INTRODUCTION

Alopecia areata (AA) is a high-prevalence immune-mediated hair loss disorder, and extrafollicular affections, including nail and ocular abnormalities, are classically related to a worse prognosis of the disease. Previous studies have suggested that the presence of a persistent nuchal nevus flammeus (NNF) also indicates a greater severity and duration of the disease. The association between AA and persistent NNF was first described by Hatzis et al in 1988, who demonstrated that the relation was statistically evident and not due to a simple observer bias. Objectives: To determine and compare the presence/absence and size of the NNF in 80 individuals (40 patients diagnosed with AA and 40 controls). Results: We found a statistically significant association not only between AA and the presence of NNF, but also with its size. Moreover, we found that the size of the NNF was also associated with the severity of AA. Conclusion: The size of the NNF in AA patients might be a useful marker of widespread and chronic disease.

Key words: Alopecia areata, nevus simplex, nuchal nevus flammeus, salmon patch
MATERIALS AND METHODS

We determined and compared the presence/absence and size of the NNF in 80 individuals (40 patients diagnosed with AA and 40 controls). Examination of all cases and controls was performed by the same two experienced clinicians. The diagnosis of NNF was based on the presence of a congenital pink patch on the nape or in the occipital area and exclusion of other possible causes [Figure 1].

The AA patients were classified into four groups according to the severity of AA: Group 1 or focal alopecia areata (FFA, patchy <25% of the scalp area without involvement of the periphery of the scalp); Group 2 or multifocal AA (MFAA, multiple patchy, >25% of the scalp area without involvement of the periphery of the scalp); Group 3 or AA totalis (AAT); and Group 4 or AA universalis (AAU). The control group was enrolled in the same calendar period from patients visiting the dermatology department for other dermatological issues unrelated to AA and NNF. None had a previous personal or familiar history of AA.

Statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Pearson’s Chi-squared test was used to compare categorical variables and Mann–Whitney test was used to compare continuous variables not normally distributed. Values of \( P < 0.05 \) were considered statistically significant.

RESULTS

The patients diagnosed with AA included in our study were 29 women and 11 men with a mean age of 38.5 years (range 13–80). The control group was composed of 28 women and 12 men, with a mean age of 38.28 years (range 15–80). We found no statistically significant differences in age and sex between the two groups [Table 1].

NNF was evidenced in 30 patients with AA and in 14 controls. As observed, the prevalence of NNF was higher in the AA group (75%) than in the control group (35%), and the difference was statistically significant \( (P < 0.001) \).

Regarding the size of the NNF, we found that the mean area of the NNF in patients diagnosed with AA was 15.4 cm\(^2\) (standard deviation 15.9), whereas the mean area in the control group was 2.7 cm\(^2\) (standard deviation of 4.9). The difference in size between the patient group and the control group was statistically significant \( (P < 0.001) \).

Moreover, we observed that the prevalence of the NNF was higher in patients with a severe form of the disease (AAMF, AAT, and AAU), and that the size of the NNF was also directly related to the severity of AA, being larger in those diagnosed with AAMF, AAT, and AAU \( (P = 0.04) \). All these results are summarized in Table 2.

DISCUSSION

Taking into consideration the results obtained, we agree with the previous studies\(^{[1‑4,9]}\) and confirm that the prevalence of NNF is higher in patients diagnosed with AA. Moreover, we found not only a statistically significant association between AA and the presence of NNF but also with its size, which confirms our initial hypothesis.

Table 1: Data of cases and controls \((n=80)\)

|                | Cases               | Controls             |
|----------------|---------------------|----------------------|
| Age (years)    |                     |                      |
| Mean (SD)      | 37.7 (15.09)        | 37.8 (13.76)         |
| Median (range) | 38 (13‑80)          | 37.5 (15‑80)         |
| Sex (%)        |                     |                      |
| Female         | 29 (72.5)           | 27 (67.5)            |
| Male           | 11 (27.5)           | 13 (32.5)            |
| Type of AA (%) |                     |                      |
| AAF            | 5 (12.5)            | 40 (100)             |
| AAMF           | 21 (52.5)           |                      |
| AAT            | 5 (12.5)            |                      |
| AAU            | 9 (22.5)            |                      |
| No AA          |                     |                      |
| NNF (%)        |                     |                      |
| Presence       | 30 (75)             | 14 (35)              |
| Absence        | 10 (25)             | 26 (65)              |
| Size of NNF (cm\(^2\)) |          |                      |
| Mean (SD)      | 15.4 (15.99)        | 2.7 (4.99)           |
| Median (range) | 9 (0‑56)            | 0 (0‑24)             |

SD – Standard deviation; AA – Alopecia areata; AAF – AA focal; AAMF – AA multifocal; AAT – AA totalis; AAU – AA universalis; NNF – Nuchal nevus flammeus
Regarding subgroups of AA patients (AAF, AAMF, AAT, and AAU), we found that the prevalence of NNF was higher in patients diagnosed with severe forms of AA (MFAA, AAU, and AAT) than in patients diagnosed with a milder form of AA (FAA). Moreover, we also observed that the size of the NNF was also directly associated with the severity of AA, having a larger birthmark those diagnosed with MFAA, AAT, and AAU. We believe that this observation could be a useful marker of widespread and chronic disease.

**CONCLUSION**

To our knowledge, this is the first study associating the size of the NNF and the severity of AA. However, the clinical association between the salmon patch and AA is still uncertain because of AAs and NNF’s high prevalence in the general population, and the fact that the exact pathogenesis of this association is still unclear.

Further studies with a greater number of patients are necessary to validate this association and determine which molecular pathways or genetic markers are involved to elucidate the link between both diseases. We hope that further investigations may reveal clues as to a possible link between these two phenomena.

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**Conflicts of interest**

There are no conflicts of interest.

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