Modifying Dupilumab Dosing Frequency in Patients Exhibiting Dupilumab induced Psoriasiform Dermatitis : A Case-based Approach

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Dupilumab associated psoriasis (DAP)

- Since the first report in 2018,
  an increasing number of psoriasis cases have been documented in
  atopic dermatitis (AD) patients receiving **dupilumab**.
- **Psoriasiform eruptions** have also been reported after dupilumab use for
  non-AD conditions, including asthma, alopecia areata, and chronic rhinosinusitis
  with nasal polyposis.
- Dupilumab exposure was associated with a significantly increased risk of
  psoriasis (hazard ratio 1.58).
- A large-scale retrospective cohort study found
  that the incidence of switching from AD to psoriasis during dupilumab treatment
  was 2.0% compared with 1.1% in controls,
  with a 3-year cumulative incidence of **2.86%** versus 1.79%.

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Dupilumab associated psoriasis (DAP)

- **Plaque psoriasis** was the most common subtype.
- The dupilumab-associated psoriatic plaques were often described as well-demarcated erythematous scaly plaques, showing no difference from classic psoriatic plaques.
- **Extremities** were the most common sites, especially bilateral extensor surfaces of upper and lower extremities, consistent with classic psoriasis.
- Additionally, trunk and scalp were other common locations.

Table 1. Clinical characteristics of de novo psoriasis associated with dupilumab[a]

Characteristics	
Gender	$n = 35$
Male	19 (54.3%)
Female	16 (45.7%)
Age, years, mean (range)	48.6 (22–92)
Time to onset, months, mean (range)	$n = 34$[b]
	4.3 (1–18)
Lesion types	$n = 35$
Plaque psoriasis	27 (77.1%)
Pustular psoriasis	3 (8.6%)
Guttate psoriasis	2 (5.7%)
Erythrodermic psoriasis	1 (2.9%)
Reverse psoriasis	1 (2.9%)
Sebopsoriasis	1 (2.9%)
Lesion location	
Extremities	27 (77.1%)
Trunk	13 (37.1%)
Scalp	11 (31.4%)
Face and neck	4 (11.4%)
Nail	2 (5.7%)

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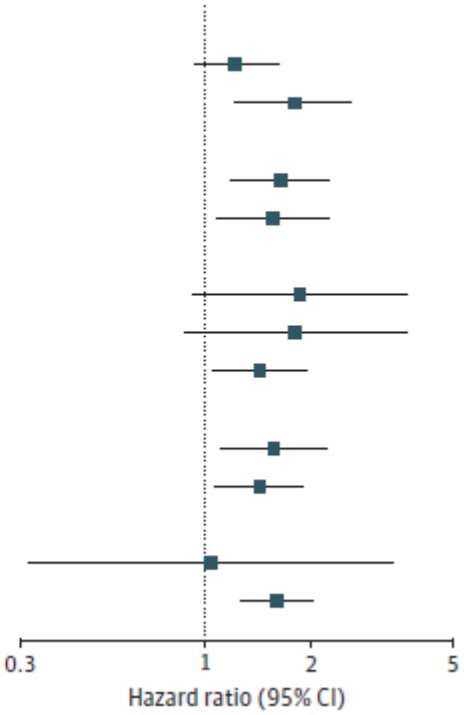
DAP is influenced by age, race, and IgE levels

- Nationwide population-based epidemiologic studies demonstrate that elderly atopic dermatitis (AD) patients (**age > 60**), **Asian** individuals, and those with pretreatment **low IgE** levels below 200 IU/mL who are treated with dupilumab have a higher risk of developing psoriasis (PsO) compared to their matched controls.
- These findings aligned with previous reports that elderly individuals, Asian individuals, and those with intrinsic AD groups with a stronger baseline **Th17 profile**, may be more prone to dupilumab associated PsO.

Subgroup analyses	Event/No. Dupilumab	Event/No. Control	Hazard ratio (95% CI)
Age, y			
18–60	122/7136	91/7136	1.23 (0.94-1.61)
>60	77/2586	42/2586	1.77 (1.22-2.58)
Sex			
Female	104/5257	59/5257	1.63 (1.19-2.24)
Male	79/4016	47/4016	1.55 (1.08-2.22)
Race			
Asian	24/997	12/997	1.85 (0.93-3.71)
Black	22/1681	11/1681	1.81 (0.88-3.73)
White	104/4888	70/4888	1.43 (1.05-1.93)
Atopic comorbidities			
Yes	90/4752	53/4752	1.56 (1.11-2.19)
No	115/5175	77/5175	1.42 (1.06-1.89)
Ever blood IgE >200 IU/mL			
Yes	10/539	10/539	1.04 (0.32-3.40)
No	192/9358	112/9358	1.59 (1.26-2.01)



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Results

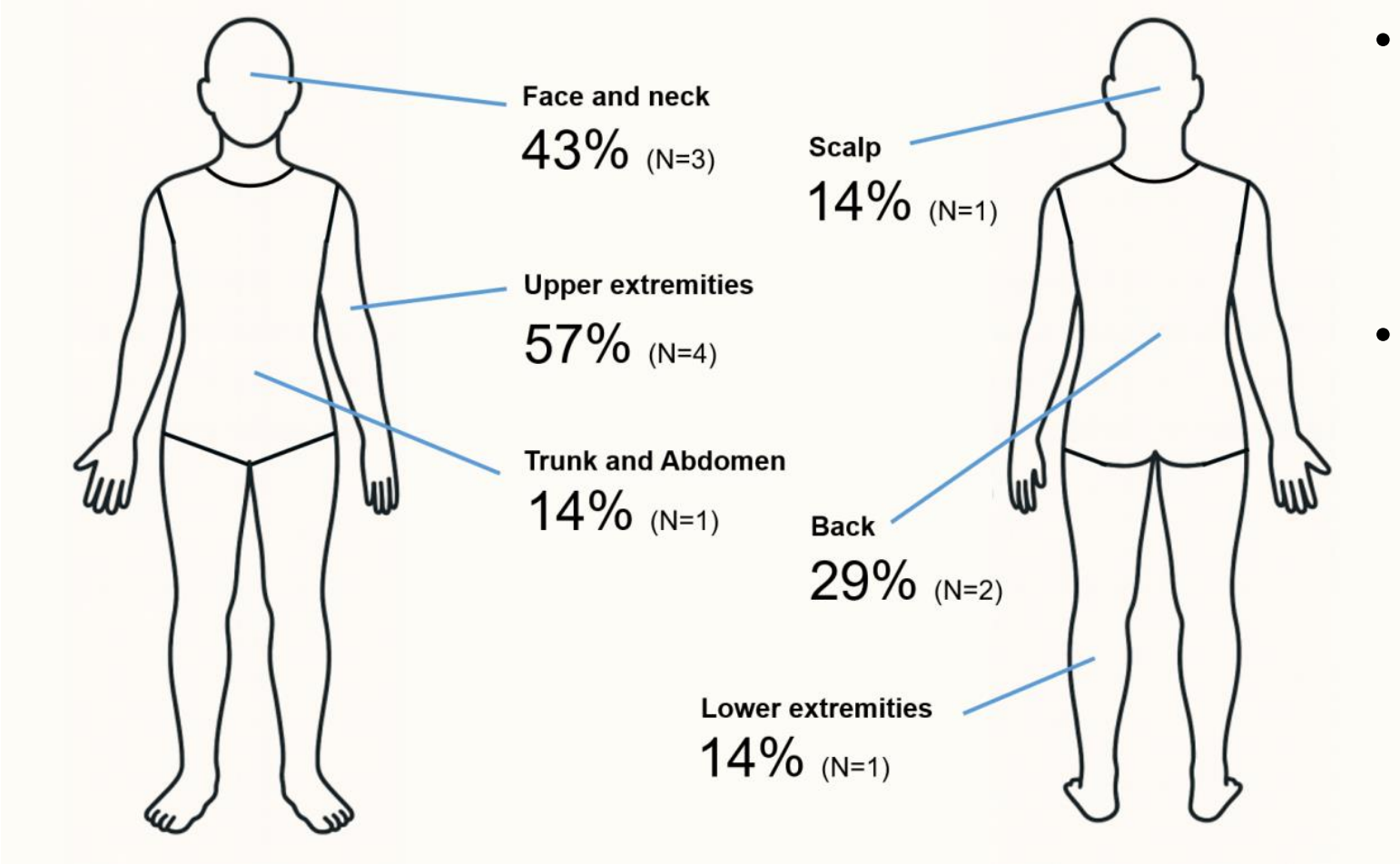
Clinical findings of DAP

- The mean age was 61.3 years (range: 28–87).
- The mean age of AD onset was 34.6 years (range: 0–68).
- The mean duration of AD was 8.3 years.
- All subjects achieved EASI 75–90 responses to dupilumab.
- Among them, two patients also presented with dupilumab-induced facial redness.

Characteristic		No. (%) Patients (N=7)
Age, mean (SD), year		
	Current age	61.3 (19.2)
	AD onset age	34.6 (24.3)
Sex		
	Female	0 (0)
	Male	7 (100.0)
Comorbidity		
	Food allergy	1 (14.3)
	Allergic rhinitis	1 (14.3)
	None	5 (71.4)
IgE in blood, mean (SD), IU/L		4459.3 (7690.7)
	<100 IU/dL	2 (28.6)
Baseline pNRS, mean (SD)		7.7 (1.1)
Baseline EASI, mean (SD)		25.6 (3.1)
EASI at 16w, mean (SD)		3.3 (2.3)
EASI at 40w, mean (SD)		2.9 (1.9)
EASI at 64w, mean (SD)		3.2 (2.2)
Latency to PD, mean (SD), month		17.7 (11.9)
Time to PD remission, mean (SD), month		6.5 (2.9)

Results

Clinical characteristics and sites of DAP



- Psoriasiform dermatitis developed a mean of 17.7 months (range: 3–35 months) after initiation of dupilumab therapy.
- The most commonly affected sites were the upper extremities, particularly the elbows and hands.
  - The head and neck area represented the next most frequent sites of involvement.

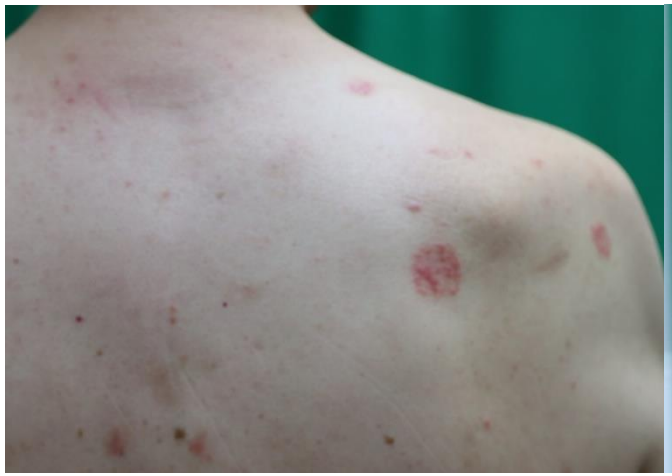
Results

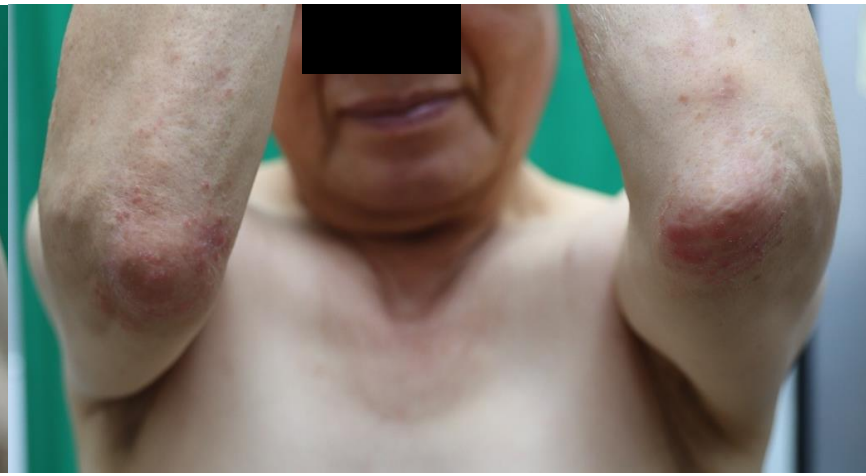
Management of psoriasiform dermatitis

	No. (%)
	Patients (N=7)
Topical agents	
Coticosteroids	2 (28.6)
Vitamin D derivatives with combination TCS	3 (42.9)
Calcineurine inhibitors	2 (28.6)

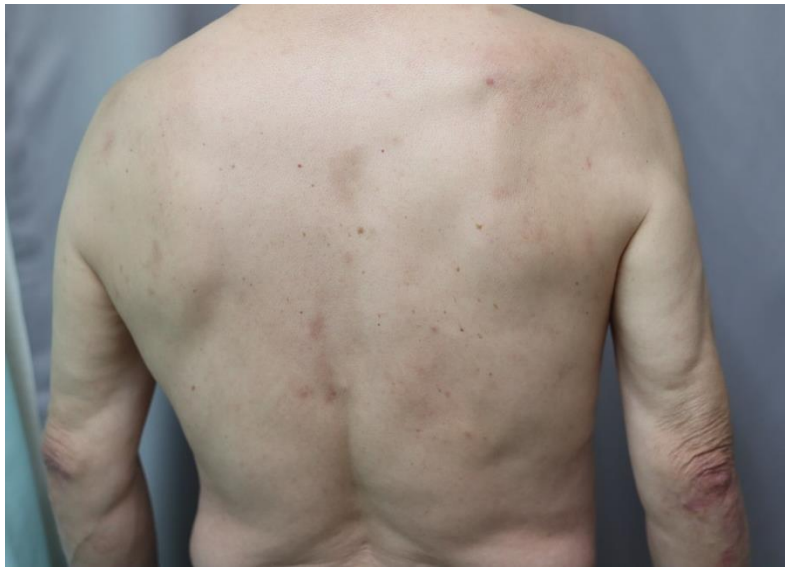
- Psoriasiform dermatitis were controlled by adjusting the dosing interval to every 3 to 4 weeks in combination with topical treatments.
- Other systemic agents were not used.
- In six patients, complete remission of psoriasiform dermatitis was achieved after a mean of 6.5 months (range: 4–11 months).
- However, in one patient, psoriasiform dermatitis did not improve despite adjustment of the dupilumab dosing interval.
- The dosing schedule was reverted to every 2 weeks, but the condition persisted, and a switch to a small-molecule therapy is being considered.

Case





- Psoriasiform dermatitis was reported after 64 weeks of dupilumab treatment (following the 28th injection).
- The affected sites included the back and upper extremities, particularly the elbows.
- Dupilumab administration was modified to a 3-week interval.
- The patient also used topical corticosteroids.
- After 6 months, clinical improvement of the psoriasiform lesions was achieved.



Discussion

- In our cohort, psoriasiform dermatitis developed after a mean of 17.7 months of dupilumab therapy, which is consistent with previous studies reporting that psoriasis can occur 1 to 30 months after treatment initiation.
- The most commonly affected sites were the upper extremities, particularly the elbows and hands. This finding aligns with previous studies showing that DAP most frequently occurs at the extremities.
- The mean age of our subjects was 61 years, suggesting that elderly Asian male patients with atopic dermatitis may be more susceptible to developing psoriasiform dermatitis.

Potential mechanisms for the atopic dermatitis - psoriasis phenotypic switch

- Recent studies have found that PsO and AD are not isolated diseases but two opposite poles of the same Th17-Th2 cell polarization spectrum.
- Dupilumab blocks IL-4 and IL-13 signaling, suppressing the Th2 pathway.
- This blockade removes the inhibitory effect of IL-4/IL-13 on IL-23 production and Th17 cell activity, resulting in upregulation of IL-23 and de novo IL-17A expression.
- The immune balance shifts toward Th17 polarization, driving keratinocyte hyperproliferation and psoriasiform inflammation.
- Patients with a higher intrinsic Th17 component (e.g., Asian ethnicity, chronic AD) may be more susceptible to this immune shift.
- Additionally, AD-related barrier dysfunction can lead to more frequent self-stranded DNA recognition and thus lead to the development of psoriasis.

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Extending the dosing interval of dupilumab

- Psoriasiform dermatitis during dupilumab treatment represents a dynamic immunophenotypic shift rather than simple treatment failure.
- Extending the dupilumab dosing interval and using adjunctive topical therapies provided effective management tailored to individual disease activity.
- By extending the dosing interval of dupilumab, serum drug levels and IL-4/IL-13 blockade intensity may partially decline, allowing some recovery of IL-4 signaling.
- This might restore a more physiological Th2/Th17 balance and reduce the risk or severity of DAP.

Algorithm of management of DAP: we suggest