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MOLECULAR DIAGNOSIS OF FAMILIAL MEDITERRANEAN FEVER IN ARMENIANS

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Abstract

Familial Mediterranean Fever (FMF) is an inherited, recessively transmitted inflammatory condition usually occurring in populations from Mediterranean decent (Armenian, Arab, Jewish, Greek, Turkish and Italian populations). Identification of MEFV gene mutations has been of tremendous help for early diagnosis of most cases. The frequency of FMF is different. The prevalence of heterozygous carriers of one of the mutations of MEFV gene is as high as 1 in 5 healthy individuals in Armenia. Genetic testing of this rare Mendelian disorder (MIM no 249100) is efficient for early and prenatal diagnosis of the disease, especially for atypic cases, for carrier screening and pregnancy planning since certain mutations have been shown to have significant correlation with renal amyloidosis (RA), the most severe possible manifestation of FMF. Also genetic testing is very important for colchicine therapy correction. Twelve MEFV mutations are identified in 7000 Armenian FMF patients. Investigation of MEFV mutations in FMF patients (heterozygotes, homozygotes and compound heterozygotes) in comparison with healthy individuals revealed the most frequent mutations and genotypes, and the information was received about the heterozygous carriers and genotype - phenotype correlation. In heterozygote carriers the most prevalent and severe cases are caused by the presence of a single M694V mutation. Our results could confirm that the MEFV gene analysis provides the first objective diagnostic criterion for FMF (characterization of the two MEFV mutated alleles in more than 90% of the patients). Molecular testing is also used to screen the MEFV gene for mutations in patients with a clinical suspicion of FMF. We also demonstrated the unfavorable prognostic value of the M694V homozygous genotype, and provided the first molecular evidence for incomplete penetrance and pseudo-dominant transmission of the disease. Overall, these data, which confirm the involvement of the MEFV gene in the development of FMF, should be essential in clinical practice, leading to new ways of management and treatment of FMF patients.

Keywords: FMF, MEFV gene mutations, genotype and phenotype correlations.

Introduction

Medical genetics concerns the relationships that exist between human genes, the variations and mutations that occur within these genes, and the phenotypes that result from these mutations. At least 5000 monogenic diseases have been documented in the Online Catalogue of Mendelian Inheritance in Man (OMIM). The number of disease genes increases and now is over 1000. Many still remain to be described (*Brunner H., 2007; McKusick V., 2007*).

Center of Medical Genetics and Primary Health Care of Armenia has experience for many years in genetic testing of different inherited

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