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Research Article

White Hair Follicles in Alopecia Areata.

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Abstract

Background: Alopecia areata (AA) is a common, non-scarring type of patchy or diffuse hair loss with possible remaining or regrowing white hair follicles (WHF). **Aim**: to examine white hair follicles within AA patches, evaluating their melanocytic components using several melanocytic markers and to compare that to expression in AA patches without white hairs. **Methods**: The study was conducted on AA patients attending the dermatology outpatient clinic, Minia University Hospitals. Biopsies were taken from the lesion in each patient, in group 1 the biopsies taken from AA with white hair and group 2 the biopsies taken from the AA without white hair. Processed routinely for transverse sections and stained for Sox 10, CD117, Melan A and HMB-45 melanocytic markers. The sum of the positive stained cells recorded and the average follicular expression was calculated. **Result**: There was an apparent expression of all of the tested melanocytic markers within AA patches in both groups except for HMB45 which showed minimal values, There was a statistically significant decline of the expression of Sox10 marker in white hair group 1.

Keywords: Alopecia areata; melanocyte markers; white hair.

Introduction

Alopecia areata (AA) is a prevalent type of non-scarring hair loss, thought to result from an immune-mediated reaction. This likely involves autoreactive T cells targeting antigens in the hair follicle. While the specific antigen remains unidentified, some researchers suggest that molecules associated with melanogenesis could trigger the autoimmune response [1].

There is a strong link between AA and the formation of white hair. As AA progresses, it can present various clinical forms of white hair. Again, at the initiation of the disease, white hair tends to remain unaffected since AA primarily targets pigmented hair [2].

The mechanism behind the selective retention of white hair in AA can be illustrated by the sudden graying observed during the acute onset of diffuse AA. This phenomenon, known as the rapid whitening of hair within a short time[3]. is famously exemplified by the case of French Queen Marie Antoinette. At the age of 38, she reportedly turned gray overnight before her execution, leading to this occurrence being referred to as Marie Antoinette syndrome[4].

Given the association between AA and white hair, it is likely that hair follicle melanocytes play a role in AA's pathogenesis[5]. It has been found that AA can be triggered by inducing CD8 (+) T cell-mediated immunity against hair follicle melanocyte lesions[6]. This supports the hypothesis that hair follicle melanocytes are targets of AA. Various studies have suggested that MAGE-A3, Melan-A/Mart-1, gp100, and gp100-

derived peptides (G9-209, G9-280) may be involved in inducing the autoimmune attacks that cause AA[7]. However, the specific autoantigen responsible for AA has not yet been confirmed.

Aim of work: to examine white hair follicles within AA patches, evaluating their melanocytic components using several melanocytic markers including CD117, Melan A, Sox10 and HMB-45 and also to compare that to AA patches without white hair follicles.

Patients and methods

1: Selection of cases

The patients were recruited from the dermatology Outpatient Clinic at Minia University Hospitals. Eight cases with alopecia areata were included in the study. Four patients with white hair follicles within AA patches and another 4 cases of AA without the existence of leukotrichia.

2: Clinical data

- A complete medical history was obtained from each patient, including their personal history (age, sex, and occupation), present history (onset, course, and duration of the condition), past history (previous diseases or medications), and family history of AA.
- The cases underwent general and dermatological examinations. The diagnosis was made by clinical examination.

3: Ethical approval

Informed consent was obtained prior to participant recruitment, which allowed participants the choice to withdraw from our research at any moment and we avoided using misleading techniques. Additionally, this study was approved by the ethics committee of the Minia University faculty of medicine. Approval number: 1011/01/2024.

4: Skin biopsy

After infiltrating the skin with local anesthesia consisting of two percent lidocaine (Debocaine, Sigma-Tec, Egypt), skin biopsy specimens were retrieved using 3 mm punches. In group (1) the biopsies were taken from the the alopetic patch with white hair and in group (2) the biopsies were taken from alopetic patch without white hair.

Samples were processed routinely for transverse sections and stained for Sox 10, CD117, Melan A and HMB-45 melanocytic markers.

5: Immunohistochemical staining

A dilution guideline for different 4 concentrated primary antibodies was used.

1- **Melan-A**: was ready to use. Cells were considered positive if they showed cytoplasmic staining.
2- **C-kit**: the cells were stained with 1:100 dilution and considered positive if they showed cytoplasmic staining.
3- **Sox10**: was used at a dilution of 1:300 and considered positive if they showed nuclear staining.
4- **HMB45**: was ready to use. Cells were scored positive if they showed cytoplasmic staining.

The slides were examined in the Western University Department of Pathology and laboratory medicine using an Aperio glass slide scanner. The Scan-Scope can convert slides from a light microscope into a digital image that can be examined using virtual microscope software at 20x, and 40x magnifications. Images can be seen and edited with free software (Aperio Scan ScopeTM). Representative photos were taken using this software.

6: Assessment of the antibody staining

Detection of Sox 10, CD117, Melan A and HMB-45 expression marker was done for all cases and the sum of the positive stained cells of all follicles related to each case was calculated and the average follicular expression was calculated.

Results

The study included 8 patients with AA; four cases with white hair follicles within AA patches (Figure 1) and 4 cases without WHF.

The transverse sectioned biopsies including cross sectioned follicles were examined. .

- All melanocytic markers were examined at the lower segment of the hair follicles at cross sections. (Figure 2)
- Positive cells at hair bulb and outer root sheath (suprabulbar) were recorded for each marker.
- Group 1 biopsies with white hairs included 37 follicles and group 2

biopsies without white hair follicles included 21 follicles.

- The average follicular expression values of all melanocytic markers are reported in Table 1,2 and Figure 3.
- There was an apparent expression of all melanocytic markers within AA patches in both groups except for HMB45 which showed minimal values.
- There was an apparent lower expression in AA patches including white hair follicles in group I compared to group 2 cases.
- There is a statistically significant decline in the expression of Sox10 marker in white hair group 1.

Table (1): The average expression values of all markers in both groups:

	case	sox10	CD117	Melan A	HMB-45
Group(1)	1	0.44	1.11	1.4	1
	2	0.722	1.38	0.16	0
	3	2.2	16	1	0.6
	4	2.6	5.4	5.2	0
Group(2)	5	5.72	8.36	3.36	0.09
	6	5.5	9	3	0
	7	6.5	9.75	7.75	0
	8	16	19	12	0

Table (2): statistical data evaluation.

	Group 1	**Group** 2	**P value**
CD-117			
Mean ±SD	5.9±6.9	11.5±5	0.14
Median	3.3	9.3	
Range	1.11-16	8.36-19	
SOX-10			
Mean ±SD	1.49±1.06	8.4±5	0.02*
Median	1.4	6.1	
Range	0.44-2.6	5.5-16	
Melan A A			
Mean ±SD	1.94±2.2	6.5±4.2	0.08
Median	1.2	5.5	
Range	0.16-5.2	3-12	
HMB-45			
Mean ±SD	0.40±0.48	0.02±0.04	0.32
Median	0.30	0	
Range	0-1	0-0.09	

*p value is considered statistically significant at <0.05.

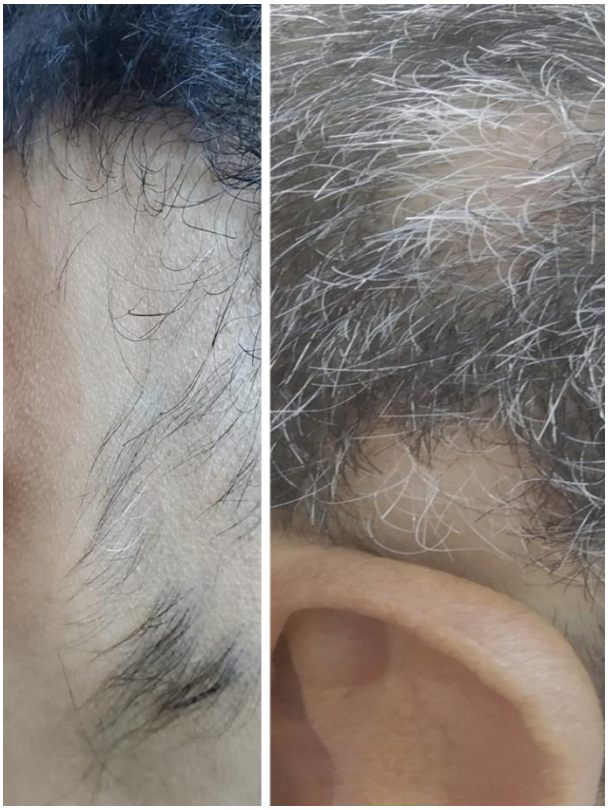

Figure (1): Cases with Alopecia areata with white hair follicles.
Right panel. with remaining canities white hairs.
Left panel. With regrowing white follicles.

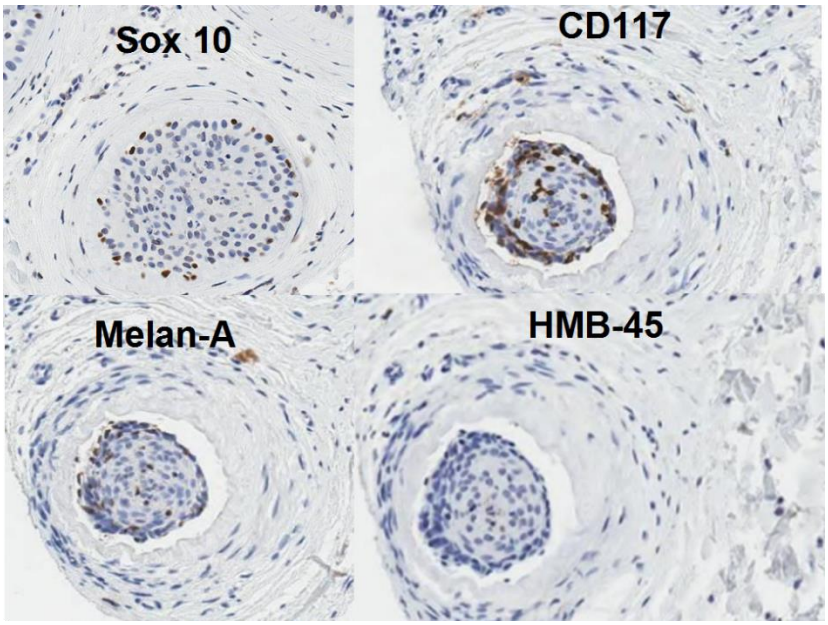

Figure (2): Follicular expression of melanocytic markers, C-Kit, MelanA, Sox-10, and HMB-45, in lower follicular segments in AA with NO WHF.

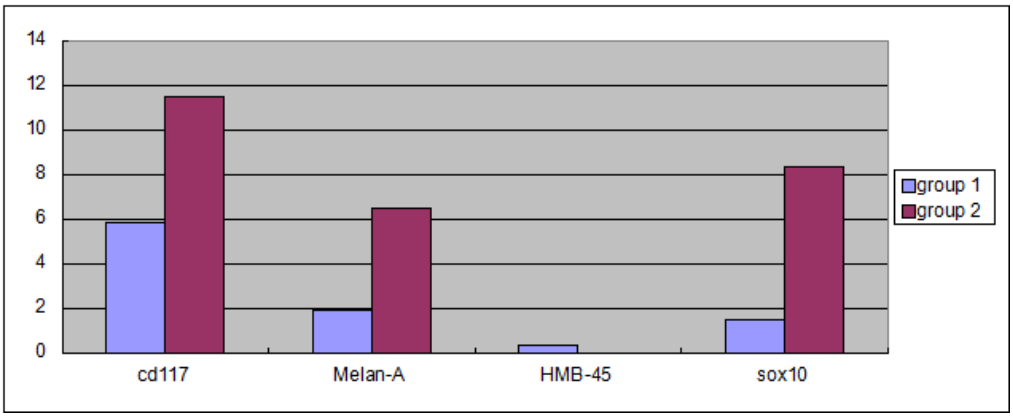

Figure (3): Bar chart represents average follicular expression values in studied groups.

Discussion

Alopecia areata (AA) is an autoimmune disorder characterized by non-scarring hair loss. It presents as well-defined patches of hair loss, which can occur on one or multiple areas of the scalp or body, and it may be diffuse and affect the whole scalp or extend to affect the whole body [8].

White hair can not only be spared during the onset of AA but can also be regenerated during the recovery phase. During the recovery process of most AA patients, thin and fragile white vellus hair often temporarily regenerates, usually lasting no longer than the first cycle of hair regeneration. Over time, this hair gradually regains its length, diameter, and pigment, eventually becoming healthy, pigmented hair [1].

It is clearly demonstrated that all melanocytic markers are expressed in hair follicles within AA patches regarding lower follicular components, including hair bulbs or suprabulbar ORS.

Comparing AA patches with white hair follicles against other AA patches without white hair follicles was done in this study and confirmed the real decline of melanocytes at different stages at different levels of hair follicles lower segment. C-Kit as a melanocyte receptor existed but with lower values in group 1 with white hair follicles. Melan-A, as a famous and specific structural melanocytic marker, also existed with a clear decline in group 1 with white hair follicles. Sox10, as a nuclear transcription factor in melanocytes, again significantly declined in AA with white hair follicles. HMB45 as a gp100 marker related to the final melanogenesis stages did not show considerable values of expression in both groups.

The All or None Rule does not apply here regarding the expression of melanocytic markers in AA follicles. This explains the existence of those melanocytic markers in both groups. Remaining hair germs within the dermis still exist even in patches with no macroscopic apparent hair remaining. A new anagen phase is expected to evolve with new possible pigmented HF due to the reviving process that can happen from hair follicle stem cells (HFSCs) and melanocyte stem cells (MSCs), unless opposed by a new attack of the cytotoxic immune process.

The successful early white regrowing hair in AA cases escapes new cytotoxic immune attacks as they lack the main bulk of antigenicity. White hair means no matrical melanogenesis and no melanocytic immune targets in the hair bulb.

The main pathology of AA is the cytotoxic lymphocytic attack aimed at the bulbar region, which should possess the main volume of functional melanocytes with ample gp100 proteins, not targeting other follicular components like the ORS area with existing nonfunctioning melanocytes with no melanin production is required [9,10]. That is why the HMB45 expression

was absent or the least to be found in the 8 cases.

The melanocytic markers CD117 and Melan A expression were decreased but not to the same extent as SOX10, which showed a significant difference between both groups. Sox10 is considered a perfect immunohistochemical stain for detecting melanocytes because of its nuclear staining pattern and low cytoplasmic reactivity [11].

Conclusion

The white hair follicles within alopecia areata could be remaining canities hair, spared as a result of their lacking expression of the melanocytic antigens, or regrowing white hair follicles; losing their active bulbar melanocytes after the immunogenic cytotoxic reaction during the active phase of the disease. Follicles in AA can still express melanocytic proteins, although several melanogenic antigens are suspected targets in the disease. gp100 is a very possible suspect for the immune-cytotoxicity in AA as HMB-45 showed significantly low expression values in remaining or regrowing white hair follicles or on other AA patches without WHF.

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