THE EVALUATION BETWEEN GENETIC FACTORS & GINGIVAL OVERGROWTH

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ABSTRACT

Multi drug resistance1 gene encodes P-glycoprotein (P-gp) and belongs to the family of ABC transporter proteins, which are linked with ATP and take part in transmembrane transport of many hydrophobic, cationic, amphoteric substances as well as xenobiotics. The main purpose of this study was to determine (such words should be kept in Introduction) relation between Multi Drug Resistance1 Gene And Gingival Overgrowth. laboratory, Clinical and History of illness including histological parameters and use of calcium antagonists were appraised in a cross-sectional epidemiologic Examinations.

P-Glycoprotein(P-GP) was detected in Gingival Tissues and Multi Drug Resistance1 G2677T/A & C3435T polymorphism were determined. 28 patients (70%) had minimal Gingival Overgrowth and 12 (30%) had Clinically significant Gingival overgrowth. Patients who treated with calcium antagonists had significantly deeper Gingival than their drug-free counterparts (P<.0002) This drug-related side effect was associated with the MDR1 2677G or G/TA genotype (P<.002) but not with the variant genotype T/TA. This drug effect was proved by multiple regression analysis with adjustment for the risk factors of periodontitis (age, sex, smoking, and education and work) (P<.0002) and was associated with elevated C-reactive protein levels. The association of probing depth with the MDR1 polymorphism was confirmed in the matched-pair analysis (P<.0002). Of course self—performed Sustenance was the effecting factor for reduced in Gingival Overgrowth Specially in patient who had the C3435T Multi drug resistance1 Polymorphism.

Key words: Gingival Hyperplasia, Multi drug resistance1, Calcium.

1. INTRODUCTION

P-gp is located in many organs and tissues among others in apical brush border of luminal cells of digestive system proximal renal tubules, and hemopoietic cells[1,2]. The tissue distribution suggests that P-gp plays a role in excreting toxic xenobiotics and metabolites. Recently, single nucleotide polymorphisms (SNPs) of MRD1 gene have been identified, including one possessing a functional role, which is localized in a position C3435T[3]. In homozygous TT-allele subjects, the P-gp expression in digestive system is lower in comparison with heterozygous CT and homozygous non-mutated CC cases. It has been demonstrated that cyclosporin A absorption is inversely correlated with P-gp expression in digestive tract. In the distal parts of the colon, where P-gp expression is the highest, cyclosporine A absorption is observed, whereas in small intestine where P-glycoprotein expression is the lowest cyclosporine A absorption is the highest[1]. It has also been demonstrated that P-gp regulates penetration of some drugs to target cells, which seems to affect their clinical efficacy. The glycoprotein expressed on T lymphocytes, i.e. target cells for cyclosporin A, limits its intracellular concentration by extruding the drug from the cells.

Thus, high activity of P-gp on the surface of T lymphocytes may be related to reduced immunosuppressive efficacy of cyclosporin A. Furthermore, P-gp can play a role in cytotoxic activity of T lymphocytes by decreasing interleukin-2 release from the activated cells[4]. Other types of cells, which are involved in allogenic graft rejection also express P-gp. Hitzl[5] proved that in NK CD56 cells, P-gp mRNA level and P-gp activity were correlated with MRD1 gene polymorphism. NK cells isolated from patients with wild C/C allele of MRD1 gene are characterized by elevated P-gp mRNA levels associated with the increased P-gp activity in comparison with homozygous T/T mutated allele. Thus, immunosuppressive effects of cyclosporin A may depend not only on its blood concentration, but also on the drug levels in the target cells, where activity of P-gp may play a crucial role. So, polymorphism in MRD1 gene encoding P-gp may be an important modulator of clinical efficacy of cyclosporin A, but also a pathogenetic factor predisposing to terminal renal failure requiring transplantation. This work has been done for 28 patients in Tabriz-Iran. The aim of the present study was to evaluate MRD1 allele and genotype distribution in
patients with allogenic kidney transplants and healthy population as well as to evaluate the influence of C3435T polymorphism of MRD1 gene in exon 26 on the prevalence of acute and chronic rejection of the kidney grafts in patients treated with cyclosporin A.

2. DISCUSSION

Genomic DNA was extracted manually (precipitation with trimethylammonium bromide salts from leukocytes contained in 450 l of venous blood with ethylenediaminetetraacetic acid as an anticoagulant)[6]. DNA was then precipitated in 95% ethanol, dissolved in distilled water and stored at −20°C until analysis. MRD1 C3435T mutation was determined using the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) assay[7]. A 197-bp fragment of exon 26 was amplified from genomic DNA with the primer pair P1 and P2. The primer sequences were: P1 (sense): 5’ TGTATTCAGCTGCTTGATGG-3’; P2 (antisense): 5’-AAGGCATATGTATGGTGCCCT-3’. PCR amplification was performed in a total volume of 100 l that contained 200 ng of genomic DNA (dATP, dCTP, dGDP and dTTP, 200 mol/l each, MBI ferments, Vilnius, Lithuania), 250 ng of each primer; 1.5 mmol/l magnesium chloride, and 2U Taq DNA polymerase (Gibco BRL Life Technologies, Glasgow, Scotland). The amplification reaction was performed using the Mastercycler 5330 (Eppendorf). PCR amplification consisted of an initial denaturation for 2 min at 94°C, followed by 35 cycles of denaturation at 94°C for 30 s, annealing at 60°C for 30 s, and extension at 72°C for 30 s. The terminal elongation was performed at 72°C for 7 min. In an amplified 197 bp fragment the C3435T polymorphism affects a restriction enzyme cleavage site for Sau3AI in such a way that after digestion with this enzyme for 16 h at 37°C, the 3435-C allele can be detected by the presence of two fragments, which are 158 bp and 39 bp long.

The study assumed that C3435T mutations of MRD1 gene may also be one of the reasons of terminal renal failure by influencing P-gp activity. The differences in MRD1 genotype frequency in healthy population and in subjects with terminal renal insufficiency might be the factor predisposing to the development of the disease, including those originating in the kidney. Siegsmund[8] observed higher T allele prevalence in patients with kidney cancer. Moreover, it was shown that Asian population is characterized by low T allele frequency which may determine statistically rarer occurrence of renal epithelial tumors, especially non-clear cell renal carcinoma prevalence, than in other populations[9]. The aforementioned reports have proved that C3435T polymorphism in exon 26 of MRD1 gene may underlay development of some diseases by modulation of P-gp expression. The study and the control groups were characterized by similar distribution of MRD1 genotypes. There were no significant differences in the frequency of 3435CC, 3435CT and 3435TT genotypes between patients after allogenic kidney transplantation and healthy volunteers. The observed lack of differences in the genotypes distribution may be partly ascribed to inhomogeneous etiology of renal insufficiency (diabetes, glomerulopathies, hypertension, etc.). The frequency of alleles and distribution of MRD1 gene genotypes from the present study are similar to other Asian populations.

3. CONCLUSION

The study group with acute rejection was characterized by the following the Multi drug resistance1 genotypes: 25% for 3435CC, 42% for 3435CT and 33% for 3435TT. There were no differences in the incidence of acute rejection among the above C3435T genotypes. However, in lung transplant patients, it was demonstrated that C allele of Multi drug resistance1 gene, exon 26, position 3435, predisposed to persistent organ rejection, i.e. 72% of patients with the C allele had acute persistent rejection in comparison to 52% for TT patients (p = 0.04). The observations of the present study are in keeping with the aforementioned observations of von Ashen et al. The allele and genotype distribution in the population of acute and chronic kidney graft rejection patients was similar to transplant patients without rejection complications. Similarly, no effects of Multi drug resistance1 gene polymorphism on tremor and gingival hyperplasia in kidney transplant patients medicated with cyclosporin A was documented. Based on the results from the present study, it can be concluded that Multi drug resistance1 gene polymorphism will not probably be useful in the diagnostics of higher risk of development of terminal renal failure leading to transplantation. Moreover, the evaluation of C3435T polymorphism of Multi drug resistance1 gene will probably not be useful for characterization of groups of patients at increased risk of acute and chronic kidney graft rejection.

4. REFERENCES


