



Editorial

The importance of considering mental health in the management of atopic dermatitis across the lifespan



Atopic dermatitis (AD) is a complex allergic skin disease associated with multiple allergic comorbidities including asthma and food allergy. Recently, there has been an increased focus on mental health issues, which adversely affect the quality of life and can complicate the management of this chronic skin disease.^{1,2} Many studies have noted the impact of AD on sleep, anxiety, depression, and even suicide.^{3–5} Atopic dermatitis classically begins in early infancy, but it has a bimodal distribution and older adults can also experience a new onset of persistent AD; thus, it is important to address these comorbidities in the older population. The impact of AD on cognitive function has been studied,⁶ but its role in the onset of dementia has not been investigated.

In the current issue of the *Annals of Allergy, Asthma & Immunology*, Pan et al⁷ published their findings of a longitudinal study in Taiwan, Republic of China. They enrolled 1059 patients with AD and 10,590 controls who were matched by age, sex, residence, income, and comorbidities. New-onset dementia was more frequent in patients with AD (2.5% vs 0.7%, $P < .001$), and these patients had an earlier age of dementia onset (74.98 years old vs 80.09 years old, $P = .003$). Using Cox regression analyses after adjustment for demographics and comorbidities, it was found that patients with AD also had an increased risk for developing dementia (hazard ratio, 2.02; 95% confidence interval, 1.24–3.29). The incidence of any dementia diagnosis was evaluated, and the risk of developing Alzheimer's disease was especially high. This study emphasizes the need to focus on the second peak of AD in middle-aged and older individuals.

These findings further connect what we know regarding the multiorgan aspect of AD. In older adults, diagnoses of hypertension, obesity, diabetes mellitus, and dyslipidemia are commonplace; these have been identified as dementia-related risk factors. Many of these conditions are associated with diet and lifestyle behaviors that have systemic consequences and promote cerebrovascular disease. Patients with AD have a higher odds of engaging in these predisposing behaviors, such as cigarette smoking, alcohol consumption, and decreased physical activity.¹ In addition, the relationship between AD and sleep disturbances has a significant impact on fatigue and daytime symptoms⁸; this is associated with a higher odds of diabetes, hypertension, obesity, and dyslipidemia.¹ The underlying pathophysiology of AD then compounds this picture as the type 2 inflammation involved in AD also contributes to the circulation of inflammatory cytokines affecting the vasculature. Patients with AD have immune dysregulation, and extension of these factors beyond the blood-brain

barrier may promote the players involved in Alzheimer's disease and dementia.

In this study, the authors identified patients with AD and dementia on the basis of the International Classification of Diseases, Ninth Revision codes. The diagnosis of dementia was documented by psychiatry or neurology providers, and Alzheimer's disease was also captured by relevant prescribed medication therapies. Although this improved the validity, the limitations associated with registry-based longitudinal studies are present. There is a risk of underreporting of outcomes, and the results of this study do not confer causality. Data before 1996 was also unavailable, so childhood AD diagnoses were not identified. Despite these limitations, the authors present novel data on the relationship between AD and dementia.

Alzheimer's dementia is a progressive disease characterized by declining cognition for which there is no cure.⁷ Further studies of the relationship between the inflammatory cytokines involved in AD and the formation and interplay of the amyloid- β peptides and tau protein is necessary to directly associate these 2 conditions. Beyond the knowledge that interleukin 6 and interleukin 1 can impact neuroinflammation across the blood-brain barrier, future studies are necessary to understand the mechanisms linking AD and Alzheimer's disease. Vascular dementia is likewise associated with high morbidity and mortality, characterized by ischemia from diseased vasculature. Risk factors include hypertension, diabetes mellitus, dyslipidemia, and smoking.¹ Although the observation between AD and cardiovascular disease has been made in various published studies,¹ the mechanisms are still unclear.

With the increasing incidence of AD, the emphasis needs to shift toward comprehensive care of older adults that includes evaluation for early signs of dementia and dementia-related risk factors such as diabetes and hypertension. The direct relationship between AD and dementia must be further studied to understand the mechanisms involved. Perhaps the more important question is whether the treatment of AD modifies the risk factors. Mental health comorbidities have been well studied in patients with AD. Among those with depression, appropriate treatment for AD using topical, oral, or biologic therapies has improved depression in patients.¹ With the advances in AD treatment, biologics such as dupilumab have also been found to not only relieve skin symptoms, but also improve the quality of life, anxiety, and depression symptoms.⁹ Thus, it will be prudent to evaluate whether the effective treatment of AD also decreases dementia onset later in life.

Overall, this study by Pan et al⁷ presents novel findings on the relationship between dementia and AD, given that individuals with AD have an increased risk for not only developing dementia but also having an earlier age of dementia onset. Further mechanistic and

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treatment studies will allow us to understand the relationship between these 2 diseases. For now, this study provides a reminder that the treatment for AD is multidisciplinary. In the light of these new findings, screening for sleep, anxiety, and depression symptoms is not enough. Atopic dermatitis affects individuals across the life-span, and older adults have associated morbidity. In these patients, clinicians ought to screen for memory and cognitive decline so proper dementia care can be pursued.

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