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Human Herpes Virus-6 and Human Herpes Virus -7 in Pityriasis Rosea

Pitriyazis Rozea'da Human Herpes Virus-6 ve Human Herpes Virus -7

Abstract

Objective: The etiology of pityriasis rosea (PR) remains unknown despite numerous investigations. In recent years, human herpes virus-6 (HHV-6) and HHV-7 were accused as causative agents in PR. The aim of this study was to evaluate the possible role of HHV-6 and HHV-7 in the pathogenesis of PR.
Methods: Twenty three PR patients and 23 healthy blood donors as a control group were included in the study. Polymerase chain reaction (PCR) with specific primers for HHV-6 and HHV-7 DNA sequences was performed on the serum samples of 23 active PR patients and controls, and also the lesional skin biopsies from 11 PR patients. Additionally, serum levels of IgM antibodies againts HHV-7 were detected by using indirect immunofluorescence test on the serum samples of all of the study population.
Results: No statistically significant differences were detected between PR patients and controls regarding all serum results.
Conclusion: These findings do not support a primary etiological role for HHV-6 and HHV-7 in PR as in some previous studies.
Key words: Pityriasis rosea, etiology, human herpes virus-6, human herpes virus-7

Özet

Amaç: Pitriyazis rozea (PR) etiyolojisi, birçok çalışmaya rağmen halen tam olarak aydınlatılamamıştır. Son yıllarda, human herpes virus-6 (HHV-6) ve HHV-7 suçlanmaktadır. Bu çalışmanın amacı, HHV-6 ve HHV-7'nin PR patogenezinde olası rolünü araştırmaktır.
Yöntemler: Çalışmaya 23 PR hastası ile kontrol grubu olarak 23 sağlıklı kan vericisi dahil edildi. Yirmiüç aktif PR hastası ve kontrollerin serum örneklerinde ve 11 PR hastasının lezyonlu deri örneğinde "Polimeraz Zincir reaksiyonu(PZR)" yöntemi ile HHV-6 ve HHV-7 DNA'sı araştırıldı. Ek olarak, hasta ve kontrol serum örneklerinde IFA (İndirekt Immunfloresan Antikor) yöntemi ile HHV-7'ye spesifik IgM antikorları araştırıldı.
Bulgular: Tüm serum sonuçları açısından, hasta ve kontroller arasında istatistiksel açıdan anlamlı fark saptanmadı.
Sonuç: Bu bulgular, daha önce bazı çalışmalarda olduğu gibi, HHV-6 ve HHV-7'nin PR için etyolojik rolünü desteklememektedir.
Anahtar kelimeler: Pitriyazis rozea, etiyoloji, human herpes virus-6, human herpes virus-7

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Introduction

Pityriasis rosea (PR) is a common, acute, self-healing exanthem characterised by oval erythematous-squamous lesions on the trunk, arms, and legs, usually sparing the face, scalp, palms, and soles (1,2).

The etiology and pathogenesis of the disease are unknown. However, several clinical and epidemiologic features suggest that an infectious agent is involved in the pathogenesis of PR. These include higher prevalence during an altered state of immunity, seasonal variation, case clustering in families or communities and small epidemics, occasional prodromal symptoms, the evolution with a primary and multiple secondary lesions (incubation/replication), self-limiting course and low recurrence rate (1-3).

Human herpes virus-6 (HHV-6) and HHV-7 are the member of the roseolovirus genus of the β-herpesviruses (4). There are several studies investigating the role of HHV-6 and HHV-7 in the pathogenesis of PR. Because of the conflincting results of these studies, we aimed to reveal the association of PR with HHV-6 and -7, HHV-6 and HHV-7 DNA on the tissue and the serum samples and serum levels of IgM antibodies againts HHV-7 were investigated in this study.

Methods

Subjects and Sample Collection : Twenty three patients with PR (15 females and 8 males) who referred to our outpatient clinic were included in the study. The clinical dignosis of PR was made by two dermatologists, and only patients who were considered to have typical PR were included. Patients' ages ranged between 12 and 63 years. Blood samples were obtained from all of the patients, but lesional skin biopsies were obtained from only 11 patients, during the acute phase of the disease.

Twenty three healthy blood donors (12 males and 11 females) were included in the study as a control group. Only blood samples were obtained from healthy blood donors. The study was approved by the local ethic committee.

All of the skin samples were collected in plastic tubes including physiological saline for PCR. Tissue and serum samples of patients and controls were stored at -80°C until analysis, in the laboratory of Microbiology Department.

PCR Detection of HHV-6 and HHV-7 DNA

Viral DNA İsolation: Viral DNA isolation was performed by extraction of nucleic acid from serum and tissue samples (5).

PCR Amplification: HHV-6 and HHV-7 DNA were detected by using polymerase chain reaction (PCR) with specific primers for HHV-6 and HHV-7 sequences chosen from previously published research articles of Wada et al (6) on serum and tissue samples of PR patients and controls.

Serological Detection of HHV-7: HHV-7 specific IgM antibodies on serum samples were detected by using indirect immunofluorescent test (IFAT) with commercial kits (ABI Advanced Biotechnologies Incorporated, Cat No: 15-321-000, Maryland, USA) according to the manufacturer's recommended procedures.

Statistical Analysis

The data were processed and analyzed using the statistical package SPSS-11.5 for Windows. Descriptive data are presented as proportions, means, and standard deviations. The comparisons between groups were evaluated using chi-square test, Fisher's exact test and independent t test. Significant differences (two-tailed p) less than 0.05 were regarded as significant.

Results

The PR patients consisted of 15 females and 8 males. The mean age±SD was 33.36±13.83 ranging from 12 to 63. The control population of healthy blood donors consisted of 12 males and 11 females. The mean age±SD was 31.87±11.14 ranging from 18 to 52. There were no differences between patients and healthy controls in age and sex distribution (p=0.691 and p=0.234 respectively).

Detection of HHV-6 DNA and HHV-7 DNA in Skin Sample: Eleven lesional skin biopsies were taken from the patients during the acute phase of the disease.

HHV-6 DNA was detected on the tissue samples of 5 PR patients (5 of 11) while HHV-7 DNA was detected in a significant proportion of PR patients (10 of 11) (Table 1).

DNA of both viruses was found in the skin sample of 5 PR patients. Five patients were positive for only HHV-7 DNA. Overall, DNA of one or both viruses was found in the skin of 10 of 11 (90.9%) PR patients.

Detection of HHV-6 DNA and HHV-7 DNA in Serum: Twenty three blood samples were obtained from the patients during the acute phase of the disease.

HHV-6 DNA was negative in serum for all of the study population except only one PR patient. Two blood donors was positive for HHV-7 DNA but none of the PR patients (Table 1). The frequency of HHV-6 and HHV-7 DNA in serum was not significantly different in the PR patients compared with controls (p=1.000 for the HHV-6 and p=0.489 for the HHV-7).

For the 11 patients whose skin and serum samples were taken, none of the patients with positive HHV-6 or HHV-7 DNA skin samples had positive serum results.

Detection of IgM Antibodies Againts HHV-7 in Serum: HHV-7 IgM antibodies was negative on serum for all patients and controls (Table 1).

Table 1. HHV-6 and HHV-7 DNA results of the study population

Subjects	No. of Individual	HHV-6 DNA		HHV-7 DNA	
		Positive n (%)	Negative n (%)	Positive n (%)	Negative n (%)
Pityriasis rosea					
Skin	11	5 (45.5)	6 (54.5)	10 (90.9)	1(9.1)
Serum	23	1(4)	22 (96)	0 (0)	23 (100)
Blood donors					
Serum	23	0 (0)	23 (100)	2 (9)	21 (91)

Discussion

The viral origin for PR has been suggested decades ago by the light and electron microscopic observation of intranuclear and intra-cytoplasmic virus-like particles and by the detection of cytolytic degeneration of keratinocytes (7-9). Viruses taken into consideration have been arenavirus, echovirus, coxsackie virus, influenza and parainfluenza virus, parvovirus B19, cytomegalovirus, Epstein-Barr virus, and HHV 8 (1). Recently, HHV 6 and 7 have been extensively studied.

Human herpesviruses 6 and 7 are closely related viruses that belong to the genus of the β-herpesviruses (β –HHVs) and share some common antigenic epitopes. They are commonly acquired in early childhood and are largely diffused in the general population. Like other herpesviruses, HHV-6 and HHV-7 become latent in peripheral blood mononuclear cells, saliva, and other sites after primary infection and can be reactivated (1,4,10).

Primary HHV-6 and HHV-7 infections can be identified by antibody seroconversion in acute and convalescent serum samples. In addition, viral IgM and DNA parameters are enough to show acute infection in acute serum samples. Detection of the viral DNA in a cell-free body fluid such as plasma or serum has been shown to correlate better with viral replication (2,11,12).

In our study, the frequency of positive HHV-6 and HHV-7 DNA on serum was not significantly different between PR patients and controls. HHV-6 DNA was positive on the serum samples of only one PR patient. A serological assay for HHV-6 could not be performed because IFAT kit for HHV-6 could not be obtained during the study period. HHV-7 DNA and also HHV-7 IgM antibodies were negative in all serum samples of PR patients. These results, except for the patient whose HHV-6 DNA was positive on serum sample, did not indicate acut HHV-6 and /or HHV -7 infection and their possibble etiological role. As we could not take a skin sample from the patient with positive HHV-6 DNA on serum sample, we could not suggest a causative role of HHV-6 infection for this patient.

In the study, biopsy samples were obtained from only 11 of 23 patients. Though it would be more precise to have the biopsy samples of all patients, serum results for HHV-6 and HHV-7 are more valid to idantify the presence of acute infection, and clarify the etiological relationship betwee PR and the viruses. HHV-6 DNA was present in 5 of 11 (45.5%) lesional skin, while HHV-7 DNA was present in 10 of 11 (90.9%) lesional skin of PR patients. The detection of HHV-7 and HHV-6 DNA on the lesional skin samples in the acute stage of the disease, suggested that these two viruses, especially HHV-7, may play a role in the etiology. However, detection of the viral DNA in tissue samples is not sufficient to differentiate acute or latent infection, as HHV DNA persists in tissue of healthy persons. On the contrary, detection of the viral DNA in both blood and tissue samples is more efficient to identify acute infection. In the present study, none of the patients with positive HHV-6 and/or HHV-7 DNA skin samples had positive serum results.

Overall, our results failed to support the casual relationship between HHV-6, HHV-7 and PR, as in some other previously published studies (13-20). There are several studies in the literature suggesting an association of PR with HHV-6 and/or HHV-7 but no virus isolation has been performed (2, 12, 22-25). These contradictory results have not clarified whether primary or recurrent HHV-7 and HHV-6 infection can elicit PR. Further studies are necessary to elucidate the causative role for HHV-6 and HHV-7 in the etiopathogenesis of PR.

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