E-mail: howardrm@uw.edu

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Characterizing dupilumab facial redness in children and adolescents: A single-institution retrospective chart review

To the Editor: Dupilumab facial redness (DFR) is an adverse event characterized by new-onset or paradoxical flaring of facial dermatitis reported in approximately 10% of patients receiving dupilumab.[1] Unlike dupilumab ocular surface disease (DOSD), DFR was not reported in dupilumab clinical trials.[1] Although dupilumab has been approved for the treatment of atopic dermatitis in children as young as 6 years, no dedicated studies have been performed to determine whether DFR occurs at similar rates in children and adults. A total of 225 patients were included in the 2 published retrospective chart reviews describing DFR, only 9 of whom are children.[1,2] Here, this study aims to characterize DFR in the pediatric population.

The University of Connecticut Health Center medical records were queried for all patients younger than 18 years who were prescribed dupilumab. Patients were excluded if they were taking dupilumab for a nondermatologic diagnosis, had not yet taken their prescribed dupilumab, or had no follow-up visits since initiating dupilumab. Patients were categorized as prepubertal or postpubertal based on the average ages of puberty (10 years in girls and 11.5 years in boys).[3] This segmentation was performed because one explanation for DFR is that it is a seborrheic dermatitis-like process, which presumably occurs more frequently in postpubertal children.[1,4] This protocol was approved by the University of Connecticut Health Center institutional review board.

Table I. Patient demographics

Variable	Patients with DFR, n (%)	Patients without DFR, n (%)	*P* value
Sex			>.99
Female	4 (31)	9 (69)	
Male	3 (27)	8 (73)	
Age, y			.63
≤10	1 (17)	5 (83)	
11-15	3 (27)	8 (73)	
16-18	3 (43)	4 (57)	
Puberty			.62
Prepubertal	1 (14)	6 (86)	
Postpubertal	6 (35)	11 (65)	
Dosing frequency			.69
Every 1 week	1 (50)	1 (50)	
Every 10 days	0 (0)	1 (100)	
Every 2 weeks	6 (33)	12 (67)	
Every 4 weeks	0 (0)	3 (100)	
Treatment duration, mo			.33
≤6	2 (20)	8 (80)	
7-12	4 (50)	4 (50)	
>12	1 (17)	5 (83)	
Ocular symptoms			.29
No	6 (26)	17 (74)	
Yes	1 (100)	0 (0)	

DFR, Dupilumab facial redness.

We identified 24 children receiving dupilumab (Table I). All children were prescribed dupilumab for treatment of AD. Overall, 7 of 24 (29%) children had documented worsening or new-onset facial dermatitis after starting dupilumab, 2 of whom had documented neck involvement (29%). DFR occurred more frequently in postpubertal children compared to prepubertal children (35% and 14%, respectively; $P = .63$), and there was a higher incidence of DFR with increasing age (17%, 27%, and 43% for ≤10 years, 11-15 years, and 16-18 years, respectively; $P = .63$). Although trends were apparent, they did not achieve statistical significance. Sex, dosing frequency, and dupilumab dosage were not significantly associated with DFR based on chi-square analysis. Additionally, although anecdotal reports have associated DFR with DOSD, only 1 patient (4%) with DFR experienced DOSD in our study (statistical test, $P = .29$).

Our findings suggest that DFR occurs in children and may occur more frequently in postpubertal children. This finding could be explained by a seborrheic dermatitis−like etiology of DFR with interleukin 4 receptor blockade facilitating a T helper

type 17—predominant hypersensitivity response.[5] Importantly, observation of DFR in prepubertal patients does not rule out *Malassezia*-induced seborrheic dermatitis as an etiology because prepubertal patients also develop seborrheic dermatitis, albeit at lower rates.[4] The observed rates in children cannot be directly compared to previously published rates of DFR in adults, because misclassification bias may have underestimated the rates in adults. We treat these patients empirically for a seborrheic dermatitis—like etiology of DFR with ketoconazole 2% cream.

Limitations include this study's retrospective nature, single-institution cohort, small sample size, and risk of misclassification bias. Our study, to our knowledge, is the first dedicated pediatric study for DFR. It suggests that DFR may be more common in postpubertal children than in prepubertal children, which may support a seborrheic dermatitis—like etiology for DFR.

Sonal Muzumdar, BA,[a] Micaella Zubkov, BA,[a] Reid Waldman, MD,[a] Madeline E. DeWane, MD,[b] Rong Wu, PhD,[c] and Jane M. Grant-Kels, MD[a]

From the Department of Dermatology, University of Connecticut Health Center, Farmington, Connecticut[a]; Yale New Haven Hospital, New Haven, Connecticut[b]; and Connecticut Convergence Institute for Translation in Regenerative Engineering, Farmington, Connecticut.[c]

Authors Muzumdar and Zubkov are cofirst authors.

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Reprint requests: Reid A. Waldman, MD, UCONN Dermatology Department, 21 South Rd, Farmington, CT 06032

E-mail: waldman@uchc.edu

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Heritability of tanning addiction: A twin concordance study

To the Editor: Tanning addiction is a dermatologic-psychiatric disorder with characteristics of behavioral addiction, substance use disorder, and other psychiatric disorders. Minimal information exists regarding the unique contribution of genetic components and environmental exposures to tanning addiction. The objective of this study was to estimate concordance rates and heritability of tanning addiction in a twin cohort.

We administered a questionnaire to monozygotic (MZ) and dizygotic (DZ) twin pairs at the 2018 Twins Day Festival (Twinsburg, OH) to evaluate for tanning addiction using the previously validated tanning-modified *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition survey (DSM-IV-TR) (Supplementary Methods; available via Mendeley at http://doi.org/10.17632/k3vwsj4px9.1). We calculated probandwise concordance rates and tetrachoric correlations with 95% confidence intervals (CIs) to measure the degree of concordance for tanning addiction within twin pairs. Structural equation and liability threshold models (Additive genetic variance, Common/shared environmental factors, and individual environmental factors plus measurement Error [ACE model]) (Supplemental Fig 1; available via Mendeley at http://doi.org/10.17632/k3vwsj4px9.1) were created to estimate the liability of additive genetic effects (heritability) and the unique environmental effects of tanning addiction after controlling for age and sex.[1] Both heritability estimates and 95% CIs were determined by using the best-fit model.[2] All analyses were performed using R (R Core Team, Vienna, Austria). This study was approved by the institutional review board of University Hospitals Cleveland Medical Center.

Our sample included 147 DZ and 24 MZ twin pairs; 33.0% of the study population met criteria for tanning addition. Sociodemographic and dermatologic sample characteristics are provided in Table I, Supplemental Table I, and Supplemental