Triggering Role of Stressful Life Events in Patients with Alopecia Areata

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SUMMARY Recent clinical studies examined the role of stress as a potential trigger for alopecia areata. However, it is still questioned whether and to what extent stress plays a role in its pathogenesis. We determined whether stressful life events are risk factors in the onset and course of alopecia areata among our population. The study included 61 consecutive patients with alopecia areata who were all outpatients at dermatology clinics of Semnan city. Sixty age- and sex-matched individuals selected among healthy subjects with respect to the diagnosis of alopecia areata served as controls. Stressful events were assessed using Traumatic Events Questionnaire (TEQ). No differences were found in the number as well as mean scores of physical and sexual stressful life time events across the two groups, while patients experienced a greater number of emotional stressing events with higher mean scores than the healthy group. Among different TEQ items, alopecia patients tended to have higher scores on the items indicating history of loss of a family member during childhood and a history of emotional neglect by relatives. In conclusion, loss of family members and emotional neglect by relatives might have major roles in triggering the onset and exacerbation of alopecia areata.

KEY WORDS: alopecia areata, stress, life

INTRODUCTION

Alopecia areata as one of the most important forms of hair loss affects nearly 1%-2% of the population of children or adolescents. Alopecia areata is commonly characterized by sudden onset patchy hair loss on the scalp that can occasionally evolve into loss of all scalp hair or even body hair. Although the pathogenesis of this disorder is thought to be dependent to autoimmune conditions, especially T-cell-mediated attack on anagen hair follicles of the hair (1), its exact pathogenesis remains unclear. However, new basic science evidence is available for stress as a contributing factor in the development of alopecia areata. It has been suggested that some stress-induced antigens such as MICA gene and its interactions with natural killer cells might be associated with alopecia areata (2) and can prove its both immune and psychological pathogenesis. In addition, recent clinical studies (3,4) examined the role of stress as a potential trigger for alopecia areata. Other researches with stress models have indicated that immune system activation can modulate the hypothalamic-pituitary-adrenal axis, which is involved in stress response. In fact, alopecia areata patients might have an aberrant stress response because of the influence...
of the chronic inflammation of alopecia areata on this axis (5). Furthermore, by comparing individuals who experienced a greater number of uncontrollable life time mental stressors, it has been shown that alopecia areata tend to be associated with high avoidance in attachment relationships, high alexithymic characteristics, and poor social support (6). In total, although the neuroendocrine-immune connection and its modulation by stress as well as direct influence of psychological factors may also be triggering factors, whether and to what extent stress plays a role in its pathogenesis is still questioned. The aim of this study was to determine whether stressful life events are risk factors in the onset and course of alopecia areata among our population.

SUBJECTS AND METHODS

The study included 61 consecutive patients older than 18 years with alopecia areata, all outpatients at dermatology clinics of Semnan city between January and December 2009. All patients had been diagnosed with alopecia areata by dermatologic examination. Those with local skin infections, a history of head radiotherapy or chemotherapy as well as users of drugs for skin disorders were excluded. Sixty-one age- and sex-matched subjects selected from healthy individuals with respect to the diagnosis of alopecia areata served as controls. The study was explained to all eligible patients who were then invited to participate. Those who accepted signed an informed consent form and were assigned to a research dermatologist who carried out a face-to-face interview in a quiet and comfortable room. The study protocol was approved by the institutional ethics committee of the Semnan University of Medical Sciences.

Stressful events were assessed using Traumatic Events Questionnaire (TEQ). The 14-item TEQ assesses 9 events such as experiencing a serious accident (industrial, farm or car), receiving news of serious injury or death of someone, and being a victim of physical or sexual abuse. It also allows for an unspecified traumatic event to be examined. For each event endorsed, respondents are asked to provide the frequency, age at the time(s) of the event, degree of injury, degree of life threat, degree of how traumatizing the event was at the time, and degree of how traumatizing the event is currently. Besides total score (the sum of all trauma), a separate subscale can be calculated for emotional, physical, and sexual traumatic events. A 7-point scale (1 = “not at all” to 7 = “extremely”) is used for each of the degree questions. The TEQ is suitable for research and clinical purposes (7). We used the validated Iranian version.

Results were reported as mean ± standard deviation (SD) for quantitative variables and as percentage for categorical variables. The groups were compared using Student’s t-test or Mann-Whitney U test for continuous variables and χ²-test (or Fisher exact test if required) for categorical variables. Predictors exhibiting a statistically significant relation with physical, emotional and sexual triggering factors in the two groups in univariate analyses were taken for multivariate logistic regression analysis to investigate their independence as predictors. Odds ratio (OR) and 95% confidence intervals (CI) were calculated. This study was done with the power of 90%. P values of 0.05 or less were considered statistically significant. All statistical analyses were performed using the SPSS version 13.0 (SPSS Inc., Chicago, IL, USA) and SAS version 9.1 for Windows (SAS Institute Inc., Cary, NC, USA).

RESULTS

A total of 61 patients with alopecia areata (mean age 30.28±7.66 years, 66% of male) and 61 comparison healthy subjects (29.55±7.37 years, 65% of male) were included in the study. Only one healthy subject refused to participate. In all patients, the onset of alopecia areata dated back to no more than six weeks. Alopecia patients and comparison subjects did not differ in terms of age and gender distribution. Table 1 reports comparisons between alopecia patients and control subjects with regard to different categories of life time stressful events. No differences were found in the number as well as mean scores of physical and sexual stressful events across the two groups, while patients experienced a greater number of emotional stress events with higher mean scores than the healthy group, which was confirmed using a multivariable logistic regression analysis. As shown in Tables 2 and 3, among different TEQ items, alopecia patients tended to have higher scores on the item indicating history of loss of a family member during childhood and history of emotional neglect by relatives. However, there were no substantial differences between alopecia patients and comparison subjects in the mean scores on other items.

DISCUSSION

An association between stressful events and the onset of alopecia areata has been suggested by some anecdotal reports, case-control studies as well as uncontrolled retrospective studies (6,9-12). However, Liakopoulou et al. found only a marginally significant association (13), and Russiello et al. report negative results (14). Another study that included patients experiencing an exacerbation recorded negative results.
Table 1. Overall incidence and scores of life time stressful factors in patients with alopecia areata and healthy subjects

<table>
<thead>
<tr>
<th>Factor</th>
<th>Overall incidence</th>
<th>Mean score</th>
<th>Univariate P-value</th>
<th>Multivariate P-value</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alopecia group (n=61)</td>
<td>Healthy group (n=60)</td>
<td>Alopecia group (n=61)</td>
<td>Healthy group (n=60)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional</td>
<td>43 (70.5)</td>
<td>21 (35.0)</td>
<td>1.61±1.58</td>
<td>0.50±0.81</td>
<td>&lt;0.001</td>
<td>0.029</td>
</tr>
<tr>
<td>Physical</td>
<td>26 (42.6)</td>
<td>16 (26.7)</td>
<td>0.57±0.78</td>
<td>0.33±0.62</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Sexual</td>
<td>3 (4.9)</td>
<td>2 (3.3)</td>
<td>0.08±0.42</td>
<td>0.03±0.18</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Total</td>
<td>45 (73.8)</td>
<td>25 (41.7)</td>
<td>2.26±2.25</td>
<td>0.87±1.21</td>
<td>&lt;0.001</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS = nonsignificant

Table 2. Overall incidence of life time stressful events in patients with alopecia areata and healthy subjects

<table>
<thead>
<tr>
<th>Patient group (n=61)</th>
<th>Healthy group (n=60)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of a family member</td>
<td>13.1</td>
<td>3.3</td>
</tr>
<tr>
<td>Family problem</td>
<td>13.1</td>
<td>3.3</td>
</tr>
<tr>
<td>Death of a family member</td>
<td>6.6</td>
<td>6.7</td>
</tr>
<tr>
<td>Death of a family member</td>
<td>1.6</td>
<td>0.0</td>
</tr>
<tr>
<td>Threat to life from illness</td>
<td>9.8</td>
<td>1.7</td>
</tr>
<tr>
<td>Divorce of your parents</td>
<td>3.3</td>
<td>1.7</td>
</tr>
<tr>
<td>Your own divorce</td>
<td>4.9</td>
<td>0.0</td>
</tr>
<tr>
<td>Victim of violence from others</td>
<td>1.6</td>
<td>1.7</td>
</tr>
<tr>
<td>Emotional neglect by family</td>
<td>13.1</td>
<td>3.3</td>
</tr>
<tr>
<td>Emotional neglect by relatives</td>
<td>14.8</td>
<td>5.0</td>
</tr>
<tr>
<td>Emotional neglect by non-family members</td>
<td>13.1</td>
<td>5.0</td>
</tr>
<tr>
<td>Misbehaving of family members</td>
<td>13.1</td>
<td>5.0</td>
</tr>
<tr>
<td>Misbehaving of relatives</td>
<td>19.7</td>
<td>5.0</td>
</tr>
<tr>
<td>Misbehaving of non-family members</td>
<td>13.1</td>
<td>5.0</td>
</tr>
</tbody>
</table>

NS = nonsignificant

While providing preliminary evidence for the role of stressful events, many of these studies used life event checklists rather than interviews or were conducted with patients whose onset dated back many months or even years. Hence, these studies carry a considerable risk of fall off in event recall and recall bias (16). Also, most studies investigated only the role of life events and neglected other factors potentially modulating susceptibility to disease, such as social support (17,18) attachment security, or alexithymia (19). Contradictory results have been reported in different psychiatric studies, ranging from the finding that as many as 93% of patients with alopecia areata have a serious mental disorder (20), to the conclusion that there is no evidence that psychological factors have a significant role in either the causation or precipitation of alopecia areata attacks (21).

Our results suggest that some emotionally life-time events including loss of a family member during childhood and a history of emotional neglect by more distant family members or relatives are significantly more often reported by patients with alopecia compared with a healthy control population, while physically traumatic lifetime events have no triggering role in the onset of the disorder. These events are related to the adverse events which occurred potentially during childhood. It seems that adverse childhood experiences are not only a risk factor for stress-related diseases such as depression or substance abuse, but they seem to be linked to an increased risk of adult disease with enhanced susceptibility for stress (22-24). According to the study by Willemsen et al. (25), emotional neglect and emotional abuse within family occurred mainly between 8 and 9 years.
for patients with alopecia areata and at the age of 10 years for the control group.

CONCLUSION

It has been suggested that besides other psychological factors, loss of family members and emotional neglect by relatives might have major roles in triggering the onset and exacerbation of alopecia areata. However, psychological disturbances also contribute to the complex puzzle of etiologic theories on alopecia. Also, the role of treatment of concomitant psychopathological disorders seems to be a vital one. Indeed, this treatment might positively affect how the patient adapts to his/her alopecia and social setting, and perhaps might even lead to a better dermatological evolution of the alopecia (26). However, these hypotheses should be additionally tested and studies using modern psychiatric methodology for their confirming seem to be necessary.

Acknowledgment

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