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Subclinical Microbial Infection in Patients with Chronic Plaque Psoriasis

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Epidemiological evidence implicates bacterial infection as a common triggering stimulus for psoriasis. Recent studies suggest that continuing, subclinical streptococcal and staphylococcal infections might be responsible not only for relapse of acute guttate psoriasis but also for a new episode of chronic plaque psoriasis. In this study 195 patients suffering from a severe form of chronic plaque psoriasis hospitalized between 1996 and 1998 were examined. The presence of subclinical microbial infection of the upper respiratory tract was studied by the cultivation of pathogens from this area. Patients with other provoking factors, such as a positive history of taking any drugs that may exacerbate psoriasis, endocrine and metabolic factors, alcohol abuse, trauma, dental focus and clinically evident bacterial infection, were excluded. Subclinical streptococcal and/or staphylococcal infections were detected in 68% of tested patients and in only 11% of the control group. The results of this study indicate that subclinical bacterial infections of the upper respiratory tract may be an important factor in provoking a new relapse of chronic plaque psoriasis. Searching for, and eliminating, microbial infections could be of importance in the treatment of psoriasis. ***Key words: triggering factors; autoimmunity; superantigens.***

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INTRODUCTION

Understanding the pathogenesis of psoriasis remains a significant challenge in dermatological research. A major thrust of recent research has been the clarification of the molecular basis for psoriasis and the relative importance of genetic and environmental factors in triggering it. There is no doubt that psoriasis is a hereditary disease, although the mode of inheritance is still not clear. Psoriasis appears to be a genetically heterogeneous disease with multiple and complex biological system abnormalities (1). Different factors are now accepted as being of importance in provoking a new episode of the disease. A wide range of local stimuli, including physical, chemical, surgical, infective and inflammatory insults, are recognized as eliciting psoriatic lesions (2). The role of bacterial infection in provoking acute guttate psoriasis has frequently been described (3, 4). Both older and newer studies suggest that continuing subclinical streptococcal infection may also be responsible for refractory chronic plaque psoriasis (5, 6). As more is learned regarding the pathogenesis of psoriasis, it is becoming clear that T-lymphocyte activation and infiltration play an important role in the initiation and maintenance of clinical disease (7, 8). Some bacterial antigens appear to have a potential role in the induction of the localized inflammatory response that leads to the clinical lesions of psoriasis (7, 9, 10). These "superantigens" bypass the most restrictive features of antigenic T-cell activation and stimulate a large proportion of the T-cell population (11). Recently, it has been shown that intradermal injections of streptococcal extracts into normal skin of patients with psoriasis can lead to lesions pathohistologically consistent with psoriasis (12). T lymphocytes obtained from patients with psoriasis have been demonstrated to have an enhanced proliferative response to group A streptococcal antigens (13).

The main aim of this study was to determine the frequency of subclinical microbial infection in patients suffering from a severe relapse of chronic plaque psoriasis.

MATERIALS AND METHODS

Patients

Inpatients at The Department of Dermatology, University Medical Center Ljubljana between 1996 and 1998 were enrolled in the study. Of the 195 patients enrolled, 122 were female (17–83 years old, median age 51 years) and 73 were male (18–74 years old, median age 47 years).

The following inclusion criteria were used: worsening of chronic plaque psoriasis, with >25% of the skin area affected; and no change of treatment in the month before the worsening. For exclusive evaluation of the role of microbial infections, patients with clinically evident microbial infections, dental focus or any other known triggering factor were excluded. The following triggering factors were considered: major trauma during month before treatment; known metabolic or endocrine disease; a positive history of taking any drugs that may exacerbate psoriasis; and alcohol or illegal drug abuse.

Study design

The study was designed to be retrospective. The data were obtained from documentation of history, investigations and results of patients with psoriasis hospitalized in our Department who were selected using the aforementioned inclusion and exclusion criteria. We considered a microbial infection to be confirmed when ≥1 of the following tests were positive: identification of pathogenic bacteria in a pharyngeal or nasal swab (considered positive with the presence of 1% of pathogenic bacteria in the culture); or pathologically elevated values of antistreptolysin titers (>240 IU/ml). Candidal infection was assumed to be confirmed if yeasts from *Candida* spp. were isolated and identified from a pharyngeal swab.

RESULTS

Of the 195 patients enrolled in the study, bacterial or yeast infections were searched for in only 117 patients (60%). Of these, infections were confirmed in 89 patients (76%). Only one pathogen was detected in 33 patients (28%) and multiple infective organisms were detected in 56 patients (48%). In 80 patients (68%) infection with *Streptococcus haemolyticus group A* and/or *Staphylococcus* spp. was demonstrated. Considering only the microbes identified from pharyngeal and nasal swabs, the following were isolated most frequently: *S. haemolyticus group A* (42.6%); *Staphylococcus* spp. (29.9%), of which *S. aureus*

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comprised 86%; *Haemophilus influenzae* (8.1%); *Klebsiella oxytoca* (5.4%); *Moraxella catarrhalis* (5.4%); *Escherichia coli* (2.7 %); and *Candida albicans* (5.4%).

DISCUSSION

This study began out of curiosity. Our national insurance company, in its endeavor to provide only the bare minimum of funding to hospitals and private practitioners, is on perpetual guard for investigations which are not clinically important and therefore unnecessary. Having at our disposal both literature data and our clinical (but unproven) impressions that microbial infections may very often lead either to the first exacerbation of psoriasis or to worsening of an otherwise stable disease, we designed the present study.

The aforementioned percentage of positive identification of infectious pathogens in our patients served our objective very well; however, the high incidence of bacterial infection was quite surprising. Therefore we enrolled a smaller control group (55 patients; 30 women, 25 men; age 15–57 years; average age 37 years) of patients with alopecia areata of unknown etiology. In common with psoriasis, alopecia areata has previously been considered by some authors to be connected with microbial focuses. In this group of otherwise healthy patients, with no known endocrinological or autoimmune disease, the same tests were conducted as for the psoriasis group. Microbial infections were detected in 9 (16.3%) of the tested patients: *S. aureus* in 3; *S. haemolyticus group A* in 2; and *S. haemolyticus group D* in 1. Subclinical streptococcal or staphylococcal infections was also found in 11% of patients in the control group. *Haemophylus influenzae*, *M. catarrhalis* and *C. albicans* were also isolated in 1 patient each.

Although the control group is smaller than the psoriasis group and not adjusted with regard to the age and sex of the patients, the data showed a statistically significant higher incidence of microbial infections in psoriasis patients ($p < 0.005$) when analyzed using the χ^2 test. We believe that the surprisingly high incidence of microbial infections in psoriasis patients supports the immunological theory in which microbial infections are an important factor in the pathogenesis of psoriasis. However, many of the possible mechanisms and pathways are still being discussed in the scientific community. Some authors assert the concept of autoimmunity (14), where the patient's immune system reacts inadequately against his/her own tissues, as if they were a foreign pathogen. However, many other authors dispute this hypothesis (15–17). A second possibility is the development of a complex immune response to microbial antigens present in tissues (18, 19). Findings supporting this option were published as long ago as the late 1970s (20), which became very probable with the publication of microbial findings in 1990 (21). In recent years more and more scientists have mentioned superantigens as one of the most important psoriasis-triggering mechanisms (11, 22).

Considering all this evidence, and taking the results of our study with a pinch of salt, we share the opinion of Rosenberg et al. (23) that in patients with a severe relapse of chronic plaque psoriasis microbial infections should be searched for and, if possible, eliminated.

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