

IL-10 Levels in Patients with Warts

VERRÜLÜ HASTALARDA IL-10 SEVİYELERİ

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Abstract

Objective: Warts are benign epitheliomatous proliferations caused by human papilloma virus infection. IL-10 is an inhibitor cytokine which is mainly secreted from T helper 2 subtype lymphocytes. IL-10 shows its inhibitory effect by decreasing the cytokine secretion of T helper 1 lymphocytes and is important in limiting the inflammatory reaction. In this study, we decided to evaluate IL-10 levels of the patients with warts comparing with the healthy, age and sex matched volunteers.

Material and Methods: 54 patients (31 female (57.4%) and 23 male (60.7%)) with warts who attended to Ankara Numune Education and Research Hospital, 1st Dermatology Clinic between 2004 and 2005 years are included in the study. 28 healthy volunteers (17 female (60.7%) and 11 male (39.3%)) were also taken into the study. IL-10 levels from the serum were measured with solid phase sandwich ELISA kit (Biosource International Inc, USA) and absorbance levels were recorded. The statistical analysis was performed using chi-square, t-test, Mann-Whitney using SPSS 11.5 packet programme.

Results: IL-10 levels were higher in the patients group. This difference between the patients and controls groups was statistically significant (p<0.01).

Conclusion: IL-10 is an inhibitory cytokine that limits the inflammatory response in especially cellular immunity. In our study, we found an increased IL-10 levels in wart patients controlled with the healthy volunteers. This immunologic dysfunction may give additional data about the pathogenesis of the warts.

Key Words: Warts, interleukin-10

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Özet

Amaç: Verrümler deri ve mukozaların papilloma virüsler ile enfeksiyonu sonucu oluşan benign epitelyal proliferasyonlardır. IL-10 özellikle T helper 2 subtipindeki lenfositlerden salgılanan inhibitör bir sitokindir. Bu inhibitör özelliğini T helper 1 lenfositlerden salınan sitokinleri azaltarak gösterir ve inflamatuvar reaksiyonların sınırlandırılmasında önemli rol üstlenir. Verrülü hastaların serum IL-10 seviyelerini ölçerek, yaş ve cinsiyet uyumlu sağlıklı kontrollerle karşılaştırmayı amaçladık.

Gereç ve Yöntemler: Çalışmaya 2004 ve 2005 yılları arasında Ankara Numune Eğitim ve Araştırma Hastanesi 1. Dermatoloji Kliniğine başvuran 54 verrülü hasta (31 kadın (%57.4) ve 23 erkek (%60.7)) ve 28 sağlıklı gönüllü (17 kadın (%60.7) ve 11 erkek (%39.3)) alındı. Serum IL-10 absorbans seviyeleri solid faz sandwich ELISA kit (Biosource International Inc, USA) kullanılarak ölçüldü ve kaydedildi. İstatistiksel analiz için ki-kare, t-test ve Mann-Whitney SPSS 11.5 paket programı kullanılarak yapıldı.

Bulgular: Hasta grubunda IL-10 seviyeleri, sağlıklı kontrollere göre istatistiksel olarak anlamlı derecede yüksekti (p<0.01).

Sonuç: Verrülü hastalarda yüksek çıkan IL-10 seviyelerinin, hastalık patogenezinde immunolojik önem taşıyabileceğini düşünmek-teyiz.

Anahtar Kelimeler: Verruka, interlökin 10

Warts are benign epitheliomatous proliferations caused by human papilloma virus infection. These slow

enlarging lesions may persist subclinically for years.^{1,2}

Viral warts are more common in childhood and adolescence. Lesions contagiousity depends on lesion localisation, contact way, infectious viral particle amount and HPV specific immunologic status of the patient. Patients with defective cellular immunology have increased susceptibility to viral warts.^{3,4}

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IL-10 is an inhibitor cytokine, main action of which is limiting and ending the inflammatory response. IL-10 strongly suppresses the secretion of IL-1 alpha, beta, IL-6, IL-12, IL-18, GM-CSF, G-CSF, TNF alpha, PAF, and IL-10 from activated monocytes and macrophages.⁵ IL-1 and TNF effects are supposed to be the key factor of IL-10 on the antiinflammatory activity.^{6,7}

There are some reports showing the increased IL-10 levels in diseases such as leishmaniasis, herpes zoster infection, and HIV infection and suggest that this elevation is important in the pathogenesis by suppressing the cellular immunity in the above disorders.⁷⁻⁹ Upregulated IL-10 expression has been shown to contribute to the persistence of parasitic and retroviral infections.¹⁰

In this study, we evaluated IL-10 levels of the patients with warts comparing with the healthy, age and sex matched volunteers. The relation between IL-10 levels and patient's age, sex, the number of lesions and duration of the disease were also examined to elucidate the possible effect of IL-10 levels in patients with warts.

Material and Methods

54 patients (31 female (57.4%) and 23 male (42.6%)) with warts who attended to Ankara Numune Education and Research Hospital, 1st Dermatology Clinic between 2004 and 2005 years were included in the study. Patients with known immunosuppression and epidermodisplasia verruciformis or patients who take any topical or systemic medication for the last one month were excluded from the study. All the included patients asked for their age, duration of the disease, clinical wart type and number of the lesions. 28 healthy volunteers (17 female (60.7%) and 11 male (39.3%)) were also taken in the study. All the healthy volunteers signed the volunteer consent form.

Serum IL-10 levels were measured after 8 hours fasting of both patients and controls with solid phase sandwich ELISA kit (Biosource Inter-

national Inc, USA) and absorbance levels were recorded. The statistical analysis was performed using chi-square for sex and age distribution, T-Test for age comparison, Mann-Whitney for the comparison of IL10 levels in independent variables using SPSS 11.5.

Results

The ages of the patients were between 6 and 71 (mean 22.50 ± 12.09) whereas the ages of the control group were between 6 and 36 (mean 22.96 ± 6.14). They were statistically matched and the age distribution was homogeneous. Sex distribution of both patient and control groups was also homogeneous. 20 patients showed verruca vulgaris, 7 showed verruca plana, 5 showed verruca filiformis, 4 showed verruca anogenitalis and 8 patients were presented with mixed warts. There were totally 5 anogenital verruca patients, one from the mixed group. The numbers and mean IL-10 levels of wart types are shown in Table I. To simplify the evaluation, patients were divided into two groups such as; genital and nongenital verruca patients. According to the number of lesions, patients were divided into 2 groups such as; patients who had lower than 10 warts and higher than 10 warts. The duration of the disease of all patients was between 1 month to 10 years. Patients were grouped as patients who show lesions for less than 1 year and more than 1 year. In both groups, 27 patients were recorded.

The results are shown in Table II.

Table 1. Mean IL 10 levels of wart types.

Wart type	n	Median IL-10 Levels (min - max) (pg/ml)
Vulgaris	20	9.08 (6.58-33.47)
Anogenitalis	4	9.03 (8.69-14.22)
Plantaris	10	8.93 (6.99-10.86)
Plana	7	8.09 (6.99-9.87)
Filiformis	5	8.29 (7.29-11.85)
Mixed	8	8.09 (6.89-9.48)

Table 2. IL-10 levels of patient and control groups and their statistical analysis.

Variables	Subgroups	IL-10 Levels (pg/ml)	p
		Median (Min – Max)	
Study Groups	Control	7.09 (5.67-12.64)	< 0.001
	Case	8.44 (6.58-33.47)	
Sex	Female	8.39 (6.58-33.47)	0.446
	Male	8.59 (6.89-10.96)	
Duration	= <1 year	8.39 (6.58-33.47)	0.938
	> 1 years	8.69 (6.89-10.96)	
Number of warts	< 10	8.39 (6.89-33.47)	0.435
	= > 10	8.49 (6.58-10.86)	

Discussion

Warts are benign epitheliomatous proliferations caused by human papilloma virus infection. Etiologically, human papilloma viruses are supposed to be the cause of viral warts. Papilloma viruses are double stranded DNA viruses that are highly type specific, thus human papilloma viruses are human specific.² According to the biological behavior of the virus, anatomical site predilection and lesional histopathology, HPV types may be classified in three groups, such as; cutaneous type (HPV-1,-2,-3,-4); genital mucosal type (HPV -6,-11,-16,-18); and epidermodysplasia verruciformis type (HPV -5, -8).¹

The incubation period of HPV infection is ranging from 1 to 18 months with a mean duration of 4 months.^{11,12} Patients with clinic and subclinic infection are supposed to be the viral reservoirs.¹ Women with cervical HPV infection have a high malignancy risk. The persistence of viral DNA is shown to be correlated with cervical dysplasia and invasive carcinoma conversion.^{1,13-15}

IL-10 is an inhibitor cytokine, main action of which is limiting and ending the inflammatory response. IL-10 inhibits monocyte, macrophage functions by decreasing monokine nitric oxide, IL-12, and MHC class II molecular expression.^{5,16} By suppression of these cells, cytokine production of T lymphocytes and NK cells are also inhibited indirectly.¹⁷ IL-10 also effects lymphoid and plasmacytoid dendritic cells. These cells secrete IFN

alpha after activation, and support the maturation of T helper 2 subtype lymphocyte that produce IL-10. IL-10 induces dendritic cell apoptosis. Hence, IL-10 shows its main effect on dendritic cells by inhibition of T helper 1 subtype lymphocytes. IL-10 also has an indirect effect on neutrophil apoptosis.¹⁸

In the review of the literature the increased IL-10 levels was found to be reported in diseases such as leishmaniasis, herpes zoster infection, and HIV infection. This suggests that elevation is important in the pathogenesis by suppressing the cellular immunity in the above disorders.⁷⁻⁹ Besides, upregulated IL-10 expression has been shown to contribute to the persistence of parasitic and retroviral infections.¹⁰ We found an increased IL-10 level in patients with warts compared with healthy controls. This result is consistent with the above mentioned inhibitory mechanisms of IL-10.

We found that patients with higher IL-10 levels have longer disease duration, although the statistical analysis was marginally insignificant (p=0.051). This result also supports the inhibitory effect of IL-10 in defense mechanisms against wart agents.

Arany et al showed that IL-10 is significantly elevated in cervical dysplasias or carcinomas as well as in the cervix of HIV-positive individuals.¹⁹ El-Sherif et al reported that increased subepithelial IL-10 synthesis may play a role in the development and progression of HPV-16 associated cervical precancer.²⁰ Besides, there are reports suggesting an increased peripheral IL-10 levels in HPV associated cervical intraepithelial neoplasia (CIN), which is correlated with the disease severity.^{21,22} Although we did not experience any difference between genital and nongenital warts, this may be due to the few number of anogenital wart cases involved in our study.

de Oliveira et al stated that patients with epidermodysplasia verruciformis (EV) showed an increased rate of low-production genotypes of IL-10 compared with control group, and concluded that IL-10 genotypes associated with low levels of

IL-10 production may have an important role in the pathogenesis of EV.²³ In our study, we were expecting to find a significantly elevated IL-10 levels in patients who have more than ten lesions compared with patients who have less than ten lesions. However, we did not find any significant difference and we think that new and larger series are needed to elucidate this condition.

Jackson et al found that IL-10 mRNA was significantly down regulated in warts compared with normal skin.²⁴ Elevated IL-10 levels observed in our results were similar to previous reports about genital warts, while being discordant with the extragenital wart studies. However, our results seem to support the inhibitory effect of IL-10.

Conclusion

As a result, we found a statistically significant increase in the levels of IL-10 in patients with warts compared with the healthy controls in our study. This increase in the cytokine levels may have an effect on inhibition of immunological response of the patients to warts and concluded that this immunologic dysfunction may give additional data about the pathogenesis of the warts.

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