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Prevalence of *Candida* Species in Patients with Psoriasis

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ABSTRACT Investigation of *Candida* yeast prevalence in patients with psoriasis has been performed with the aim of determining their possible role as a trigger factor in the pathogenic process of this disease. The purpose of our study was to investigate the prevalence of *Candida* species on the skin of intertriginous areas and psoriasis lesions as well as the prevalence of *Candida* species in the stool of patients with psoriasis. This study also examines a possible correlation between the severity of psoriasis and prevalence of isolated *Candida* species. The patients with psoriasis were divided into two groups according to the clinical type of psoriasis; a group with plaque psoriasis (PP) and psoriasis inversa (PI) (G1) and a group with psoriasis erythrodermica (PE) and psoriasis pustulosa (PPS) (G2). The group of patients with PP and PI (G1) was divided according to score on the Psoriasis Area Severity Index test (PASI) according to severity of disease into the clinical subgroup with PASI <50 and another subgroup with PASI >50. Mycological analysis of skin samples in patients of the clinical group with PP and PI showed a statistically significant difference as well as correlation between the results of isolated specimens of *Candida* species from the skin of intertriginous areas and psoriasis lesions, the clinical form of psoriasis, and the PASI score.

KEY WORDS: *Candida*; psoriasis; PASI, severity

INTRODUCTION

Psoriasis is a chronic, relapsing inflammatory skin disease characterized by abnormal keratinocyte differentiation and proliferation. Besides genetic predisposition, many endogenous and exogenous provoking factors play an important role in the development of the disease. Infections have been recognized as a trigger for the onset or exacerbation of psoriasis (1,2). Several studies suggested that various micro-organisms such as *β-hemolytic Streptococcus, Staphylococcus aureus* and *Candida albicans* may release factors that act as superantigens and thus stimulate the pathogenic process of psoriasis. Superantigens are the microbial proteins which are able to stimulate up to 20% of the naive T-cell population in a nonspecific way (3,4). It is thought to play an important role in the pathogenesis of inflammatory skin and systemic diseases, such as psoriasis, atopic dermatitis, vasculitis, T-cell lymphoma, and autoimmune diseases. The role of the superantigens in the pathogenesis of these diseases is determined by its ability to cause extensive inflammatory cytokine release after stimulation of T-cell and/or T-lymphocyte-mediated cytotoxicity, and thus damage to the tissue. Activation and infiltration of T-lymphocytes play a key role in the development and maintenance of psoriasis (5). The purpose of this study was to determine the prevalence of *Candida* species on the skin and in the intestinal tract of patients with psoriasis and to determine if there is a correlation between severity of psoriasis with the test results of isolated *Candida* species samples.

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PATIENTS AND METHODS

Patients

The study included 80 patients with different clinical types of psoriasis (29 women and 51 men, median age 45.8 years). According to the clinical type of psoriasis, the patients were divided into two groups, a group with plaque psoriasis (PP) and psoriasis inversa (PI) (G1) and a group with psoriasis erythrodermica (PE) and psoriasis pustulosa (PPS) (G2). The group of patients with PP and PI was divided according to the Psoriasis Area Severity Index (PASI) score, according to severity of disease into the subgroups with PASI score less than 50 (G1A) and PASI score more than 50 (G1B). Patients with psoriasis were excluded from the study if they had received systemic or topical antimicrobial or immunosuppressive treatment during the preceding three months or if they had a previous diagnosis of diabetes mellitus.

Methods

All included patients with psoriasis gave their medical history; clinical examination of skin changes was conducted and clinical tests were performed – the auxiliary physical search method specific for psoriasis. Skin samples from psoriatic lesions and intertriginous areas as well as stool samples for fungal cultures were taken from all the study participants. In patients with psoriasis inversa, samples for mycological analysis were taken both from the skin folds with psoriatic lesions and from skin lesions suspected of intertriginous candidiasis.

Laboratory analysis

Skin samples from the intertriginous areas and psoriatic lesions, and stool samples were taken using a sterile cotton-tipped swab. Collected samples were inoculated separately into Sabouraud dextrose agar plates with the addition of antibiotics to prevent bacterial growth. Sabouraud dextrose agar plates were incubated at 37°C and examined for 48 hours. After this period, the plates with cultures were inspected and selected as positive and negative and with and without yeast growth. In this way, the isolation of yeasts was performed and the number of colonies on plates with inoculated stool samples was determined. A germination test was used for identification of *C. albicans* and its differentiation from non-*C. albicans* species. All yeast isolates were classified in two groups: *C. albicans* species (CA) and non-*C. albicans* (NCA) species, without individual identification of non-*C. albicans* species.

Statistical analysis

Analysis of statistical data was conducted using the Chi-square test and Pearson test of correlation at the level of 95% significance. All statistical calculation was done using the SPSS computer program, version 13 for Microsoft Windows (SPSS Inc, Chicago, Illinois, USA).

RESULTS

A total of 60 patients were included in the group with PP and PI (G1), and 20 patients were included in the G2 group with atypical clinical types of psoriasis (PE and PPS) (Table 1, Table 2). The average age among the total of 80 patients was 45.8 years±16.2, with the youngest patient at age 9 and the oldest at age 75. Statistical analysis did not find significant differences in age of patients between the two clinical groups (G1 and G2 groups), (x^2=5.190, *P*>0.05).

Table 1. Distribution of patients according to clinical group G1 and G2

Clinical group	Clinical form	Patients	
		n	%
G1	PP+PI	60	75.0
G2	PE+PPS	20	25.0
Total		80	100.0

G1 (PP: plaque psoriasis, PI: psoriasis inversa); G2 (PE: psoriasis erythrodermica, PPS: psoriasis pustulosa)

Table 2. Distribution of patients according to clinical subgroup G1A (PASI <50) and G1B (PASI >50)

PASI	Clinical form				Total patients	
	PP		PI			
	n	%	n	%	n	%
<50 (G1A)	32	65.3	7	63.6	39	65.0
>50 (G1B)	17	34.7	4	36.4	21	35.0
Total	49	100.0	11	100.0	60	100.0

PASI: Psoriasis Area Severity Index

Mycological analysis of skin samples

The swab findings from the skin of all patients in clinical group G1 (PP and PI) and G2 (PE and PPS) are presented in Table 3 and Figure 1.

Positive isolates from the skin of intertriginous areas and psoriatic lesions were found in 33.3% of patients with PP and PI and with PASI <50 (G1A). In the group of patients with the severe clinical type of psoriasis with PASI >50 (G1B), there were 33.3% positive isolates from the skin (Figure 1). We found a statistically significant difference between the findings of

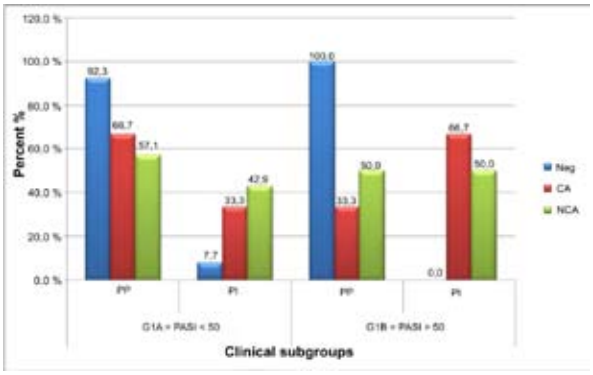

Figure 1. The skin swab findings of in patients from clinical group G1 (PP and PI) – correlation with severity of disease.

the skin swab (including both intertriginous regions and psoriatic lesions) and the clinical type of PP and PI with PASI <50, and the same clinical type of disease with PASI >50 (x^2=15.83, *P*<0.014). Furthermore, statistical analysis revealed a significant correlation between the skin swab findings (including both intertriginous regions and psoriatic lesions), clinical disease type G1 patient group (PP and PI) and the PASI score, in the sense that in severe clinical types with higher PASI scores there were more positive isolates of *Candida* species; Ro=0.378, *P*=0.018 (*P*<0.05). There was no statistically significant difference or correlation between findings of skin swabs (intertriginous regions and psoriatic lesions) of the two clinical groups, G1 and G2 (*P*>0.05).

Table 3. The prevalence of *Candida* species on the skin of intertriginous areas and psoriatic lesions (total), in patients in clinical groups G1 and G2

Yeast isolates findings	Clinical group				Total of isolates findings	
	G1		G2			
	Clinical type (PP+PI)		Clinical type (PE+PPS)			
	n	%	n	%	n	%
Neg	40	66.7	13	65.0	53	66.3
CA	9	15.0	3	15.0	12	15.0
NCA	11	18.3	4	20.0	15	18.7
Total	60	100.0	20	100.0	80	100.0

Neg: negative findings; CA: *Candida albicans*; NCA: non-*Candida albicans*

Results of the mycological findings in the stool samples

In the total sample of 80 patients, 52% had positive findings in the stool, out of which 38.8% isolates were *C. albicans* and 10.0% were isolates of non-*C. albicans* species. Mixed cultures (CA and NCA) were isolated in 3.7% patients. Statistical analysis showed no significant difference between mycological findings from the stool between the two clinical groups (G1 and G2), (*P*>0.05).

Table 4. Mycological stool findings in patients in clinical subgroups G1A (PASI <50) and G1B (PASI >50)

Yeast isolates findings	Clinical group				tTotal isolates findings	
	G1A PASI <50		G1B PASI >50			
	n	%	n	%	n	%
Neg	23	59,0	7	33,3	30	50,0
CA	11	28,2	11	52,4	22	36,7
NCA	3	7,7	3	14,3	6	10,0
CA+NCA	2	5,1	0	0,0	2	3,3
Total	39	100,0	21	100,0	60	100,0

G1 (PP: Plaque psoriasis, PI: Psoriasis inversa); G1A (clinical form PP and PI, with PASI <50); G1B (clinical form PP and PI, with PASI >50)

Results of stool mycological findings in patients from the clinical group with PP and PI (G1) according to the severity of clinical symptoms assessed using the PASI test are presented in Table 4. We did not find significant differences between the mycological findings in the stool for patients with PP and PI with PASI <50 and the same clinical type of psoriasis with PASI >50 (*P*>0.05). Furthermore, there was no statistically significant correlation between the mycological findings in the stool, clinical form of disease (PP and PI), and the PASI score (*P*>0.05).

DISCUSSION

A combination of genetic and numerous endogenous and exogenous factors are responsible for psoriasis occurrence and detection of the disease (6). Newer hypotheses on the pathogenesis of psoriasis are based on the dominant role of the cellular immune system in exacerbation of the disease (7). Many authors believe that microorganisms such as *β*-hemolytic *Streptococcus, Staphylococcus aureus*, and *Candida albicans* can act as exogenous triggers and release factors which act as superantigens. The source of these microorganisms may be in the skin or in other parts of the body such as the gut, in case of the *Candida* species. From this location, *Candida* and another microorganisms release their superantigens that reach the skin through the vascular system and start the psoriatic process (8). Sayama *et al.* concluded

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that superantigens may be factors for exacerbations or "triggers" of psoriasis, but they are not essential for disease maintenance (9). Very small amounts of data in the available literature indicate the prevalence of *Candida* yeasts in patients suffering from psoriasis, especially the prevalence in intertriginous areas of the skin and in psoriatic lesions, so this was one of the initial factors that encouraged us to engage in this study. It was suggested that cutaneous or intestinal *Candida* is a trigger of plaque psoriasis (10). Based on this, the results of some studies showed that systemic antifungal treatment with ketokonazol or nystatin was very effective in some patients with psoriasis (11). During analysis of the microflora in 297 patients suffering from psoriasis, Noah found more than 30 different microorganisms in psoriatic skin lesions, including the yeast *C. albicans* and *C. parapsilosis* (12). Rosenberg *et al.* have explored the association between microorganisms and psoriasis in 167 patients with psoriasis, and isolated an insignificant number of *Candida* yeasts in a skin fold (13). Flyström *et al*. investigated the presence of microorganisms on the intertriginous areas of the skin in patients with inverse psoriasis ("intertriginous psoriasis"). *Candida* was not isolated from the intertriginous skin region; none of the patients from the three groups studied was positive (1).

In our study, analysis of mycological findings from the skin of intertriginous areas and psoriatic lesions in patients with PP and PI, with PASI <50 and PASI >50, showed a statistically significant difference and correlation between the swab findings, clinical form of disease, and severity of the disease determined by PASI. In patients with PI and with PASI >50, there were no negative mycological findings from the skin of intertriginous areas, which was expected due to the pronounced tendency of this form of exudation and additional superinfection.

Henel *et al*. conducted tests on the incidence of *Candida* species in the stool of patients with psoriasis; these studies were based on the assumption that the intestinal *Candida* may be a "trigger" factor of psoriasis (14). The study of Menzel and Holzman found *Candida* yeasts in 92.0% of patients, while the prevalence of *Candida* was 50.0% in the control group (15). In our study, *Candida* was isolated in the stool of 52.2% patients, and *Candida albicans* dominated at 38.8%. There was higher prevalence of *Candida* species in the stool of patients with PE and PPS (60.0%). There was no statistically significant difference between the mycological findings in the stool and clinical findings in the group of patients with PP and PI and the group of patients with PE and PPS.

Analysis of the prevalence of *Candida* species in the stool of patients with PP and PI with PASI <50 and PASI >50 showed a higher prevalence of *Candida* in patients with the severe clinical form of the disease (PASI >50) (66.6%). Statistical analysis showed no significant difference between the mycological findings for *Candida* in the stool, the clinical form of psoriasis, and PASI score. In the study conducted by Waldman *et al*. which included 50 patients with psoriasis , *Candida* was isolated in the stool of 72% of patients (16). *C. albicans* was isolated at the highest percentage, namely 64.0%. The authors of this study did not find a correlation between disease severity assessed by PASI score and quantitative analysis of *Candida* in the stool of patients with psoriasis, which is similar to the results of our study.

CONCLUSION

This study revealed a significant association between psoriasis and *Candida* and also showed that the frequency of *Candida* species in the stool was higher than the frequency of *Candida* species on the skin of intertriginous areas and psoriasis lesions. Further studies are needed to establish whether the frequency of isolated *Candida* species correlates with the degree of severity of psoriasis. Use of new molecular methods applied to more patients is needed to clarify the involvement of *Candida* in the development or exacerbation of psoriasis. However, our studies suggest that an antifungal treatment should be considered as an adjuvant treatment in patients with psoriasis that have a significant quantity of *Candida* in the stool.

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