Original Article

Phenotypical Differences of Childhood- and Adult-Onset Atopic Dermatitis

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What is already known about this topic? The risk factors and clinical characteristics of adult-onset atopic dermatitis are poorly understood.

What does this article add to our knowledge? Adults with atopic dermatitis have high rates of self-reported adult-onset atopic dermatitis, lower prevalence of personal or family history of atopic disease, and distinct phenotypes with less flexural lesions and more involvement of the hands and/or head/neck.

How does this study impact current management guidelines? Clinicians caring for patients with atopic dermatitis should recognize the phenotypes associated with adult-onset atopic dermatitis. Further studies are needed to determine whether these phenotypes are associated with different treatment outcomes.

BACKGROUND: Little is known about adult-onset atopic dermatitis (AD).
OBJECTIVE: To determine the associations and clinical characteristics of adult-onset AD.
METHODS: A prospective study of 356 adults with AD (age ≥18 years) was performed using standardized questionnaires and examination. AD severity was assessed using the Patient-Oriented Eczema Measure, Eczema Area and Severity Index, Scoring Atopic Dermatitis, body surface area, and numeric rating scale for itch and sleeplessness. Latent class analysis was used to determine dominant clinical phenotypes. Multivariate logistic regression was used to determine the relationship between adult-onset AD and distinct phenotypes.
RESULTS: One hundred forty-nine adults (41.9%) reported onset of AD during adulthood, with 87 (24.4%) after the age of 50 years. Adult- versus childhood-onset AD was associated with birthplace outside the United States (χ^2, $P = .0008$), but not sex, race/ethnicity, current smoking status, or alcohol consumption ($P \geq .11$); and decreased personal history of asthma, hay fever, and food allergy and family history of asthma and food allergy ($P \leq .0001$ for all). There was no significant difference in the Eczema Area and Severity Index, Scoring Atopic Dermatitis, body surface area, numeric rating scale for itch and sleeplessness, or Patient-Oriented Eczema Measure between adult- and childhood-onset AD (Mann-Whitney *U* test, $P \geq .10$). Latent class analysis identified 3 classes: (1) high probability of flexural dermatitis and xerosis with intermediate to high probabilities of head, neck, and hand dermatitis; (2) high probability of flexural dermatitis and xerosis, but low probabilities of head, neck, and hand dermatitis; and (3) lower probability of flexural dermatitis, but the highest probabilities of virtually all other signs and symptoms. Adult-onset AD was significantly associated with class 1 (multivariate logistic regression; adjusted odds ratio, 5.54; 95% CI, 1.59-19.28) and class 3 (adjusted odds ratio, 14.03; 95% CI, 2.33-85.50).
CONCLUSIONS: Self-reported adult-onset AD is common and has distinct phenotypes with lesional predilection for the hands and/or head/neck. © 2017 American Academy of Allergy, Asthma & Immunology **(J Allergy Clin Immunol Pract 2017;■:■-■)**

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Atopic dermatitis (AD) is an inflammatory skin disorder that commonly affects both children and adults. Most clinical and

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Abbreviations used
AD- Atopic dermatitis
aOR- Adjusted odds ratio
BSA- Body surface area
EASI- Eczema Area and Severity Index
IQR- Interquartile range
LCA- Latent class analysis
NRS- numeric rating scale
POEM- Patient-Oriented Eczema Measure
SCORAD- SCORing Atopic Dermatitis

epidemiological research has focused on childhood AD, but few have studied AD in adults.[1] Recent studies suggest that AD may be more common in adults than previously recognized, with 1-year US prevalence ranging from 3% to 10%.[2,3] The higher than expected prevalence of AD may be attributed to high rates of persistent childhood disease and/or adult-onset disease. One longitudinal study found that 80% of children have persistence of AD symptoms into adulthood, with only 50% achieving a period of disease clearance by the age of 20 years.[4] However, a recent meta-analysis of 44 studies suggested that 50% and 80% of children with AD achieved a period of observed clear skin by 3 and 8 years of follow-up, respectively.[5] Thus, persistence of childhood AD is likely not the only factor contributing to adult AD. Over the past decade, several studies have reported substantial proportions of adults with AD having disease onset in adulthood (≥18 years of age), that is, adult-onset AD.[6-12] We hypothesized that adults with AD have high rates of adult-onset disease.

Previous studies found that foreign-born American children had significantly lower rates of AD than those born in the United States; however, odds of AD in these children increased after having resided in the United States for more than 10 years.[13] Similarly, foreign-born American adults had significantly lower rates of asthma than those born in the United States; the odds of asthma in these adults also increased after having resided in the United States for more than 10 years.[14] These results suggest that foreign-born Americans may have later onset of AD and atopic disease. We hypothesized that adults born outside the United States have higher rates of adult-onset AD.

Still, little is known about the phenotypical differences between childhood AD and adult-onset AD. Recent studies showed an important role of barrier disruption in childhood AD and the atopic march in the development of atopic disease.[15] We hypothesized that adults with adult-onset AD have lower rates of atopic disease than those with long-standing AD and associated barrier disruption since childhood. Moreover, we hypothesized that adult-onset AD may present with different clinical characteristics than childhood disease. The present study sought to determine the proportion of adult AD with adult-onset AD, risk factors, and phenotypical differences of adult-onset AD.

METHODS

Study design

We performed a prospective dermatology practice-based study to determine the predictors of adult-onset AD. Self-administered questionnaires were completed by adult (≥18 years) patients of the eczema clinic before their encounter. Surveys included questions about sociodemographic characteristics, birthplace, and age of moving to the United States for foreign-born Americans. Patients were then evaluated with a medical history and skin examination by a dermatologist. Surveys were administered between January 2014 and June 2016. The study was approved by the institutional review boards of the Northwestern University and informed consent was waived.

Assessment of AD

AD was assessed using the Hanifin and Rajka major and minor criteria.[16] Specific elements presented in this analysis include the major criteria (pruritus, distribution of eczematous lesions, personal or family history of AD, asthma, or hay fever) and the minor criteria (xerosis, ichthyosis, palmar hyperlinearity, keratosis pilaris, age of AD onset, nipple dermatitis, cheilitis, Dennie-Morgan infraorbital folds, facial pallor/erythema, conjunctivitis and eyelid dermatitis, pityriasis alba, dermatitis of the anterior neck folds, history of cutaneous infections, clinical course worsened by environmental or emotional factors, pruritus when sweating). AD severity was assessed using the numeric rating scale (NRS) for itch and sleeplessness, body surface area (BSA) of involved skin, SCORing Atopic Dermatitis (SCORAD), Patient-Oriented Eczema Measure (POEM), and Eczema Area and Severity Index (EASI).

Data processing and statistical methods

All data analyses and statistical processes were performed using SAS version 9.4 (SAS Institute, Cary, NC). Chi-square and Fisher exact tests were used to compare the age of AD onset (<18 years vs ≥18 years) with birthplace in the United States (binary); continent of birth (North America, Canada, South America, Europe, Asia, or Africa); whether AD preceded migration; personal history of asthma, hay fever, food and medication allergy (binary); family history of AD, asthma, hay fever, food and medication allergy (binary); and distribution of eczematous lesions and other signs and symptoms of AD (all binary). Median (interquartile range [IQR]) was determined for the number of combined signs and symptoms, EASI, SCORAD, BSA, NRS-itch, and NRS-sleep. Mann-Whitney *U* tests were used to compare these outcomes between adult- and childhood-onset groups. A 2-sided *P* value of .01 or less was taken to indicate statistical significance for all hypothesis tests.

Latent class analysis (LCA) was used to examine phenotypical patterns of binary variables of 19 signs and symptoms of AD. LCA uses observed categorical or binary data, termed latent classes, to identify patterns. Subjects with similar response patterns are categorized into specific classes. Conditional probabilities were estimated using maximum likelihood to characterize the latent classes by indicating the chance that a member would give a certain response (yes or no) for the specific item. Conditional probability plots are presented, where probabilities closer to 0 or 1 indicate lower or higher chances, respectively. LCA regression models examine the differential effects of individual variables across unobserved classes. The ideal number of latent classes and best-fitting models were selected by minimizing the Bayesian information criterion, consistent Akaike information criterion statistics, and interpretability. Multivariate logistic regression was then performed to determine the association between adult-onset AD and membership in the latent classes. Sex, race/ethnicity, BSA, and EASI were included as covariates to address potential confounding. Adjusted odds ratios (aORs) and 95% CIs were estimated.

Sample size calculation

A priori sample size calculations were performed on the basis of 2 coprimary analyses: the association between adult-onset AD and