Hypertension and Cicatricial Hair Loss: Defining High Value Symptom Clusters within Reproductive Aging

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Abstract

Although hot flashes and disturbed sleep receive the most attention during reproductive aging, other concerns such as depression, weight gain, fatigue and hair loss also cause women to go to the doctor. In this cohort, African American and Caucasian women with two distinct forms of cicatrical hair loss had increased risk of hypertension as compared to their respective control groups. Hypertension has a strong association with the renin-angiotensin-aldosterone system (RAAS). RAAS participates in the generation of fibrosis. The co-occurrence of cicatrical hair loss and hypertension in women may have overlapping biologic origins.

Keywords

Hypertension, Mineralocorticoid receptor, Renin angiotensin aldosterone system (RAAS), Central centrifugal cicatricial alopecia, Frontal fibrosing alopecia

Introduction

Women have vastly different experiences during reproductive aging. Changes in appearance, particularly weight gain and hair loss, lead to medical engagement in ways preventive medicine does not. Two forms of cicatrical hair loss are increasing in frequency, central centrifugal cicatricial alopecia (CCCA) and frontal fibrosing alopecia (FFA). CCCA and FFA have epidemiologic features such as gender, racial predominance, scalp site specificity and an association with the reproductive axis that are suitable for longitudinal database modeling [1-3]. In this study, both African American and Caucasian women with cicatrical hair loss had a higher risk of hypertension.

CCCA is more common in African American women and appears at a younger age than FFA. CCCA affects the crown and vertex of the scalp [4-6]. FFA is more common in Caucasian women, appears near the menopausal transition or beyond, and affects the eyebrows and frontal hairline [7-10]. Targeted destruction of the pilosebaceous unit in women during reproductive aging may share proinflammatory mechanisms with hypertension.

Methods

This study received approval from the University of Missouri Kansas City Institutional Review Board and informed written consent was obtained from all patients. Age, BMI, race, type of hair loss, systolic and diastolic blood pressure readings and presence of antihypertensive medication were collected from each patient. Blood pressure readings were taken at every visit, in the seated position, in one arm via an automated cuff. All but one patient was seen multiple times. The highest blood pressure reading across multiple visits was recorded.

Data from 43 women with scarring hair loss was collected. 22 African American women with CCCA and 21 Caucasian women with FFA were compared to an age, race and BMI matched group of women without hair loss. The control group originated from the same clinic. To support randomness in the control group, data was collected from women attending clinic on the 1st, 15th and 30th days of the month. Descriptive statistics, such as mean, standard deviation and proportion were calculated to describe our sample. T tests were conducted to estimate and test group difference on the outcome variables. Statistical analyses were conducted using SPSS version 24.

Results

Both study groups had a mean systolic pressure of...
134 mmHg, as compared to the control group, which had a mean systolic pressure of 118 mmHg (p = value 0.002). A higher mean diastolic pressure was also noted, with mean of 85 mmHg, as compared to the control group mean of 73 mm Hg (p = value 0.092). Eleven of the 17 patients (65%) with CCCA were on antihypertensive medications, with 6 untreated (35%). Five of the 13 (38%) patients with FFA were on antihypertensive medications, with 8 untreated (62%). The control group included 8 patients with hypertension, 6 of whom were on antihypertensive pharmacotherapy.

There were significant age and BMI differences between women presenting with CCCA and FFA. The mean age of AA women presenting with CCCA was 47.31 with a self-reported age of onset at 42.36. The mean age of Caucasian women presenting with FFA was 66.58 with an age of onset at 60.72. The mean BMI in AA women with CCCA was 33.45 and the mean BMI in Caucasian women with FFA was 27.19.

**Discussion**

Two of the more common forms of cicatricial hair loss, CCCA and FFA, occur mostly in women and emerge in the later parts of the reproductive axis. Each form of hair loss has distinguishing features such as age of onset, race, predominant scalp region affected and level of overt inflammation. Research in women’s health has identified the latter aspects of the reproductive axis as a critical time in women’s health [11-16]. Coronary artery disease remains the main cause of death in women with hypertension a key modifiable feature. Hypertension appears earlier in women and is more difficult to control, as compared to men [17]. The American Heart Association now identifies menopause as a cardiovascular risk factor [17,18].

Women have vastly different experiences with reproductive aging. Hot flashes start earlier and last longer than previously recognized [19]. The most common symptoms, hot flashes and disordered sleep, correlate with fluctuations in FSH and estradiol [20]. The severity of these two symptoms is factored into cardiovascular risk models [21-24]. Women seeking care for menopausal symptoms undergo evaluation and receive non-symptom related therapies for hypercholesterolemia, hypertension and osteoporosis [25,26]. The pharmaceutical burden can be substantial and complicate the evaluation of off target effects, such as depression and hair loss [27,28].

The aldosterone-mineralocorticoid receptor axis is present in many tissues and participates in the regulation of vascular responsiveness and immune function [29]. The mineralocorticoid (MR) and glucocorticoid receptors (GR) control metabolic, hemodynamic and stress responses throughout the body [30,31]. MR and GR are functionally homologous, the engagement of one alters the behavior of the other [32]. Even though cortisol, aldosterone and progesterone all have the ability to bind the MR, the concentration gradient favoring cortisol over aldosterone and progesterone means that most MR is bound with cortisol [33]. MR ligand selectivity is controlled by 11β hydroxysteroid dehydrogenase (HSD), which has tissue specific isoforms. 11β HSD1 ensures cortisol delivery to metabolically active tissues, such as the liver and adipocyte. 11β HSD2 prevents cortisol binding to the MR by converting cortisol to corticosterone, which cannot bind the MR [34]. The clinical expression of ‘typical’ glucocorticoid or ‘typical’ mineralocorticoid response depends on cell type, the predominance of 11β (HSD) types 1 or 2, the level of obesity and the phase of circulating gonadotropin levels.

Progesterone has high affinity for the MR and in general, functions as an antagonist [35]. Progesterone competes with aldosterone during pregnancy and the luteal phase of the menstrual cycle. Ligand selectivity between progesterone and aldosterone is also controlled by enzymatic deactivation, protecting the MR during high progesterone states [36]. Synthetic progestins have varying effects on mineralocorticoid and glucocorticoid related metabolism. Progestin only contraceptives may circumvent the control mechanisms that balance MR and GR expression, as estrogen supports the expression of 11β (HSD) 2. Side effects associated with progestin only contraception, such as weight gain, mood changes and acne, may be clinical reflections of the absence of 11β HSD control of GR/MR ligand receptivity.

Clinicians evaluating women with cicatricial hair loss should assemble symptom clusters that reflect the activation profiles of the MR and GR. Predominant glucocorticoid expressions, such as obesity, history of gestational diabetes, difficulty with satiety, may require different treatment protocols than women presenting with hypertension, luteal phase fluid retention and fibrosis [36-38]. Pregnancy related hypertension and diabetes have predictive effects for cardiovascular and metabolic diseases later in life. These variables should be included in longitudinal studies of women with cicatricial alopecia and hypertension [39-43].

**Conclusions**

The co-occurrence of cicatricial alopecia and hypertension may have utility in modeling fibrosis and vascular aging in women at midlife and beyond. Hypertension has a strong association with the renin-angiotensin-aldosterone system (RAAS). RAAS is known to participate in fibrosis. The search for factors associated with cicatricial alopecia and hypertension should include a detailed pregnancy history, exposure to synthetic progestins and itemization of drugs known to influence the renin-angiotensin-aldosterone system.

**Limitations**

This is a small case control study and the results may not be generalizable. The study was not designed to
Table 1: Group statistics on women with cicatricial alopecia vs. A race, age and BMI.

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Race</th>
<th>BMI</th>
<th>Onset</th>
<th>Systolic</th>
<th>Diastolic</th>
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<td>CCCA</td>
<td>n = 22</td>
<td>47.32</td>
<td>AA</td>
<td>33.45</td>
<td>42.36</td>
<td>133.91</td>
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<tr>
<td>Control</td>
<td>n = 19</td>
<td>53</td>
<td>AA</td>
<td>33.96</td>
<td>117.72</td>
<td>72.79</td>
</tr>
<tr>
<td>FFA</td>
<td>n = 21</td>
<td>66.57</td>
<td>C</td>
<td>27.19</td>
<td>60.72</td>
<td>133.76</td>
</tr>
<tr>
<td>Control</td>
<td>n = 23</td>
<td>56</td>
<td>C</td>
<td>28.64</td>
<td>117.74</td>
<td>72.91</td>
</tr>
</tbody>
</table>

Table 2: Independent samples test for women FFA vs. control group.

<table>
<thead>
<tr>
<th></th>
<th>Sig. (2-tailed)</th>
<th>Mean Difference</th>
<th>Std. Error Difference</th>
<th>95% CI of the Difference Lower</th>
<th>95% CI of the Difference Upper</th>
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<td>16.02</td>
<td>3.19</td>
<td>9.57</td>
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<tr>
<td></td>
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<td>3.28</td>
<td>9.31</td>
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<td>8.61</td>
<td>2.34</td>
<td>3.89</td>
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<td>8.61</td>
<td>2.36</td>
<td>3.82</td>
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Table 3: Independent Samples Test for CCCA vs. control group.

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<th></th>
<th>Sig. (2-tailed)</th>
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<th>Std. Error Difference</th>
<th>95% CI of the Difference Lower</th>
<th>95% CI of the Difference Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td>Equal variances assumed</td>
<td>0.001</td>
<td>16.19</td>
<td>4.7</td>
<td>6.63</td>
</tr>
<tr>
<td></td>
<td>Equal variances not assumed</td>
<td>0.001</td>
<td>16.19</td>
<td>4.62</td>
<td>6.83</td>
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<tr>
<td>Diastolic</td>
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<td>3.09</td>
<td>9.67</td>
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<td>3.04</td>
<td>9.78</td>
</tr>
</tbody>
</table>

capture the temporal sequence of hypertension, treatment for hypertension with the onset of alopecia. The possibility of white coat syndrome was not included as a confounder (Table 1, Table 2 and Table 3).

References
Health Across the Nation (SWAN). Menopause 26: 1213-1227.


