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Association Between Cytomegalovirus Infection and Alopecia Areata In Thi Qar Province. Iraq

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Abstract

Alopecia areata (AA) is lost hair from a few or all regions of the body, for the most part from the scalp. Etiology and pathogenesis of alopecia areata being not totally comprehended, is accepted to be multifactorial in ancestry. Recently, studies suggested an association between alopecia and types of viruses, therefore we concerned to investigate the association between CMV infection and alopecia areata. This study included of 100 individuals (50 alopecia patients and 50 healthy). Mean age of study groups were 20.90 ± 11.07 and 22.64±12.29 years of cases and control group respectively. Mean of age onset of patients were 20.83 ± 10.0. Out of 50 patients 52% were male, the rest were female. However 1:1 of control group were male: female. 40% of patients had a positive family history for this disease. Alopecia areata affected on scalp in 78% of cases. All patients had a high concentration of CMV IgM. With treatment of oral ganciclovire drug, a decrease of anti-CMV IgM levels and an increase of CMV IgG levels were observed as an evidence of a previous viral infection

Keywords: Alopecia areata, CMV, IgM , IgG levels, CMV infection.

Introduction

It is a typical reason for non scarring alopecia that happens in an inconsistent, intersecting or diffuse example [1]. The condition can spread to the whole scalp (Alopecia totalis) or to the whole epidermis (Alopecia universalis). AA has an announced occurrence of 0.1–0.2% with a lifetime danger of 1.7% with men and ladies being influenced similarly [2]. Etiology

and pathogenesis of alopecia areata being not totally comprehended, is accepted to be multifactorial in ancestry [3]. However, psychological, environmental, immunological, and genetic factors are the most vigorous explanations, but the role of each of these is not perfectly known [3, 4]. Such proof supports the think that the experience of alopecia is psychologically damaging effect, causes intense emotional sufferance, and leads to personal, social, and work linked problems[5]. There is a common link between hair and identity, particularly for women [6]. The present body of evidence assists an autoimmune origin and genetic role, further modulated by unknown environmental influences [7]. Multiple genetic factors participate to the development of alopecia areata. A positive family history is apparent in approximately 10% to 25% of cases [8, 9, 10]. Immunological causes are believed to be the most significance in this regard, as their prominence has been reported from time to other time [11,12].

Cytomegalovirus (CMV) is a human β-herpesvirus that has high seroprevalence in grown-ups. CMV illness dominatingly happens as an entrepreneurial disease in patients with extreme immunosuppression and seldom happens in immunocompetent patients [13]. CMV is a member of the human herpesviridae viruses which contain a double stranded DNA, it can invade various tissues and organs of the host, especially the epithelium tissues [14]. Recently, studies suggested an association between alopecia and types of viruses such as hepatitis B and hepatitis C virus [15]. However, the effect of CMV infection on the occurrence of alopecia areata patients is unclear. No studies have showed that anti-CMV treatment can recover the condition of patients with alopecia areata. For this reason, we concerned to investigate the association between CMV infection and alopecia areata and to presented the outcome of oral ganciclovire drug in AA.

Materials and Methods

This was a type of case control study. A fifty alopecia areata with positive serological test for CMV were recruited, who attended out-patient dermatology clinics, AL Hussein-Teaching hospital Dhi-Qar, Iraq, during the period of January’ to May’ 2017. The patients included of (26 males, 24

females) , age ranging from 3 to 50 years. A clinical examination was done, and the site and type of the lesions were observed. The control group compromised of 50 healthy individuals matched by age, sex, and socioeconomic status to the patient group, with no history of either alopecia areata or viral infection. The clinical finding of patients was refined by expert dermatologist. Each of the patient and healthy filled up a questionnaire form that included personal, information, socio-economic data, history and present status of disease, family history. The types of the patients who had no formal instruction were rounded out with the assistance of an interrogator. Exclusion criteria were patients with previous diseases that can affect immunity results, pregnant, allergy to ganciclovire drug , other causes of alopecia , positive fungal infection.

Blood collection

Five mL of venous blood sample was gathered from the antecubital vein of each of the alopecia areata and healthy volunteers in a a sans metal sterile tube. Samples with signs of hemolysis were disposed of. The blood was then allowed to clot at room temperature for 25 minutes and centrifuged for 15 min. at 3000 r/m to isolate the serum. The serum was aliquoted into 1.5 microcentrifuge tubes and stored at −80°C for analysis of anti-cytomegalovirus (Immunoglobulin G and Immunoglobulin M). Serum separation and blood collection were carried out in a sterile environment [16].

Detection of anti- cytomegalovirus IgG and IgM antibodies

Enzyme –linked immunosorbent assay (ELISA) test was used for the detection of antibodies to CMV in human sera. In brief, 100 µl of diluted patients serum (1:100 with serum diluents), one well negative and two wells positive controls were pipetted in duplicates into wells of microtiter plates precoated with HCMV antigen. After incubation for 15 min at 25°C, the plates were rinsed 5 times with 300 µl diluted washing solution to remove residual serum. 100 µl of enzyme-labelled antibodies to human IgG conjugate were added and incubated as above. Then well washed 5 times

(300 µl washing solution) to remove unbound material. Then 100 µl of substrate solution (tetramethylbenzidine) was pipetted and incubated for 15 min to induce development of colour. The reaction was terminated by the addition of stop solution and the resulting dye was measured in a spectrophotometer (Awareness Technology, Palm City, USA) at a wave length of 450 nm against the substrate blank. The results were interpreted according to the manufacture instruction. For IgG ELISA, a sample was considered to be negative and positive when the absorbance of individual values was found <1.0 and >1.1, respectively. Test results were labeled as equivocal means when the absorbance value was found to be between 1.0 and 1.10. For IgM ELISA, a sample was considered as negative and positive when the absorbance of individual values was found <0.90 and >1.1. Samples were considered equivocal when absorbance of individual values was between 0.90 and 1.10 [17].

All those patient with positive test for CMV were given full course of ganciclovire drug (5mg/kg for 10 days) and follow him for 3 months with monthly clinical, photographic and laboratory assessment [16,17].

Statistical Analysis

The SPSS (Version 17) was utilized to analyze the data. Descriptive statistics were utilized for all variables. Data process on categorical scale was presented as frequency, percentage, mean, and standard deviation and was analyzed by chi-square test.

Results

The clinical features of patients are showed in table 1 . This study included of 100 individuals (50 alopecia patients and 50 healthy) , aged 3 to 50 years with mean age of 20.90 ± 11.07 years and 22.64±12.29 years of cases and control group respectively. The patients and control group were divided in age groups ranging 1-9 years, 10-19 years, 20-29 years , 30-39 years and above 40 years. Mean of age onset of patients were 20.83 ± 10.0. 26 of patients were male , the rest were female. However 25:25 of control

group were male : female. 30 patients had no family history of alopecia areata , while 20 patients had a positive family history, the majority of patients were affected with alopecia before aged 40 years with mean age of onset 20.83±10.0 .

Table 1 : The clinical features of patients and control group.

Parameter	Patients		Control		*P*-value
	n	%	n	%	
Age (years)					
Mean ± SD	20.90 ± 11.07		22.64±12.29		1.00
Mean Age of onset	20.83 ± 10.0				
Gender					
Male	26	52%	25	50%	0.50
Female	24	48%	25	50%	
Total	50	100%	50	100%	
Family history					
Positive	20	40%	—	—	
Negative	30	60%	—	—	
Total	50				

P-value ≤ 0.05 : Significance

In present study, Scalp was observed in 39 (78%) patients alone , however scalp with beard involved 6 (12%) cases. In otherwise alopecia areata affected on scalp and eyebrow of 5 (10%) of cases. This is shown in figure 1.

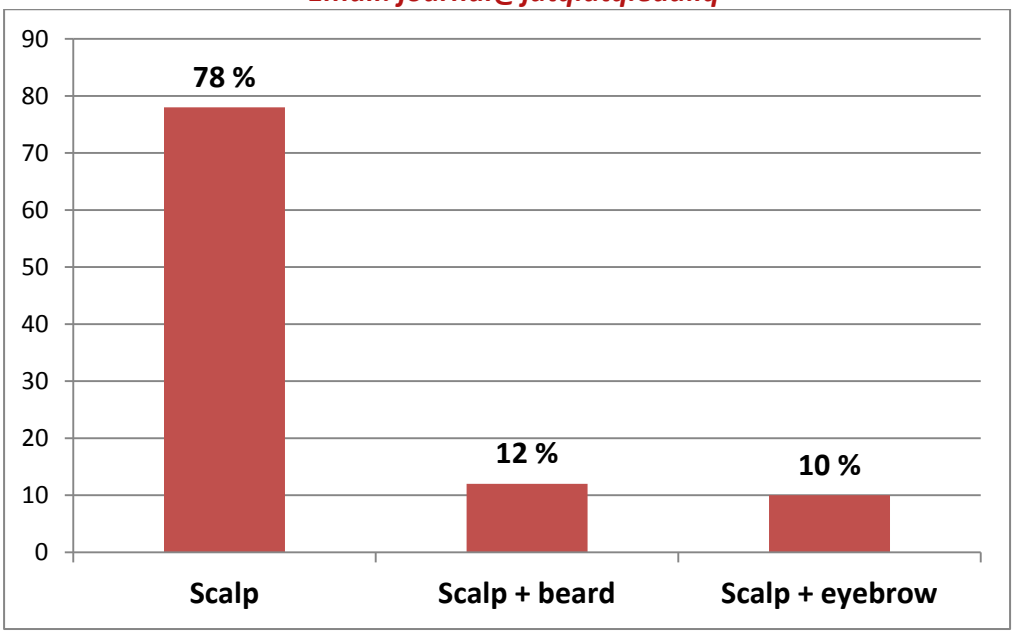

Figure 1: Site of Alopecia Areata lesion

CMV IgM antibodies were higher in all patients at visited the outpatient clinic of dermatology. We found in 20 (40%) of patients had a concentration between 1-5 g/L of CMV IgM while 6 (12%) had a concentration more than 10 g/L of CMV IgM . However 24 (48%) of patients had a concentration between 6-10 g/L of CMV IgG , (Table 2).and clinical response was followed (figure 2).

Table 2. CMV IgM , IgG detection in alopecia areata Prior and Post treatment .

Immunoglobulin (g/L)	Prior treatment of ganciclovire			Post treatment of ganciclovire		*P*-value
	Range	n	%	n	%	
CMV IgM in patient sera	< 1	0	0%	40	80%	0.00
	1 – 5	20	40%	6	12%	
	6 – 10	24	48%	4	8%	
	> 10	6	12%	0	0%	

	Total	50	100%	50	100%	
CMV IgG in patient sera	< 1	47	94%	0	0%	0.00
	1 – 5	3	6%	30	60%	
	6 – 10	no	–	17	34%	
	> 10	no	–	3	6%	
	Total	50	100%	50	100%	

P-value ≤ 0.05 : Significance.

A **B**

Figure 2: patient with AA: (A) before using oral ganciclovire , (B) after the treatment

Discussion

In this study, the majority of patients were affected with alopecia before aged 40 years with mean age of onset 20.83±10.0 . With similar finding Ejaz *etal.* [4] showed the most of patients were in age groups 20-40 years with mean age of onset 21.4 years. the frequency of male patients with alopecia areata group was same as compared to females. This finding is

similar with Kutrev *et al*. [18] who also suggested that both sexes in alopecia areata were equal. However, Ahmed *et al*. [19] showed a female preponderance in alopecia areata. Also Seyrafi *et a*l. [20] found a female preponderance to male in their study. In this study, 40% of patients had a positive family history of alopecia areata . This finding was higher compare with other studies [8,9,10] , they reported a positive family history was apparent in approximately 10% to 25% of cases. Regarding the site of lesion, we found the most common site affected by alopecia areata was scalp, either alone in 78% of cases or affected with other sit such as beard or eyebrow. This finding resemble with Bharathi *et al* .[21] who observed that the scalp was involved in 88% of cases.

The correlation between CMV and alopecia areata was first described by Skinner *et al* [22] who found no association between CMV and development of alopecia areata. We studied the prevalence of CMV antibodies among alopecia areata. In this study ,we showed that the levels of anti-CMV (IgM) in patient sera were increased that indicates the involvement of the CMV as a cause of alopecia areata. With treatment by oral ganciclovire drug, a decrease of anti-CMV IgM levels and disappearance of CMV antigens were observed in the early stage of alopecia areata, maybe due to host defenses against viral infection. Contrariwise, we observed an increase of IgG levels, this indicates to a cure from previous viral infection.

Conclusion

Based on the this findings, we think there is a significant association between CMV infection and Alopecia areata and CMV may resulting in A.A and so anti CMV drug play a role and advice screening test for CMV in patients who suffering from AA.

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الخلاصة

يعرف داء الثعلبة على انه فقدان للشعر في منطقة او مناطق مختلفة من الجسم، على الاغلب في منطقة الراس. المسببات المؤدية لداء الثعلبة غير معروفة بشكل كاف لحد الان، فهو مرض متعدد العوامل. مؤخرا اشارت دراسات الى ارتباط بين داء الثعلبة وعدد من الاصابات الفايروسية لذلك درسنا العلاقة بين هذا المرض وفايروس المضخم الخلوي. شملت الدراسة 100 شخص (50 مصاب بداء الثعلبة و50 اصحاء) وكان معدل العمر 20.90 ± 11.07 و 22.64 ±12.29 سنة لمجموعتي المرضى والمقارنة على التوالي. اما معدل عمر الاصابة فقد كان 20.83 ±10 . 52% من المرضى كانوا ذكور اما البقية فكانوا من جنس الاناث. اما نسبة الذكور الى الاناث في مجموعة المقارنة فكانت 1:1 . 40%من المرضى امتلكوا تاريخ عائلي للمرض . 78% من الاصابات كانت في منطقة الراس. وجد ان الاجسام المضادة للفايروس من نوع ميو كانت مرتفعة عند كافة المرضى، ومع استخدام العلاج المضاد للفايروس لوحظ انخفاض نسبة الاجسام المضادة ميو وارتفاع نسبة الاجسام المضادة كاما كمؤشر على وجود اصابة فايروسية سابقة.