The Association between Nuchal Nevus Flammeus and Alopecia Areata: A Case-Control Study

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Introduction

Nevus flammeus or salmon patch consists of a congenital faint pink, blanchable patch with irregular borders. Histologically, no abnormality may be apparent in infancy, but persisting nuchal lesions in adults show dilatation of subpapillary capillaries. There is evidence of a definite genetic influence in its etiology, and both nuchal and facial salmon patches seem to be inherited in an autosomal dominant manner [1–3]. Studies document a prevalence of 42% in white neonates, 31% in blacks [4] and 23.4% in Chinese and Malaysian infants [5]. It is most commonly located on the nape of the neck (81%), the eyelids (45%) and the glabella (33%) [6]. Those on the face fade rapidly, and most will have more or less disappeared within a year [7, 8]. Nuchal lesions tend to be much more persistent and probably remain unchanged into adult life in at least 50% of cases [7, 9].

Alopecia areata (AA) is characterized by rapid and complete loss of hair in one or, more often, several round or oval patches, usually on the scalp, in the beard area, eyebrows, eyelashes and, less commonly, in other hairy areas of the body.

Studies showed that the prevalence of nuchal nevus flammeus (NNF) was significantly increased in patients with AA, especially severer forms [10–12]. We also conducted a study to investigate whether AA is associated with NNF.

Key Words
Alopecia areata  Nuchal nevus flammeus  Salmon patch

Abstract

Background: The association of alopecia areata (AA) with nuchal nevus flammeus (NNF) has been demonstrated by previous studies. Objectives: The aim of this study was to investigate whether AA is associated with NNF. Methods: 199 AA patients and 215 controls without AA were examined for the presence of NNF. Results: 35 patients (17.6%) in the AA group had NNF. In the control group, 20 patients (9.3%) had NNF (odds ratio = 2.08, 95% confidence interval 1.43–2.73; p = 0.013). A statistically significant association was found between the presence of NNF and duration of the AA (p < 0.001). The presence of NNF was associated with severity of AA (p < 0.001).

Conclusions: The results of our study suggest a link between NNF and AA especially in severer and more chronic forms.
Patients and Methods

A case-control study was conducted from July 2002 to December 2003 and included 199 patients with AA and 215 controls without AA from Razi Hospital, Tehran, Iran.

We completed a questionnaire concerning age, sex, age at onset and duration of AA, family history of AA in the first-degree relatives, form of AA and presence of NNF. Examination of both cases and controls was performed by the same two experienced clinicians. The diagnosis of NNF was based on the presence of a congenital pink blanchable patch on the nape of the neck or in the occipital area and exclusion of other possible causes. We tried to examine the patients and controls for the presence of NNF by parting the hair in the hairy areas. The patients were classified into five groups according to the severity of AA: (i) patchy (<25% of the scalp area without involvement of the periphery of the scalp); (ii) multiple patchy (>25% of the scalp area without involvement of the periphery of the scalp); (iii) ophiasis; (iv) totalis; (v) universalis. The patients were 95 women and 104 men with a mean age of 24.7 years (range 3–60). 215 controls were enrolled in the same calendar period among patients visiting the same department for other dermatological diseases unrelated to AA and nevus flammeus. None had a previous history of AA. The control group was 109 women and 106 men, with a mean age of 23 years (range 7–54). There were no statistically significant differences for age and sex between the two groups (p = 0.07 and 0.54, respectively). Informed consent was obtained from each patient and control.

Student’s t test was employed to compare the age of the two populations. The χ² test was used to compare the sex, family history and prevalence of NNF among populations. The odds ratio with corresponding 95% confidence intervals was calculated to determine the association between NNF and AA. The Mann-Whitney test was used to evaluate the association of NNF with severity, age at onset and duration of AA. (The data regarding age at onset and duration of AA were not normally distributed.) p < 0.05 was considered statistically significant.

Results

31 of 199 patients (15.6%) had a positive family history of AA, compared with 6 of 215 controls (2.8%). The difference was statistically significant (p < 0.001).

NNF were present in 35 of 199 patients (17.6%), compared with 20 of 215 controls (9.3%). The difference was statistically significant (odds ratio = 2.08, 95% confidence interval 1.43–2.73; p = 0.013).

The mean age at onset of the AA was 19.5 years (range 3–60). A statistically significant association was not found between the presence of NNF and age at onset of disease (p = 0.43).

Table 1 shows the prevalence of NNF in AA patients according to duration of the disease. A statistically significant association was found between the presence of NNF and duration of the disease (p < 0.001).

<table>
<thead>
<tr>
<th>Duration of disease</th>
<th>With NNF n</th>
<th>With NNF %</th>
<th>Without NNF n</th>
<th>Without NNF %</th>
<th>Total n</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 year</td>
<td>5</td>
<td>7.9</td>
<td>58</td>
<td>92.1</td>
<td>63</td>
<td>100</td>
</tr>
<tr>
<td>1–5 years</td>
<td>10</td>
<td>13.7</td>
<td>63</td>
<td>86.3</td>
<td>73</td>
<td>100</td>
</tr>
<tr>
<td>&gt;5 years</td>
<td>20</td>
<td>31.7</td>
<td>43</td>
<td>68.3</td>
<td>63</td>
<td>100</td>
</tr>
</tbody>
</table>

n = Number of patients.

Patchy AA was the most common form (42.7%), followed by universalis (26.7%), diffuse patchy (17.6%), ophiasis (8.5%) and totalis (4.5%). Table 2 shows the prevalence of NNF in AA patients according to the form of disease. A statistically significant association was found between the presence of NNF and severity of disease (p < 0.001).

In the AA group, 5 of 35 patients (14.3%) with NNF had a positive family history of AA, compared with 26 of 164 patients (15.9%) without NNF. The difference was not statistically significant (p = 0.816).

Discussion

The results of our study suggest an association between NNF and AA especially in severer and more chronic forms of AA.

A summary of previous studies is shown in table 3. The association between AA and NNF was statistically significant in the studies by Hatzis et al. [10], Orecchia and Perfetti [11] and Camacho and Navas [12]. All the above studies [10–12] showed that NNF was more prevalent in severer forms of AA. NNF was less prevalent in patients with AA than controls in the study of Van Baar et al. [13]. The difference was statistically significant.

The exact pathogenesis of this association remains unclear. It has been suggested that the high prevalence of NNF in patients with AA is more likely to be a sign of epidermal atrophy visualizing ectatic subpapillary vessels on the nape of patients with AA than a concomitant skin abnormality [14]. However, in the study of Hatzis et al. [15], no signs of epidermal atrophy were observed.

We tried to examine the patients and controls for the presence of NNF by parting the hair in the hairy areas; however, it is possible that some faint NNFs were overlooked in these areas. This can be a possible observation.
bias in our study. The result of the previous studies may also be affected by this bias.

The population of AA patients in our study may not be representative of the population of AA patients in the community, because patients with severer forms of AA are referred to Razi Hospital more frequently than patients with less severe forms.

We hope that further investigations may reveal clues to the pathogenesis of the association between these two phenomena.

**Table 2. Prevalence of NNF in AA patients according to the form of the disease**

<table>
<thead>
<tr>
<th>Clinical form</th>
<th>With NNF</th>
<th>Without NNF</th>
<th>Total</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Patchy</td>
<td>10</td>
<td>11.8</td>
<td>75</td>
<td>88.2</td>
</tr>
<tr>
<td>Multiple patchy</td>
<td>5</td>
<td>14.3</td>
<td>30</td>
<td>85.7</td>
</tr>
<tr>
<td>Ophiasis</td>
<td>6</td>
<td>35.3</td>
<td>11</td>
<td>64.7</td>
</tr>
<tr>
<td>Totalis</td>
<td>2</td>
<td>22.2</td>
<td>7</td>
<td>77.8</td>
</tr>
<tr>
<td>Universalis</td>
<td>12</td>
<td>22.6</td>
<td>41</td>
<td>77.4</td>
</tr>
</tbody>
</table>

n = number of patients; p value, showing significance of the association between the presence of NNF and the form of disease.

**Table 3. Summary of previous studies of the association between NNF and AA**

<table>
<thead>
<tr>
<th>Source</th>
<th>Cases</th>
<th>Controls</th>
<th>Prevalence of NNF in cases and controls, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ophiasis-extensive group: 22.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mild forms group: 3.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Control group: 4.5</td>
</tr>
<tr>
<td>(1989)</td>
<td></td>
<td></td>
<td>Patchy form group: 48</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Total patients with AA: 53</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Controls younger than 14 years: 18.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Normal adults: 10.8</td>
</tr>
<tr>
<td>(1992)</td>
<td></td>
<td>II: 1,027</td>
<td>Multiple patches: 8.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>AA totalis: 86.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>AA universalis: 95.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ophiasis: 55.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Total patients: 43.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Control I: 26.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Control II: 15.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Control group: 57.50</td>
</tr>
</tbody>
</table>

I = Control group I, patients with androgenetic alopecia; II = control group II, newborns.

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References