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Research Article

Significance of Angiotensin Converting Enzyme and Role Alopecia Areata

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Abstract

Alopecia Areata is a chronic inflammatory diseases of hair follicle exact pathology are unknown it is related with T cells immune response it's an autoimmune disease. On the other hand, it is related with RAAS system. And serum ACE Analysis is done to know its effect in Alopecia Areata.

Keywords: Autoimmune diseases, Alopecia Areata, Hair follicle, ACE, RAAS, T cells and Inflammation.

1. Introduction

Alopecia areata is an immune-dependent disorder characterized by the interaction of T-lymphocytes with follicular antigens. It is the most common cause of immune-mediated nonscarring alopecia, with a female to male ratio of about [1]. Angiotensin-converting enzyme (ACE) is a membrane-bound zinc-dependent dipeptidase that catalyzes the conversion of angiotensin I to a physiologically active peptide named angiotensin II. Recent studies have shown the presence of a local renin–angiotensin system in some organs such as the brain, kidneys, epithelial cells, heart and skin, which works separately from its circulating counterpart. In this local renin–angiotensin system system, ACE has a role in autoimmunity and inflammation.

The aim of this study was to evaluate the levels of ACE activity in the serum and skin of alopecia areata patients in order to show a possible role of the local renin–angiotensin system in the pathogenesis of this disease. We did not find any previous reports of evaluation of both serum and tissue ACE activity in alopecia areata [2].

Table 1: Demographic and clinical characteristics of alopecia areata patients (n=25), and correlation of the clinical characteristics with serum ACE activity [3].

Clinical characteristics	n (%)	Mean rank of serum ACE	P
Pattern of hair loss			
Patchy (scalp, beard)	20 (80)	11.4	0.029
Nonpatchy	5 (20)	19.3	
Universalis	1 (4)		
Ophiasis	1 (4)		
Patchy and ophiasis	2 (8)		
Diffuse	1 (4)		
Duration of current episode of hair loss			
<3 months	19 (76)	11.7	0.186
3-12 months	2 (8)	13.0	
12-24 months	0	-	
2-5 years	0	-	
>5 years	4 (16)	19.1	
Hair loss activity			
Losing	17 (68)	13.2	0.960
Stable	6 (24)	12.8	
Growing	2 (8)	11.8	
Pull test			
Positive	14 (56)	12.4	0.647
Negative	11 (44)	13.8	
Exclamation mark hair			
Positive	5 (20)	10.4	0.408
Negative	20 (80)	13.7	
Amount of hair loss according to SALT scores			
S1 (≤25%)	19 (76)	11.2	0.030
More than S1 (>25%)	6 (24)	18.6	
S2 (26-50%)	4 (16)		
S3 (51-75%)	1 (4)		
S4 (76-99%)	0		
S5 (100%)	0		
Diffuse	1 (4)		
Body hair loss			
B0 (no involvement)	21 (84)	11.8	0.068
Not B0 (body involvement present)	4 (16)	19.1	
B1 (some body hair loss)	2 (8)		
B2 (100% body involvement)	2 (8)		
Nail involvement			
N0 (no nail involvement)	22 (88)	11.8	0.027
Not N0 (nail involvement)	3 (12)	21.7	
N1a (20-nail dystrophy or trachyonychia)	2 (8)		
Leukonychia	1 (4)		
Eyebrow, eyelash alopecia			
Present	4 (16)	15.0	0.592
Absent	21 (84)	12.6	

[Mann-Whitney U-test. SALT: Severity of alopecia tool, ACE: Angiotensin-converting enzyme

Tissue ACE	Cases, n (%)	Controls, n (%)	P
Tissue ACE activity			
Epidermis			
0	4 (18.2)	1 (4.2)	0.016
1+	15 (68.2)	11 (45.8)	
2+	3 (13.6)	12 (50)	
Follicular epithelium			
0	7 (31.8)	1 (4.2)	0.004
1+	15 (68.2)	17 (70.8)	
2+	0	6 (25)	
Endothelium			
Negative	15 (68.2)	9 (37.5)	0.037
Positive	7 (31.8)	15 (62.5)	
Tissue ACE distribution			
Epidermis			
Basal layer	18 (100)	23 (100)	
Full thickness	0	0	
Follicular epithelium			
Basal layer	10 (66.7)	11 (50)	0.500
Full thickness	5 (33.3)	11 (50)	

E: Angiotensin-converting enzyme

Table shows that there is no effect in gender and value of serum of ACE is low in the patients as shown in the table and figures below [4].

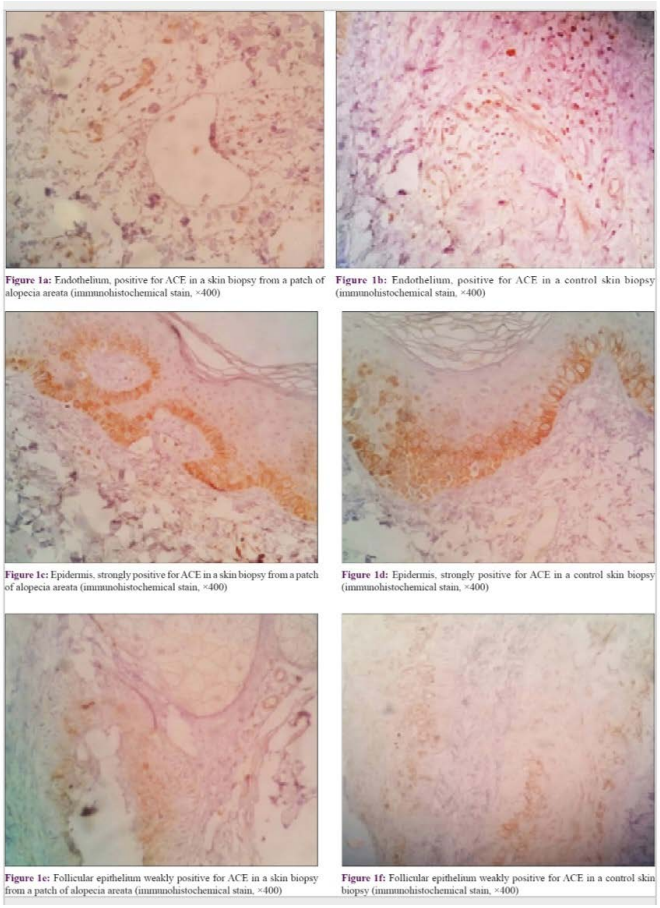

Figure 1: showing the immuno histology of the Alopecia Areata [5]

In case of severe diseases of alopecia areata the level ACE was higher than normal serum level so as it is related to activation of the angiotensin, so it has an indirect correlation with alopecia areata. [6]

2. Results

There is the indirect correlation of ACE in alopecia areata as it activates the angiotensin system.

3. Discussion

Although the exact etiopathogenesis of AA is unknown, recent studies yield considerable evidence in support of a T-cell mediated autoimmune mechanism. Coexistence of AA with other autoimmune diseases and presence of autoimmune antibodies including autoantibodies against hair follicles have been reported [7]. Rich inflammatory cell infiltrates consisting mainly of T-cells are present in and around hair bulbs. Many studies have shown that cytokines may play an important role in the disease process. A Th1 cytokine profile with elevated levels of TNF-α, IL-1, IL-2, and IFN-γ and low levels of TGF β1 due to improper function of regulatory T- (T reg) cells has been reported in this disease. IFN-γ play an important role in the pathogenesis of AA, and IFN-γ level may be an indicator of disease activity [8].

Besides its major role in the control of the arterial (vascular) pressure, several studies suggest an important role for the RAAS in inflammatory and autoimmune processes [9]. In a study by Sagawa et al. ARBs cause a decrease in IFN-γ production and lymphocyte proliferation and also improvement of the clinical and histopathologic features of arthritis in mice. Shao et al. reported an increase in IFN-γ (a Th1 cytokine) and a decrease in IL-4 (a Th2 cytokine) following infusion of angiotensin II into mice. Administration of ARBs led to the improvement of this imbalance.

To the best of our knowledge, this is the first study to evaluate the role of RAAS in AA as an autoimmune disease. There are many experiments on other autoimmune diseases like RA and multiple sclerosis (MS) where Th1 cytokines play a key role. A study on MS by Platten et al. showed increased activity of the RAAS. AT1 receptor was positive regulation in CD4+ T-cells involved in the autoimmune process. Negative regulation of the RAAS by ACEIs and ARBs suppressed autoreacitve Th1 and Th17 cells and induced T reg cells. In studies by Çobankara et al. and Veale et al., serum ACE levels were higher in RA patients than in the control group, but no statistically significant difference was seen. On the other hand, ACE activity was significantly higher in synovial fluids of the patients. Similarly, in our study, mean serum ACE activity was higher (17%) in AA patients than in controls but no statistically significant difference was observed. Which increase the serum ACE activity may indicate the local involvement of RAAS in the pathogenesis of AA.

The RAAS is traditionally known to regulation in blood circulation but recent researches provide evidence on the existence of this system in tissues. Platten et al. confirmed increased activity of the RAAS in brain lesions of MS. Go to et al. obtained peripheral monocytes of RA patients and on observation we found that, in a serum-free condition, these monocytes spontaneously produced and released increased amounts of IL-1 and ACE. Çobankara et al. found that ACE levels were significantly raised in synovial fluids of RA patients. They lead to conclude that increased production of ACE led to joint destruction in this disease. Veale et al. also found that ACE levels were significantly higher in synovial fluids of RA patients. They used anti ACE monoclonal antibodies to stain synovial membrane samples of RA patients and localized ACE to endothelial cells and mononuclear cells of macrophage origin. They concluded that ACE is produced by the synovial membrane in RA. Due to some limitations in the present study, it was not feasible to measure local and serum ACE activity concomitantly. The increased serum ACE activity found in this study, although statistically insignificant, may indicate locally increased activity of the RAAS, since the soluble form of ACE may be an indicator of turnover and clearance of the membrane-bound form Therefore, our findings suggest that the RAAS may be involved in the pathogenesis of AA. However, assessment of ACE activity in tissue samples of AA patients seems to be a more sensitive indicator of the activity of this system in this condition.

4. Conclusion

There is relation between ACE and alopecia areata studies have been proved.

Conflict of interest

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