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GENETIC DISEASES AND MOLECULAR GENETICS

SP027 KILLER CELL IMMUNOGLOBULIN LIKE RECEPTOR GENOTYPE DISTRIBUTION IN FAMILIAL MEDITERRANEAN FEVER: NO ASSOCIATION WITH DISEASE PHENOTYPE AND RENAL AMYLOIDOSIS

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Introduction and Aims: Familial mediterranean fever (FMF) is an autosomal recessive autoinflammatory disease affecting populations of Mediterranean origin which is characterized by recurrent episodes of inflammation with fever, serositis and arthritis. The most devastating complication of FMF is type AA amyloidosis leading to nephrotic syndrome and chronic renal failure. The gene associated with FMF is the MEFV (MEditerranean FeVer) gene which encodes a protein called pyrin. Mutations of pyrin lead to uncontrolled inflammatory attacks while subclinical inflammation continues during attack free intervals. Other than MEFV mutatations some genetic, immunologic and envorimental factors also effect the disease phenotype. Natural killer (NK) cells are cytotoxic lymphocytes that take part in innate immunity. Killer cell immunoglobulin like receptors (KIR) are a group of regulatory receptors expressed on NK cells and cytotoxic T cells. KIR genes have remarkable allelic polymorphism. This polymorphic variation may effect the immune response of the NK cell. Aim of the current study is to define immunogenetic determinants in the pathogenesis of FMF and look for if KIRs are related to disease phenotype and complications like renal amyloidosis.

Methods: One hundred and five Turkish unrelated FMF patients and 100 healthy controls with similar demographic features were involved in the study. Nine patients had marked proteinuria (>2 gram/day) with biopsy proven renal amyloidosis. Peripheral blood samples were obtained from the patients in attack free periods. Isolated DNA was amplified by sequence spesific PCR probes and analysed by Luminex for KIR genotypes. Variation of KIR gene distribution was evaluated by Fisher Exact test. KIR genes / genotypes were evaluated in FMF patients with and without amyloidosis and arthritis. Additionally, relationship between individual KIR genes / genotypes and the age of onset of the disease, serum CRP levels and common MEFV mutations were evaluated.

Results: The framework genes KIR2DL4, 3DL2, 3DL3 and 3DP1 were found in all of the patients and healthy controls. An activator KIR gene KIR2DS2 was significantly more frequent in FMF patients (p=0.036). There was no significant difference between KIR gene frequencies and genotypes of the patients with and without renal amyloidosis. None of the KIR genes was associated with age of disease onset. KIR3DL1 which is an inhibitor gene was significantly more common in patients with high serum CRP levels (>0.8mg/dl), (p=0.016). Associations with KIR genes and common MEFV mutations were not observed.

Conclusions: KIR genes have too many variations among different ethnic groups. In a study by Mahfouz et al. showed a higher prevalence of a pseudogene KIR 3DP1*003 in 56 Lebanese FMF patients. In this study we found KIR2DS2 to be more frequnet in 105 FMF patients, which is the first study to demonstrate the KIR genotype of Turkish patients with FMF. We suggest that the presence of KIR2DS2 which is an activator gene for NK cell functions might be related to occurence and severity of FMF. Association of KIR3DL1 with high CRP needs further investigation. The potential effect of KIR genes on predisposition to renal amylodosis and other clinical features is needed to be studied on greater sample size.

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