Is androgen excess masked in alopecia areata patients: a retrospective data analysis of 1,587 patients

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Introduction

Alopecia areata (AA) is a common non-scarring inflammatory hair loss. AA is considered to be a T cell dependent autoimmune disease in which a complex interplay between genetic and epigenetic factors leads to a heterogenous clinical presentation and disease progression.

Current evidence suggests that environmental triggers, such as emotional stress, increase the release of stress induced corticotropin-relasing hormone (CRH) thus altering the hypothalamic pituitary axis (HPA) as well as the hair follicle microenvironment, potentially playing a role in the severity or course of AA[(Ito,Kim,Islam)].

Objective

The objective of this study was to assess for the prevalence of a hormonal and/or endocrine disorder among AA patients.

Materials & Methods

A retrospective study was conducted using an institutional review board approved database of 1,587 AA patients diagnosed at the Cleveland Clinic Department of Dermatology from 2005 to 2015. Inclusion criteria included available laboratory hormonal levels and/or past gynecological history. Patients were categorized into one of four AA subtypes: patchy alopecia, alopecia areata ophiasis subtype, alopecia totalis, or alopecia universalis. To compare the prevalence of hormonal dysfunction compared to the general population levels of polycystic ovarian syndrome (PCOS), 95% confidence intervals for the prevalence were created, and tests against 6% (the upper limit for PCOS prevalence in the general population) were performed. The distribution of dysfunction types were compared using one-sample goodness of fit chi-square tests. Pearson chi-square tests were used to compare groups defined by diagnosis or dysfunction on various characteristics. One-sided one-sample t-tests compared diagnosis groups against the lower normal limit for vitamin D (20ng/mL). Analyses were performed using SAS software (version 9.3; Cary, NC).

Table 1.

Comparison of Hormonal Dysfunction Prevalence Against Prevalence of PCOS in Normal Population.

Group	Hormonal Dysfunction	Total	%	95% CI	Population Level	p-value
AA	226	1587	14.2	(12.6, 16.1)	6%	<0.001

Table 2a-b.

Comparisons of distribution of dysfunction overall and by subtype. For all subtypes, statistically significant results were observed (p<0.001 for all except FFA (p=0.001)).

A.

Distribution of dysfunction type for all AA PCOS patients.

Factor	Total (N=226) n	Summary	P-value
Overall Dysfunction	226		<0.001
. 1.Clinical: Hirsutism Only		35(15.5)	
. 2.Adrenal: Androgen Excess/PCOS		96(42.5)	
. 3.Adrenal: Low Androgens		39(17.3)	
. 4.Adrenal: Low/High Androgens		10(4.4)	
. 5.Adrenal: Hirsute/Low Androgens		4(1.8)	
. 6.Ovarian: Cyst Only		37(16.4)	
. 7.Ovarian: Cyst/Low Testosterone		5(2.2)	

B.

Distribution of dysfunction type for Patchy AA PCOS patients.

Factor	Total (N=177) n	Summary	P-value
Overall Dysfunction	177		<0.001
. 1.Clinical: Hirsutism Only		25(14.1)	
. 2.Adrenal: Androgen Excess/PCOS		73(41.2)	
. 3.Adrenal: Low Androgens		36(20.3)	
. 4.Adrenal: Low/High Androgens		8(4.5)	
. 5.Adrenal: Hirsute/Low Androgens		3(1.7)	
. 6.Ovarian: Cyst Only		28(15.8)	
. 7.Ovarian: Cyst/Low Testosterone		4(2.3)	

Table 3.

AA Overall Dysfunction Comparison

Factor	1.Clinical Evidence (N=35)	2.And. Excess PCOS (N=96)	3.Other Adrenal (N=53)	4.Ovarian Dysfunction (N=42)	p-value
No Labs	19(54.3) [23]	3(3.1) [14]	0(0.0) [14]	27(64.3) [23]	***<0.001***[c]
anemia*	9(26.5)	24(25.0)	18(34.0)	13(31.0)	0.67[c]
Menstrual Irregular?*	5(14.7)	25(26.0)	9(17.3)	17(41.5)	***0.023***[c]
Trouble Conceiving?*	1(2.9)	6(6.3)	10(19.2)	4(9.8)	***0.034***[c]
Vit D Deficiency	15(42.9)	59(61.5)	33(62.3)	18(42.9)	0.062[c]
Seb Derm	2(5.7)	19(19.8)	5(9.4)	3(7.1)	0.057[c]
Adult Acne	8(22.9)	39(40.6) [4]	17(32.1)	6(14.3) [2]	***0.013***[c]
Hirsutism	35(100.0) [234]	32(33.3) [14]	14(26.4) [14]	2(4.8) [123]	***<0.001***[c]
Obesity	13(37.1)	37(38.5)	20(37.7)	16(38.1)	0.99[c]
Overweight	4(11.4)	24(25.0)	11(20.8)	11(26.2)	0.36[c]
Diabetes	4(11.4)	5(5.2)	7(13.2)	3(7.1)	0.34[c]
Polycystic ovaries	0(0.0) [2]	21(21.9) [14]	3(5.7)	1(2.4) [2]	***<0.001***[c]
Ovarian Cyst	1(2.9) [4]	10(10.4) [4]	8(15.1) [4]	33(78.6) [123]	***<0.001***[c]
FH Diabetes	15(42.9)	35(36.5)	23(43.4)	21(50.0)	0.50[c]

*Data not available for all subjects..
Values presented as N (column %).
p-values: c=Pearson's chi-square test.
[1]: Significantly different from 1.Clinical Evidence
[2]: Significantly different from 2.And. Excess/PCOS
[3]: Significantly different from 3.Other Adrenal
[4]: Significantly different from 4.Ovarian Dysfunction
A significance level of 0.008 was used for pairwise ad-hoc comparisons.

Results

- A total of 226 alopecia areata patients demonstrated either objective laboratory evidence of hormonal imbalance (i.e. abnormal circulating hormone levels), and/or history of ovarian dysfunction, and/or clinical evidence of androgen excess.
- In comparison to the prevalence of PCOS in the normal population, hormonal and endocrine dysfunction is **approximately 2.4 times more** prevalent in the AA patient population.
- Androgen Excess/PCOS was the most significant dysfunction in all AA subtypes.
- Adult acne, hirsutism, PCOS, and ovarian cysts were significant clinical makers that predicted androgen excess.

Conclusions

The data in the present study revealed an increased prevalence of sex hormone dysfunction among alopecia areata patients. This suggests that altered sex hormone balance may be involved in modulating AA. From this study, however, we were unable to ascertain a causal relationship with AA onset or progression. As sex hormone imbalance may play a role in the course of AA, we suggest androgen excess screening (total testosterone, free testosterone, free testosterone %, DHEAS and androstenedione) in patients that have menstrual irregularities, trouble conceiving, PCOS, ovarian cysts, and/or have clinical evidence of elevated androgens (hirsutism or adult acne). Further studies will be needed to elucidate the benefit of anti- androgen therapy in the clinical management of AA patients.

Acknowledgements

This research was funded by the Health Service Scholorship. Special thanks to my mentor Dr. Wilma Bergfeld M.D.