Understanding and Managing Atopic Dermatitis in Adult Patients

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Atopic dermatitis (AD) in adults is an important dermatologic disease. Even in patients in whom the clinical presentation is mild, the burden of disease can be considerable. Relatively little has been published on adult AD compared to the body of literature devoted to AD in children, although adults with severe AD are greatly affected by the disease. Even when AD is a mild clinical disease in adults, the psychosocial and economic burden of the disease can be profound. Patients are likely to find it useful if these nondermatologic comorbidities of AD are addressed by health care providers in clinical encounters. The treatment options for AD in adults are the same as those for children with AD, with some modifications.
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In about 90% of patients with atopic dermatitis (AD) in childhood, the disease is diagnosed before 5 years of age. In an estimated 70% to 90% of patients, it resolves before adulthood. Thus, the disease persists into adulthood in 10% to 30% of those diagnosed in childhood, with an estimated prevalence of AD in adults of 1% to 3%.[1] In the older or elderly adult population, the prevalence appears to be much lower,[2,3] but as the ESTHER study (**E**pidemiologische **S**tudie zu Chancen der Verhütung, Früherkennung und optimierten THerapie chronischer **ER**krankungen in der älteren Bevölkerung) in Germany demonstrated, AD incidence is increasing among elderly patients in industrialized countries.[3]

Why Does AD Persist in Some Patients?

The reason for resolution of childhood AD in most patients or for persistence of AD into adulthood in some patients has not been established, but recent research demonstrates that—

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like the predisposition to develop AD itself—persistence or resolution of the disease is genetically determined.

Progress has been made within the last decade toward understanding the long-observed familial predisposition to develop AD, advances made possible by completion of the mapping of the human genome. Loss-of-function mutations in the filaggrin gene (FLG) have been identified as being strongly associated with the development of AD.[4] Subsequent studies determined that the number of FLG copies within genes can vary, with alleles encoded for 10, 11, or 12 copies of the filaggrin monomer.

Based on this understanding, Brown and colleagues[5] conducted a genetic study of more than 800 children with AD and determined that the number of copies of the filaggrin monomer affect how much filaggrin protein is expressed in skin. They demonstrated that the number of copies of FLG is associated with the tendency to develop AD, and speculated that the number of FLG copies might be associated with disease severity in a "dose-dependent" manner—fewer copies, more severe disease; more copies, less severe disease.

Adult-Onset AD

AD beginning in adulthood is an unusual presentation. In 2000, Bannister and Freeman[6] noted that their extensive review of published articles yielded only occasional mentions of adult-onset AD in epidemiologic studies. In their own review of 2604 patients seen in a contact dermatitis clinic, 243 (9%) had onset of AD at 20 years of age or older and had no evidence of contact dermatitis. These authors note that clinicians encounter patients with adult-onset symptoms characteristic of AD, with cases being sometimes severe and disabling. Some of these patients are diagnosed with adult-onset AD because they have a clinical presentation that suggests AD (such as flexural involvement) or because their eczematous dermatitis is accompanied by a history of allergic disease (such as asthma or hay fever) or a family history of atopic disease.

Ozkaya[7] argues that adult-onset AD may demonstrate the typical clinical pattern seen in adults who have maintained their childhood AD (which includes flexural involvement with lichenification), but also may affect the trunk and extremities, with or without flexural involvement. In a retrospective study of 376 consecutive patients with diagnoses of AD (according to the Hanifin-Rajka criteria[8]), Ozkaya[7] found 63 patients (17%) who reported onset of AD symptoms after 18 years of age (reported onset ranged from 18 to 71 years of age, with a mean of 28 years). Seven (11%) of the 63 patients had nonflexural involvement, and, in these patients, patch testing was done to exclude detectable contact dermatitis.

Additional studies are required to characterize further, delineate, and determine criteria for the diagnosis of adult-onset AD. Meanwhile, symptomatic therapy is indicated, following the same strategy that is used for patients with AD in whom the disease has persisted since childhood.

Clinical Presentation

The presentation of AD in adults may differ from that seen in children with the disease. As in childhood, the sites of involvement in adult AD can be anywhere on the body, but the most common areas of involvement in adults are the flexural areas of the arms and legs, the nape of the neck, and the hands. In adults, AD is characterized by a more lichenified, drier appearance than is usually seen in children with AD.

The psoriasiform presentation in adults might be explained by a shift in T helper (T_H) type 2 cells toward the T_H1 phenotype.[9] In a complicated study of 121 elderly patients (mean age, 69 years), Bozek and colleagues[10] found that 25 (21%) of these patients had AD with negative allergy testing and low levels of total IgE. Patients in this group tended to have T_H1 cytokine profiles. However, sensitivity to aeroallergens, especially dust mites, often persists in adults.

Although signs and symptoms tend to be less severe in adults than in children, milder presentations can be severely problematic for adult patients, particularly when the exposed areas of the body are involved, such as the hands, neck, and face. Moreover, a subset of adults can have severe AD that is challenging to manage (Figure 1).

Figure 1 Atopic dermatitis in an adult. This patient has had atopic dermatitis since childhood. At the time of this clinical visit, the patient complained of pruritus and the affected areas were dry and lichenified. In such cases, bacterial colonization is likely, particularly in crusted areas such as the periorificial region shown here. Photo courtesy of Charles N. Ellis, MD.

Infectious Comorbidities in Adult AD

Skin infection is not as common a problem in adults as in children. However, colonization with *S. aureus* in adult patients with AD is high—reported as 86% in one study[11]—and is associated with the severity of disease.[11,12] In addition, colonization with yeast organisms—typically, *Malassezia* species—is common in the head and neck areas.[13,14]

Eczema herpeticum (EH) can be a life-threatening or disfiguring complication of AD in adults as well as in children. The risk for this complication is increased in individuals with AD who have or acquire herpes simplex virus (HSV) infections. Patients with AD should take steps to avoid exposure to individuals with HSV infections, whenever possible. In addition, live vaccination for smallpox (for example, in the military) may generalize to cause eczema vaccinatum in patients with AD. Therefore, these individuals should avoid vaccinations, and those who share a residence with patients with should also avoid such vaccinations to prevent transmission to the patient with AD. Recently, Leung and colleagues[15] reported that it may be possible to determine which patients with AD are at risk for EH infections. In a study involving 64 subjects—24 with a history of this complication (ADEH-positive), 20 without such a history (ADEH-negative), and 20 nonatopic individuals—these investigators found that interferon-γ protein production was significantly lower in the ADEH-positive subjects than in the ADEH-negative and the nonatopic control groups.

Psychiatric and Psychological Comorbidities

The literature on comorbidity in AD has drawn attention to concomitant depression in teenagers and adults (well-established), as well as other mental disorders, including attention-deficit/hyperactivity disorder and autism (under investigation, with emerging evidence). AD is among the group of dermatologic conditions (also including psoriasis, chronic idiopathic urticaria, and alopecia areata) in which a number of psychiatric disorders—including depression—are considered comorbidities. At least 30% of patients with dermatologic diseases have been reported to experience psychiatric disturbances and psychosocial problems.[16] Even mild degrees of severity of AD may be accompanied by a psychiatric comorbidity.[16]

Gupta et al[17] examined the relationship between pruritus and depression in 252 patients with mild to moderate psoriasis (n = 77), AD (n = 143), or idiopathic urticaria (n = 32). Patients were asked to rate the severity of their pruritus on a 10-point scale devised by the investigators. They also completed psychologic rating scales to assess depression (Carroll Rating Scale for Depression), levels of anger, anxiety, and curiosity (Spielberger State-Trait Personality Inventory), and psychopathologic symptom dimensions such as depression, somatization, phobic anxiety, and paranoid ideation (Brief Symptom Inventory). In this study, the severity of pruritus in all groups of patients correlated with their levels of depression, which suggests that patients with more severe depression have a lower itch threshold, or that more severe pruritus results in higher depression scores.

Suicidal ideation is a risk in patients with depression, and Kimata[18] reported that such ideation is common in patients with AD. Symptoms of major depression may be detectable during a brief office visit, but clinicians also should be alert to the possibility that patients with AD may be experiencing subclinical depression, characterized by less dramatic manifestations, such as a decrease in energy and interest in activities that usually bring satisfaction; individuals with subclinical depression often do not perceive themselves as feeling sad.[16]

In addition to frank psychiatric disturbances, AD is associated with psychosocial and quality-of-life impairment, a relationship that has long been recognized by clinicians and patients, and is supported by a large body of evidence in the literature.

In the landmark International Study of Life with Atopic Eczema (ISOLATE),[19] 38% of patients with AD said that their disease affected their choice of occupation, and even those with mild to moderate AD reported an increase the number of sick days taken from work, as well as early retirement. Ten percent of respondents said that they believed they had experienced discrimination in their workplace; one in seven patients said that their careers had been impaired by their disease.

Psychosexual issues also were common: 58% of individuals with AD reported that they had decreased desire for sex, and 37% of partners of those with AD said the condition adversely affected their sexual relationship. Forty-three percent of adults with AD said that they felt awkward about having a partner see or touch their body during a flare of the disease.[19]

Adults with AD also avoid other activities at work and in social- and home-life. The findings in ISOLATE have been supported by other studies.[19-23]

Unfortunately, such issues often are inadequately addressed in clinical encounters involving adult patients.[19,21-23] Only 26% of patients in ISOLATE said that their physicians acknowledged and discussed such problems with them.[19]

Issues that may affect quality of life deserve more attention, and clinicians may wish to consider screening their patients with AD for possible clinical or subclinical psychiatric disturbances. Some patients may benefit from treatment with antidepressants or other psychotropic medications, as well as psychotherapy. Dermatologists and other clinicians who treat adult patients with AD also should be prepared to refer these patients to appropriate mental health professionals for evaluation and possible treatment when these issues are identified.

Treatment of AD in Adults: Special Considerations

With a few modifications, treatment options for adults with AD are the same as those for children with the disease (see the article by Paller et al[24] on page S10 of this supplement). Because adult patients tend to have thicker, more lichenified skin, more aggressive measures may be needed to bring signs and symptoms under control. Unfortunately, only 25% of

patients and their caregivers in the ISOLATE study feel confident that they can manage AD flares adquately, and 75% reported that being able to have such control would be "the single most important improvement" in their quality of life.[19]

For mild to moderate disease in adults, higher-potency topical agents (corticosteroids or topical calcineurin inhibitors [TCIs]) are the mainstays of therapy. However, the ISOLATE survey[19] revealed that 58% of patients restricted their use of topical corticosteroids because of concerns about side effects, and 66% said they use these medications "only as a last resort." Thus, it is evident that adult patients with AD require education from their health providers about the realistic risks and benefits associated with the use of topical medications, including both corticosteroids and noncorticosteroid agents such as TCIs.[25,26]

For adult patients with severe AD that does not respond to topical therapy, treatments include phototherapy—narrowband ultraviolet B, ultraviolet A, or both.[27-29] Systemic immunosuppressants also are recognized therapeutic options in severe cases of AD. Patients in whom these agents are used—including methotrexate, azathioprine, mycophenolate mofetil, and oral calcineurin inhibitors (cyclosporine or tacrolimus)—should be followed carefully, and laboratory monitoring should be performed, as described in the article by Paller et al.[24]

If the skin in an adult patient with AD looks superficially infected (for example, the presence of pustules or weeping of serous fluid), bacterial cultures should be obtained and appropriate antibiotic therapy instituted. In some patients, antibiotic treatment may be helpful, even in the absence of frank infection.

Emerging understanding of the underlying pathogenesis and related molecular processes of AD has led to attempts to influence these mechanisms. For example, based on the discovery of the association between IgE-mediated inflammatory responses and eczematous skin signs and symptoms, and on the success of treatment to reduce IgE serum levels in patients with asthma, some have proposed the potential benefit of reducing serum IgE levels in patients with AD. A study of a small group of adults with severe AD did not yield promising results.[30] However, Vigo and colleagues[31] studied the effects of anti-IgE treatment on skin symptoms in two pediatric and five adult patients with AD who were being treated with the anti-IgE monoclonal antibody omalizumab for their asthma. In this study, the anti-IgE strategy showed substantial benefit for the skin component.

Similarly, the association of IgE-mediated activation of skin mast cells in patients with AD, the advances in understanding of the roles of innate and adaptive immunity and skin barrier function/dysfunction,[32] and the success of the leukotriene receptor antagonist montelukast in asthma and allergic rhinitis prompted the study of this agent in AD. However, a 4-week, randomized, double-blind, placebo-controlled trial of 59 adult patients with moderate to severe AD by Veien and colleagues[33] failed to demonstrate a significant difference in efficacy between the montelukast and placebo-treated groups. A subsequent 8-week, randomized, placebo-controlled trial of montelukast in adults with AD conducted

by Friedmann and colleagues[34] also failed to demonstrate significant benefit.

Others have examined the potential benefits in AD of topical cromolyn sodium lotion[35] (some success), probiotic treatment with microorganisms such as *Lactobacillus*[36] and oral supplementation with essential fatty acids[37] (no significant benefit likely), and Chinese herbal remedies[38] (not enough evidence from clinical trials to establish or rule out benefit).

Conclusion

Relatively little has been published on AD in adults compared to the literature available regarding AD in pediatric patients. Treatment of AD signs and symptoms in adults is not radically different from that used in younger patients; all of the options available for children may be considered for adults, and modalities—such as ultraviolet therapy—that may not be suitable for some (especially the youngest) pediatric patients may be quite effective in adults.

A substantial gap exists in treatment of AD in adults with respect to the recognition and management of quality-of-life issues and psychiatric comorbidities. Addressing these comorbidities provides an important opportunity to improve the treatment of AD in adults.

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