Title
Alopecia Areata is Associated with Risk of Inflammatory Arthritis

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Alopecia areata is associated with risk of inflammatory arthritis

To the Editor: Genome-wide association studies in patients with alopecia areata (AA) suggest that susceptibility loci predispose them to a range of autoimmune conditions.[1] Patients with AA have a high burden of comorbid inflammatory conditions such as atopic dermatitis, psoriasis, and systemic lupus erythematosus.[2] At our institution, it has been observed that many patients with AA have a personal or family history of inflammatory arthritic conditions [N.A.M.]. In this study, we utilized a global health research network database consisting of medical records from 75 health care organizations (TriNetx) to determine if an association between AA and inflammatory arthritis exists.

After obtaining a cohort of patients with AA from the database, a control cohort of age, sex, and race matched patients without AA was generated. International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) codes were used to identify the prevalence and risk of various inflammatory arthritic conditions in the AA cohort. Odds ratios (ORs) were subsequently generated by TriNetx and validated by research statisticians.

A total of 46,682 patients with AA were identified, 65% female, mean age 34.7 years (Table I). Patients with AA had a significantly higher risk of developing psoriatic arthritis (OR = 2.344, $P < .0001$), rheumatoid arthritis (OR = 2.09, $P < .0001$), and ankylosing spondylitis (OR = 1.68, $P = .0021$) compared to controls (Table II). The mean age of these AA-arthritis subgroup cohorts at the time of data collection was 49.2, 52.1, and 44.3 years old, respectively. Patients with AA and concomitant inflammatory arthritis were predominantly female, with the highest proportion being in the AA and rheumatoid arthritis subgroup (84% female). Similarly, AA was found to be associated with the development of "other crystal arthropathies" (OR, 1.763; $P < .0001$; mean age, 67.3 years old) and "other inflammatory arthropathies" (OR, 1.631; $P < .0001$; mean age, 56.2 years old). Gout occurred at similar rates between the cohorts.

These findings of AA associated with inflammatory arthritis support outcomes from genome-wide association studies identifying shared polymorphisms in human leukocyte antigens and interleukin genes amongst inflammatory diseases.[1] For example, human leukocyte antigen-B27 has been identified as a high-risk haplotype for developing AA (patchy and totalis/universalis), and significant in recurrent AA patients, but not those with a positive family history.[3] The observed association of AA with rheumatoid arthritis supports results from a previous study in a young Taiwanese population (AA onset 11-20 years old; OR, 2.57).[2] Therapies targeting Janus kinase pathway inhibition have demonstrated efficacy in rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, and AA.[4] Importantly, increased risk of gout was absent in patients with AA, relevant as probenecid, an organic anion transporter 3 (OAT3) inhibitor, can interact with baricitinib and require dosage adjustment.[5]

In this large-scale cohort study, patients with AA and inflammatory arthritis were older (average age, 54.4 years old), raising the question of whether we should screen patients with AA for arthritis and at what age. Initiation of systemic treatment, such as JAK inhibitors, may hold benefits for comorbid diseases. Study limitations include the retrospective nature of data collection, potential misclassification of ICD-10 coded diagnoses, and inability to establish the sequence of arthritis and AA diagnoses in the prevalence analysis with certainty.

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Conflicts of interest

None disclosed.

Table I. Patient demographic information for alopecia areata cohort and control cohort after propensity score matching for age, sex, and race (left)

	AA and control cohorts			Prevalence of inflammatory arthritic conditions in AA cohort					
	All AA (*n* = 46,682)	Control cohort (*n* = 46,682)	*P* value	PsA (*n* = 363)	AS (*n* = 135)	RA (*n* = 1761)	Gout (*n* = 979)	Other crystal arthropathy (*n* = 271)	Other inflammatory arthropathy (*n* = 1091)
Age, mean (SD) y	34.7 (20.8)	34.8 (20.9)	.36	49.2 (15.3)	44.3 (16.8)	52.1 (16.8)	57.6 (15.1)	67.3 (13)	56.2 (15.6)
Sex, no. (%)									
Female	30,506 (65)	30,506 (65)	1	274 (75)	97 (72)	1483 (84)	546 (56)	216 (80)	891 (82)
Male	16,176 (35)	16,176 (35)	1	89 (25)	38 (28)	278 (16)	433 (44)	55 (20)	200 (18)
Race, no. (%)									
White	26,841 (58)	26,841 (58)	1	292 (80)	97 (72)	1199 (68)	650 (66)	204 (75)	767 (70)
Black or African American	7744 (17)	7744 (17)	1	18 (5)	14 (10)	314 (18)	198 (20)	38 (14)	184 (17)
Asian	1966 (4)	2095 (4)	.038	9 (3)	6 (5)	36 (2)	27 (3)	7 (3)	21 (2)
Other/ unknown	10,131 (21)	10,002 (21)	.31	44 (12)	18 (13)	212 (12)	104 (11)	22 (8)	119 (11)

Overall prevalence of inflammatory arthritic conditions in alopecia areata cohort and each group's respective demographic information (right).
ICD-10 codes used: AA = L63.x; PsA = L40.5; RA = M05.x, M06.x; Gout = M10.9, Other crystal arthropathies = M11.x; AS = M45.x; Other inflammatory arthropathies = M46.1, M46.8, M46.9.
AA, Alopecia areata; *AS*, ankylosing spondylitis; *PsA*, psoriatic arthritis; *RA*, rheumatoid arthritis.

Table II. Risk of developing inflammatory arthritic conditions in alopecia areata cohort compared to control cohort ($n = 46{,}682$ each). Timeframe: any time after index event (ie, AA diagnosis)

Arthritis type	AA, no. (%)	Control, no. (%)	OR	95% CI	*P* value
Psoriatic arthritis	271 (0.581)	116 (0.248)	**2.34**	**1.88-2.91**	**<.0001**
Rheumatoid arthritis	1248 (2.673)	597 (1.279)	**2.09**	**1.92-2.34**	**<.0001**
Other crystal arthropathies	176 (0.377)	100 (0.214)	**1.76**	**1.38-2.25**	**<.0001**
Ankylosing spondylitis	94 (0.201)	56 (0.12)	**1.68**	**1.20-2.34**	**.0021**
Other inflammatory arthropathies	636 (1.362)	392 (0.84)	**1.63**	**1.43-1.85**	**<.0001**
Gout	666 (1.427)	608 (1.302)	1.09	0.98-1.22	.1019

Bold text denotes significance at $P \leq .05$.
AA, Alopecia areata; *OR*, odds ratio.

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Comparative efficacy of biologics and oral agents in palmoplantar psoriasis and palmoplantar pustulosis: A systematic review and network meta-analysis of randomized clinical trials

To the Editor: Topicals and phototherapy often fail to improve the diseases palmoplantar psoriasis (PP) and palmoplantar pustulosis (PPP); however, the comparative efficacy of biologic and oral agents in PP/PPP are not well established.[1] Here, we compare the efficacy of biologic and oral treatments in PP and PPP using a network meta-analysis (NMA).

Eligible publications were phase 2 to 4 randomized controlled trials (RCTs) reporting the severity metrics of palmoplantar disease at 12 to 16 weeks.