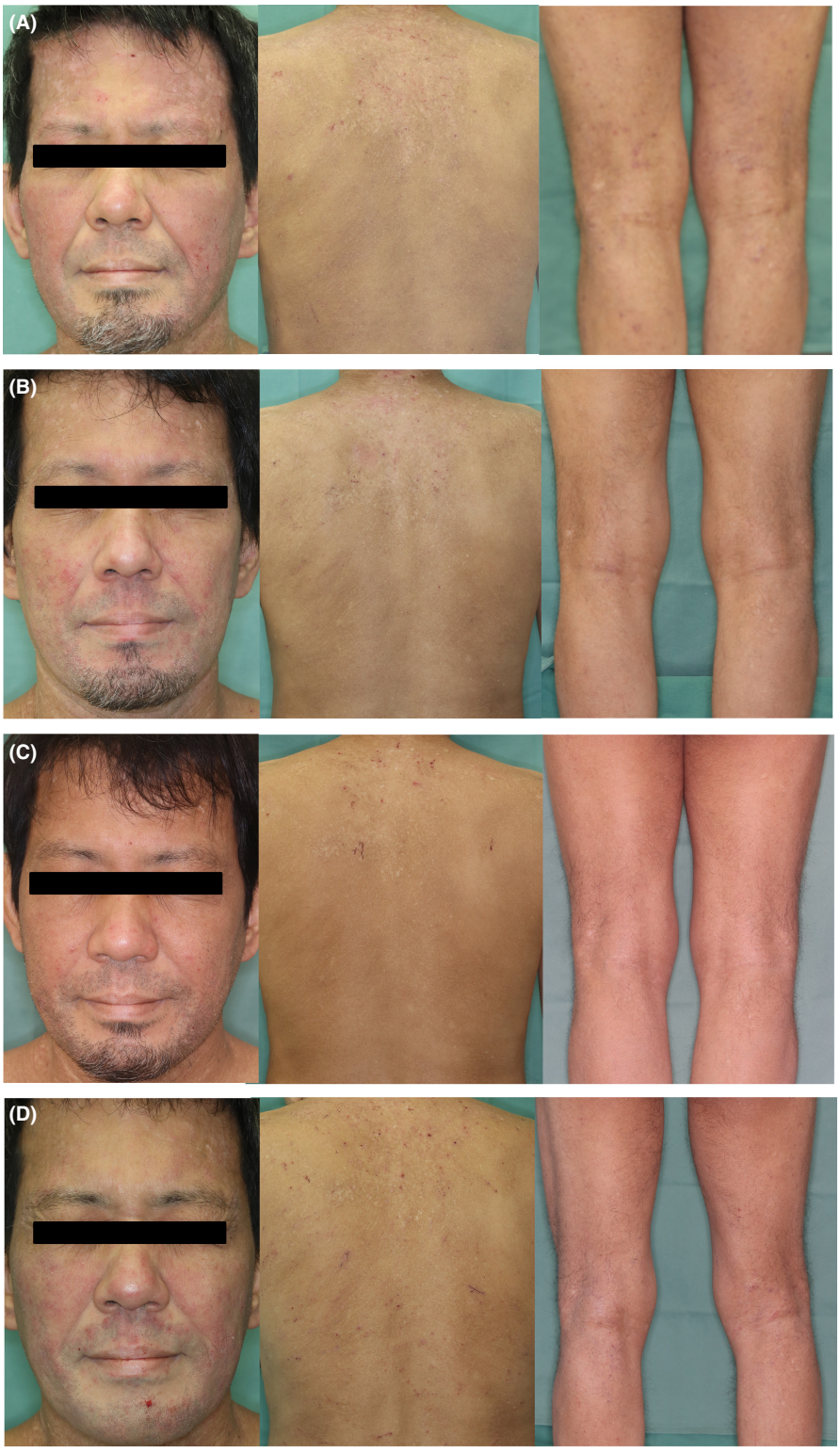

FIGURE 1 Clinical manifestations of the 50-year-old patient with atopic dermatitis (A) before initiating dupilumab, (B) 12 months after starting treatment with dupilumab, (C) 12 weeks after switching from dupilumab to upadacitinib, and (D) 2 weeks after switching from upadacitinib back to dupilumab.

3 | CASE 2

A 19-year-old male with a history of AD since childhood had been treated with topical corticosteroid and tacrolimus, which did not improve his AD symptoms. At our department, he presented with erythema and red papules on his entire body (EASI, 18.8; affected BSA, 40%: VAS score of pruritus, 65 mm). He was treated with 30 mg/day of upadacitinib. Three months later, although upadacitinib improved AD symptoms (EASI, 1.6; affected BSA, 1%; VAS score of pruritus, 8 mm), upadacitinib was switched to dupilumab due to acne on his face. He suffered from pruritus 1 day after the first dupilumab treatment, and erythema and red papules began to appear. Three days after initiating dupilumab, 150 mg/day of cyclosporine was added to dupilumab, which improved the exacerbation. Cyclosporine was tapered and withdrawn 4 months after initiation of dupilumab.

4 | DISCUSSION

We experienced immediate exacerbation of AD symptoms upon switching from upadacitinib to dupilumab in two patients. This phenomenon is attributed to the difference in elimination half-life of the two drugs and a slower onset of efficacy of dupilumab than upadacitinib. The elimination half-life of upadacitinib is about 8–12 h, whereas that of dupilumab is about 5–9 days according to the description in the package insert published by Pharmaceuticals and Medical Devices Safety in Japan. Furthermore, dupilumab showed a slower onset of efficacy than 30 mg of upadacitinib.[4] Upon switching from upadacitinib to dupilumab, upadacitinib wears off immediately, but it takes a while for dupilumab to exert efficacy. Short-term concomitant use, intensifying topical treatment, and/or rescue with cyclosporine should be considered.

There is also a paucity of literature on the concomitant use of classic immunosuppressants including cyclosporine (the elimination half-life is about 1 h), methotrexate (about 2–3 h), and mycophenolate mofetil (about 13–16 h) with dupilumab at transitioning from classic immunosuppressants to dupilumab. Ludwig et al.[8] published an article on a practical guide about the transition, in which they recommend concomitant use with a tapering dose of classic immunosuppressants for 12 weeks, considering that steady-state concentration of dupilumab was achieved by week 16 and that efficacy reached steady state by week 16 in clinical trials. In pediatric AD patients, Ludwig et al.[9] recommend that regardless of dupilumab dosing regimen, it is reasonable to decrease the immunosuppressant dose by half every 2 weeks after the loading dose and discontinue fully by week 8.

Due to a lack of evidence, safety during the concomitant period remains unknown. Although safety data during concomitant use of upadacitinib and dupilumab have not been reported, those of patients who switched from dupilumab and upadacitinib have been reported.[10] Given the half-life elimination time of dupilumab, patients were considered to be under the effects of both dupilumab and upadacitinib for a few weeks after switching from dupilumab to upadacitinib. In the patients, no new safety risks were observed, which suggests tolerable safety of short-term concomitant use with a tapering dose of upadacitinib when transitioning from upadacitinib to dupilumab. However, further accumulation of evidence is needed.

CONFLICT OF INTEREST STATEMENT

M.K. received honoraria for lectures from AbbVie. Y.T. received grants for research from AbbVie and honoraria for lectures from AbbVie.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, M.K., upon reasonable request

ETHICS STATEMENT

Approval of the research protocol: Not applicable.

Informed Consent: The patients in this manuscript have given written informed consent for the publication of their case details.

Registry and the Registration No. of the study/trial: N/A.

Animal Studies: N/A.

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