Psoriasis - investigating the link between genetics and comorbidities in a Romanian population

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INTRODUCTION

Psoriasis is one of the most frequently encountered and yet one of the least understood skin diseases in current clinical practice. Genetic study progresses made in the last decades [1] and the efforts put into understanding the immunological mechanisms involved in psoriasis have given birth to the current concept that psoriasis is a systemic inflammatory disease. This permanent subclinical inflammatory state apparently leads to an increased cardio-cerebro-vascular morbidity in these patients, when compared to the general population.

Metabolic syndrome (MS) has been proven to represent a multi-systemic aggressor, affecting the musculoskeletal, cardiovascular, digestive, endocrine and cutaneous systems.

SNPs (single nucleotide polymorphisms) are the most common type of genetic variation. A SNP represents a mutation characterized by the difference of a single nucleotide in the DNA of a gene. Some SNPs can influence the affected gene's activity.

METHODS

This was a cross-sectional study, carried out between April 2014 and May 2016. *Inclusion criteria:* a clinical and histopathological diagnosis of psoriasis, age between 18-90 years old. *Exclusion criteria:* the presence of systemic infectious or neoplastic diseases.

Metabolic syndrome was defined using the 2006 IDF (International Diabetes Federation) criteria [2].

Patient general data: age, sex, height, weight, PASI score [3], DLQI score, metabolic syndrome IDF criteria, and comorbidity data.

The DNA necessary for genotyping was extracted and quantified using QIAamp DNA Mini Kit (QIAGEN). Only after having verified the quantity and purity of the extracted DNA did we proceed to the genotyping phase which was done *via* rt-PCR using TaqMan® (Life Technologies, SUA) probes, specific to each studied allele.

In light of the data from previous studies, the following SNPs were included: **rs361525** (TNF-238 G/A), chromosome 6, TNF gene, position 31575324 promoter region; **rs1800629** (TNF-308 G/A), chromosome 6, TNF gene, position 31575254 promoter region; **rs1800896** (IL10-1082 G/A), chromosome 1, position 206773552; **rs610604**, chromosome 6, TNFAIP3 gene, position 137878280; **rs17782313**, chromosome 18, MC4R gene, position 60183864.

Data analysis. Raw data were collected using the Light Cycler® 480 Gene Scanning Software and then imported into LightCycler® 480 Endpoint Genotyping which automatically performed genotyping into one of the following: ancestral homozygote (AA) or mutant homozygote (MM) and heterozygote (AM). Statistical analysis was performed using SPSS v20 (IBM, USA) with significance being established at <0.05 (CI 95%).

CONCLUSIONS

- Patients with **psoriasis and MS** have a **higher risk** of developing **psoriatic arthropathy**, a severe and debilitating complication.
- Being heterozygote for SNPs **rs610604** and **rs17782313** strongly influences the presence of DM, while the latter also influences the presence of obesity alone.
- SNPs **rs361525** and **rs1800629** did not show any influence in the statistical model, possibly due to the low incidence of hetero- and homozygote mutants in the general population, coupled with the relatively low number of patients in the study group.

REFERENCES

1. Campalani E, Barker JN. The clinical genetics of psoriasis. Current genomics. 2005 Feb 1;6(1):51-60.
2. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome--a new world-wide definition. A Consensus Statement from the International Diabetes Federation. Diabet Med. 2006;23(5):469-80.
3. Fredriksson T, Pettersson U. Severe psoriasis--oral therapy with a new retinoid. Dermatology. 1978;157(4):238-44.

OBJECTIVES

This study aims to link certain SNPs to an accelerated disease progression and/or a higher number of comorbidities in psoriatic patients, in relation to the concomitant presence of metabolic syndrome.

RESULTS

In total, 82 patients were enrolled: 46 males and 36 females, mean age of 49.96 ± 14.54 . Median disease duration was 14.64 years with a mean age at diagnosis of 36.31 ± 15.85 years.

There was no statistically significant difference concerning disease severity (PASI score) at enrollment ($p = 0.225$) between the group presenting with psoriasis and MS and the group with psoriasis alone.

Patients presenting both psoriasis and MS were, in average, 11.56 years older than patients with psoriasis alone ($t = -3.957$, $p < 0.001$). Also, MS patients were diagnosed with psoriasis, in average, 8.38 years later ($t = -2.4$, $p = 0.019$).

***Disease severity.** Out of the 82 patients in the study group, the majority had mild psoriasis ($N=42$). Our data showed no significant influence ($p > 0.05$) of the studied SNPs on disease severity.

***Psoriatic arthropathy and MS.** Not only was the number of patients showing psoriatic arthropathy higher ($\chi^2 = 5.13$, $p = 0.023$), but the relative risk of patients with both psoriasis and MS for developing psoriatic arthropathy was 3.58 times higher (Fig. 1).

***SNPs and psoriatic arthropathy.** SNP **rs17782313** significantly influenced the presence of psoriatic arthropathy ($\chi^2 = 5.374$, $p = 0.05$). More AA patients ($N = 7$) were affected by arthropathy than AM ($N = 1$) or MM ($N = 2$) patients.

***SNPs, diabetes mellitus, obesity and MS.** SNP **rs610604** was significantly involved in the presence of **diabetes mellitus** (DM) in our patients ($\chi^2 = 5.543$, $p = 0.05$). More AM ($N = 5$) met DM criteria compared to MM patients ($N = 2$) (Fig. 2). No diabetics were found among the AA patients. SNP **rs17782313** also influenced the presence of **DM** in these patients ($\chi^2 = 6.525$, $p = 0.038$). A higher number of heterozygotes had DM compared to homozygotes (5 vs. 1) (Fig. 4). Furthermore, SNP **rs17782313** influenced the presence of **obesity** ($\chi^2 = 5.761$, $p = 0.05$), with heterozygotes having a relative risk of 1.16 for developing obesity compared to homozygotes (Fig. 3).

***MS** appeared independently of all five SNPs studied in our patients.