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STUDIES ON CYTOMEGALOVIRUS INFECTION AND ANTINUCLEAR ANTIBODY AMONG VITILIGO PATIENTS IN AHWAZ IRAN

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ABSTRACT

Recently, using polymerase chain reaction (PCR) technique, the DNA of cytomegalovirus was detected from depigmented white patches in patients with vitiligo. The reactivation of infection and occasional anti-CMV IgM circulating among patients infected by cytomegalovirus has been reported for years. We have studied 26 patients with clinical signs and symptoms of vitiligo, some of whom had a history of disease for years. Of these patients, 7 cases (26.92%) showed positive for anti-CMV IgM, indicating the presence of cytomegalovirus infection among vitiligo patients which differed significantly from control subjects ($p<0.0001$). Of these 7 patients positive for anti-CMV IgM, 6 cases (85.71%) were also positive for antinuclear antibody (ANA). On the other hand, from among the 19 cases negative for anti-CMV IgM, 7 cases (36.84%) were positive for antinuclear antibody (ANA), so the difference was statistically significant ($p<0.05$). The prevalence of anti-CMV IgM was higher among the active vitiligo patients than those with stable vitiligo ($p<0.02$).

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Keywords: Cytomegalovirus (CMV), Vitiligo, Antinuclear antibody (ANA).

INTRODUCTION

It has been estimated that 1% to 3% of the world population are suffering from vitiligo.[1] The pathogenesis of vitiligo is not quite clear, however the role of autoimmunity is considered as the most probable pathogenesis. Viral infections have been implicated in the pathogenesis of a variety of autoimmune disorders, including type I diabetes mellitus, rheumatoid arthritis, lupus erythematosus, multiple sclerosis, Sjogren's syndrome and Hashimoto's thyroiditis.[2-5] Cytomegalovirus (CMV) infection has been suggested to be associated with various autoimmune manifestations, such as hemolytic anemia, granulocytopenia, and CD13-specific autoimmunity.[6] Recently cytomegalovirus DNA has been identified in skin biopsy specimens of patients with vitiligo by polymerase chain reaction (PCR) technique which significantly enhances the detection of viral genomes in tissue samples.[1] The reactivation of infection and occasional anti-CMV IgM positivity among patients infected by cytomegalovirus has been reported for years.[7] This project was carried out to reevaluate the significance of anti-cytomegalovirus IgM (CMV IgM) among patients with vitiligo.

MATERIAL AND METHODS

26 patients (14 females, 12 males) with clinical signs and symptoms of vitiligo attending the Dermatology Department of Imam Khomeini Hospital, Ahwaz were selected for the present study. Consent was obtained from all patients participating in the study. Each patient had a complete history and skin examination. The mean age of the patients was 20 years. All patients were from Khozestan province, the capital of which is Ahwaz. 15 patients had generalized vitiligo, 7 acrofacial lesions, 2 localized and 2 segmental vitiligo. The mean duration of vitiligo was 2.5 years. 26 control subjects (12 males, 14 females) with a mean age of 26 years were selected with no history of vitiligo but having other skin disorders: androgenetic alopecia 2, ingrowing nail 1, acute urticaria 2, leishmaniasis 1, lichen simplex chronicus 2, acanthosis nigricans 1, rosa-

cea 3, hand eczema 4, keloid 1, basal cell carcinoma 1, acne 4, morphea 1, melasma 2, solar keratosis 1, and drug eruption 1 case. Their sera were collected and kept at -20°C until performing ELISA. The ELISA test kit for anti-CMV IgM manufactured by Sorein company, Italy was used for this study. The test was carried out according to the manufacturer's instructions. For each anti-CMV IgM-positive sample, the test was repeated. The immunofluorescence (IF) test was carried out for detection of anti-nuclear antibody.[8] Chi-square analysis and z test were used for evaluation of statistical significance.

RESULTS

Of these 26 sera from the vitiligo patients, 7 cases (26.92%) were positive for anti-CMV IgM, indicating the presence of cytomegalovirus infection. The other 19 samples (73.08%) were negative for anti-CMV IgM. All the 26 sera of the control group were negative for anti-CMV IgM. Of the 7 sera positive for anti-CMV IgM, 6 cases (85.71%) were positive for anti-nuclear antibody (ANA) by IF test as well. Of the 19 sera negative for anti-CMV IgM, 7 sera (36.84%) showed positive for ANA test. The frequency of anti-CMV IgM positivity among the vitiligo patients versus the control subjects was statistically significant ($p<0.0001$). Of the 7 vitiligo patients with anti-CMV IgM, 3 (42.85%) were male and 4 (57.14%) were female. The differing prevalence of anti-CMV IgM among males and females was not statistically significant ($p>0.05$). The results of ANA showed that statistical significance was observed among the anti-CMV IgM-positive and anti-CMV IgM-negative cases. Of the total of 8 active vitiligo patients, 6 cases (75%) were positive for anti-CMV IgM while only 1 stable vitiligo patient (5.55%) was positive for anti-CMV IgM, a statistically significant difference ($p<0.02$).

Table I. Clinical features of anti-CMV IgM-positive and anti-CMV IgM-negative vitiligo patients.

	anti-CMV IgM positive	anti-CMV IgM negative
No. of cases	7	19
Mean age	23	17
Sex:		
Male	3	9
Female	4	10
Mean.duration	2 years	3 years
Progression:		
Active	6 (75%)	2 (25%)
Stable	1 (5.55%)	17 (94.44%)
ANA (IF)	6 (85.71%)	7 (36.84%)
Acrofacial	3	4
Generalized	3	11
Segmental	1	0
Localized	0	4

DISCUSSION

Vitiligo is diagnosed by loss of epidermal melanocytes. The destruction of melanocytes is reportedly due to humoral and cell mediated immunologic defects caused by viral infections.[9] In vitiligo a variety of similar humoral and cell-mediated immunologic abnormalities have been reported in association with CMV infection.[10] Cytomegalovirus belongs to the herpes virus family and possesses the ability to induce primary, latent, persistent, or recurrent infection.[11] Immunological abnormalities of an autoimmune nature often develop during primary human cytomegalovirus (HCMV) infection.[12] IgM antibodies reacting with the membrane of uninfected human embryonic fibroblasts can be detected in most patients undergoing a primary human cytomegalovirus infection. It was shown that there is a common antigenic epitope shared by a cell membrane component of Mr 60K (mp60), and CMV assemble protein Mr 38K (VP38) which is recognized by IgM in sera from patients with primary human cytomegalovirus infection.[12] Evidence from DNA sequence analysis showed that human cytomegalovirus encodes a molecule similar to the MHC class-1 antigen of higher eucaryotes and this protein is responsible for beta 2-microglobulin binding.[13] It was demonstrated that homology exists between a viral intermediate early protein and HLA-DR antigen. The expression of these autoreactive antigens in the plasma membrane of cells suggests that they could serve as binding sites for cytolytic IgM antibodies identified on CMV infected cells, thereby mediating cell destruction.[14] CMV infected cells also produce a glycoprotein similar to class 1 major histocompatibility complex (MHC) antigens.[15] It has been proposed that CMV infection could potentially mediate the destruction of melanocytes in vitiligo by induction of aberrant humoral and cell-mediated immunologic responses.[1] Recently, cytomegalovirus DNA was detected in skin biopsy specimens of patients with vitiligo.[1] After primary CMV infection the reactivation and circulation of anti-CMV IgM among patients infected by cytomegalovirus has been reported for years.[7] The results of the present work indicated that anti-CMV IgM testing could be applied for vitiligo patients, especially those suffering from active progressive disease.

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