Alopecia areata is a medical disease

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Alopecia areata (AA) is a common autoimmune disease characterized by nonscarring hair loss that affects all ages, both sexes, and all skin types. Despite significant advances in understanding the pathomechanism of the disease, the autoimmune comorbidities, and how quality of life (QoL) is affected, treatment for AA is still not considered medically necessary by many insurers and even some physicians.

The lifetime prevalence of AA is approximately 2%, regardless of sex or ethnicity.[1,2] AA typically affects patients <40 years of age, with roughly 50% seeking treatment before 20 years of age.[3,4] Approximately 20% of patients have a positive family history, with reported monozygotic twin concordance rates ranging from 42% to 55%.[5] Although up to 50% of patients with limited patchy hair loss might experience spontaneous regrowth, the prognosis for spontaneous regrowth in patients with extensive disease is poor, though this has not been well documented.[6]

Numerous studies support the conclusion that AA is an autoimmune disease, driven by cytotoxic T lymphocytes directed against the hair follicle.[7,8] Similar to other immune-mediated diseases, the human leukocyte antigen locus is a risk factor for AA.[9] Recently, signaling pathways that converge on downstream effector Janus kinases have been identified in the pathogenesis of AA, leading to the successful use of Janus kinase inhibitors in patients with extensive AA.[10-15]

Abbreviations used:

AA: alopecia areata
QoL: quality of life

The manifestations of AA and its associated disorders extend beyond the hair follicle. Forty-six percent of patients present with nail findings, the most common of which is nail pitting, followed by trachyonychia.[16] There is a strong association between AA and other autoimmune diseases, the most common of which is thyroid disease, with approximately 19% of AA patients affected.[17] Other autoimmune conditions associated with AA include vitiligo, psoriasis, lupus erythematosus, and rheumatoid arthritis.[18,19] Patients with AA have a significantly increased risk for atopic dermatitis, allergic rhinitis, and asthma.[20] Nutritional deficiencies,

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including vitamin D and iron deficiency, are also more common in AA patients.[18] Finally, patients with AA have been found to have higher rates of sensorineural hearing loss.[21]

Alopecia areata adversely affects QoL of afflicted patients. Hair has social and psychological significance beyond its biologic function.[22] Therefore, it is not surprising that many patients with AA experience significant psychological distress. Specifically, depression, anxiety, and sleep problems are more prevalent in both adults and children with AA compared with the general population.[17,23] Furthermore, reports of suicide in children and adults with AA are concerning.[24,25]

QoL studies have emerged as invaluable tools to understanding the impact a disease has on affected individuals. Patients with AA experience diminished QoL at levels comparable to patients with chronic skin diseases, such as psoriasis and atopic dermatitis.[26,27] The AA patients who experienced the lowest QoL scores were young (age <50 years), female, and had more widespread involvement of hair loss.[28] First-degree relatives of patients with AA also had higher rates of anxiety, affective disorders, and substance abuse.[29]

AA has a profound economic impact on patients, third party payers, and governmental agencies. Understanding the burden of the disease is key to prioritizing health care resources. In 2010, the Global Burden of Disease study estimated the disability of 291 diseases in patients of all ages within 187 countries during 1990-2010.[30,31] AA ranked 137 out of 176 in terms of disability burden; this burden was experienced across various geographic regions, with a stable ranking over the past 2 decades.[31] For comparison, AA ranked higher than psoriasis (144/176), melanoma (138/176), and nonmelanoma skin cancer (150/176).[32] Despite recent increases in National Institutes of Health's funding for alopecia areata, it is still strikingly low relative to its disease burden.[33]

In summary, AA is a complex autoimmune disease that has a severe negative impact on QoL and accounts for a significant global disease burden. In conclusion, AA should be considered in a medical context by dermatologists and other health care providers, and treatment should be a priority.

REFERENCES

1. Safavi KH, Muller SA, Suman VJ, et al. Incidence of alopecia areata in Olmsted County, Minnesota, 1975 through 1989. *Mayo Clin Proc*. 1995;70(7):628-633.
2. Villasante Fricke AC, Miteva M. Epidemiology and burden of alopecia areata: a systematic review. *Clin Cosmet Investig Dermatol*. 2015;8:397-403.
3. Shellow WV, Edwards JE, Koo JY. Profile of alopecia areata: a questionnaire analysis of patient and family. *Int J Dermatol*. 1992;31(3):186-189.
4. Kyriakis KP, Paltatzidou K, Kosma E, et al. Alopecia areata prevalence by gender and age. *J Eur Acad Dermatol Venereol*. 2009;23(5):572-573.
5. Rodriguez TA, Fernandes KE, Dresser KL, et al. Concordance rate of alopecia areata in identical twins supports both genetic and environmental factors. *J Am Acad Dermatol*. 2010;62(3):525-527.
6. Alkhalifah A, Alsantali A, Wang E, et al. Alopecia areata update: part I. Clinical picture, histopathology, and pathogenesis. *J Am Acad Dermatol*. 2010;62(2):177-188; quiz 189-90.
7. Islam N, Leung PS, Huntley AC, et al. The autoimmune basis of alopecia areata: a comprehensive review. *Autoimmun Rev*. 2015;14(2):81-89.
8. Gilhar A, Schrum AG, Etzioni A, et al. Alopecia areata: animal models illuminate autoimmune pathogenesis and novel immunotherapeutic strategies. *Autoimmun Rev*. 2016;15(7):726-735.
9. Xing L, Dai Z, Jabbari A, et al. Alopecia areata is driven by cytotoxic T lymphocytes and is reversed by JAK inhibition. *Nat Med*. 2014;20(9):1043-1049.
10. Betz RC, Petukhova L, Ripke S, et al. Genome-wide meta-analysis in alopecia areata resolves HLA associations and reveals two new susceptibility loci. *Nat Commun*. 2015;6:5966.
11. Liu LY, Craiglow BG, Dai F, et al. Tofacitinib for the treatment of severe alopecia areata and variants: a study of 90 patients. *J Am Acad Dermatol*. 2016;76(1):22-28.
12. Craiglow BG, Liu LY, King BA. Tofacitinib for the treatment of alopecia areata and variants in adolescents. *J Am Acad Dermatol*. 2016;76(1):29-32.
13. Craiglow BG, Tavares D, King BA. Topical ruxolitinib for the treatment of alopecia universalis. *JAMA Dermatol*. 2016;152(4):490-491.
14. Mackay-Wiggan J, Jabbari A, Nguyen N, et al. Oral ruxolitinib induces hair regrowth in patients with moderate-to-severe alopecia areata. *JCI Insight*. 2016;1(15):e89790.
15. Jabbari A, Nguyen N, Cerise JE, et al. Treatment of an alopecia areata patient with tofacitinib results in regrowth of hair and changes in serum and skin biomarkers. *Exp Dermatol*. 2016;25(8):642-643.
16. Tosti A, Morelli R, Bardazzi F, et al. Prevalence of nail abnormalities in children with alopecia areata. *Pediatr Dermatol*. 1994;11(2):112-115.
17. Miller R, Conic RZ, Bergfeld W, et al. Prevalence of comorbid conditions and sun-induced skin cancers in patients with alopecia areata. *J Investig Dermatol Symp Proc*. 2015;17(2):61-62.
18. Muller SA, Winkelmann RK. Alopecia areata. An evaluation of 736 patients. *Arch Dermatol*. 1963;88:290-297.
19. Chu SY, Chen YJ, Tseng WC, et al. Comorbidity profiles among patients with alopecia areata: the importance of onset age, a nationwide population-based study. *J Am Acad Dermatol*. 2011;65(5):949-956.
20. Mohan GC, Silverberg JI. Association of vitiligo and alopecia areata with atopic dermatitis: a systematic review and meta-analysis. *JAMA Dermatol*. 2015;151(5):522-528.
21. Ucak H, Soylu E, Ozturk S, et al. Audiological abnormalities in patients with alopecia areata. *J Eur Acad Dermatol Venereol*. 2014;28(8):1045-1048.
22. Cash TF. The psychology of hair loss and its implications for patient care. *Clin Dermatol*. 2001;19(2):161-166.

23. Bilgic O, Bilgic A, Bahali K, et al. Psychiatric symptomatology and health-related quality of life in children and adolescents with alopecia areata. *J Eur Acad Dermatol Venereol*. 2014; 28(11):1463-1468.
24. Sinclair RD. Alopecia areata and suicide of children. *Med J Aust*. 2014;200(3):145.
25. Layegh P, Arshadi HR, Shahriari S, et al. A comparative study on the prevalence of depression and suicidal ideation in dermatology patients suffering from psoriasis, acne, alopecia areata and vitiligo. *Iran J Dermatol*. 2010;13(54):106-111.
26. Rencz F, Gulácsi L, Péntek M, et al. Alopecia areata and health-related quality of life: a systematic review and meta-analysis. *Br J Dermatol*. 2016;175(3):561-571.
27. Liu LY, King BA, Craiglow BG. Health-related Quality of life (HRQoL) among patients with alopecia areata (AA): a systematic review. *J Am Acad Dermatol*. 2016;75(4):806-812.
28. Shi Q, Duvic M, Osei JS, et al. Health-related quality of life (HRQoL) in alopecia areata patients-a secondary analysis of the National Alopecia Areata Registry data. *J Investig Dermatol Symp Proc*. 2013;16(1):S49-S50.
29. Colon EA, Popkin MK, Callies AL, et al. Lifetime prevalence of psychiatric disorders in patients with alopecia areata. *Compr Psychiatry*. 1991;32(3):245-251.
30. Karimkhani C, Boyers LN, Naghavi M, et al. The global burden of disease associated with alopecia areata. *Br J Dermatol*. 2015; 172(5):1424-1426.
31. Hay RJ, Johns NE, Williams HC, et al. The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions. *J Invest Dermatol*. 2014;134(6):1527-1534.
32. Karimkhani C, Boyers LN, Prescott L, et al. Global burden of skin disease as reflected in Cochrane Database of Systematic Reviews. *JAMA Dermatol*. 2014;150(9):945-951.
33. Hagstrom EL, Patel S, Karimkhani C, et al. Comparing cutaneous research funded by the US National Institutes of Health (NIH) with the US skin disease burden. *J Am Acad Dermatol*. 2015;73(3):383-391.e1.