INVESTIGATION OF THE RELATIONSHIP BETWEEN DISEASE SEVERITY AND DEVELOPMENT OF AMYLOIDOSIS AND GENETIC MUTATION IN FMF DISEASE

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Aim: Familial Mediterranean Fever (FMF) is an autosomal recessive genetic disease which is characterized by episodic fever attacks and the inflammation of the accompanying of serous membranes. Amyloidosis is the most important complication of FMF that determines the prognosis of the disease. FMF is a disease associated with mutations in the MEFV gene located on the short arm of chromosome 16. Some mutations are more frequent in some ethnic groups. M694V mutations are the most common mutations in studies have donein our country. Those who are homozygous for M694V have a heavier disease and amyloidosis is more frequent. Although, the risk of developing amyloidosis is low in patients with V726A mutation, it has been shown in one study that patients with V726A and E148Q mutations amyloidosis are more common. The other genes can also be affected in FMF. In our study we have investigated the relationship between the genetic mutations with the disease severity and the frequency of development of amyloidosis in patients with FMF who applied to Samsun Ondokuz Mayis University.

Material and Method: In our study we have been evaluated genetic mutations, the severity of the disease, age at onset, gender relationship, attack frequency, the duration of attack, medication levels used in treatment of FMF, treatment response, the frequency of occurrence of clinical symptoms and the frequency of development of amyloidosis in 148 FMF patients who were admitted to Ondokuz Mayis University Medical Faculty Rheumatology and Nephrology Clinic between January 2009 and December 2015.

In our study, 148 patients were enrolled over 18 years of age. All of these patients were diagnosed according to the Tell-Hashomer criteria. Gender distribution of our patients was 80 women (54%) and 68 men (46%). Female-male sex ratio was 1.2 / 1

The mean age of the patients was 30.98 ± 11.18 (18-67) years and the mean age of onset of clinical symptoms was 13.57 ± 8.28 (2-40) years. The mean age of diagnose was 22.45± 11.15 (3-64) years.. The mean age of patients with amyloidosis was 35 ± 12.42 (18-54) years, the mean age of onset of clinical symptoms was 8.30±3.42 (2-14) years and the mean age of diagnosis in these patients was 21.61±10.62 (6-40) years.

Our patients have been divided into 3 groups according to disease duration; shorter than 5 years duration: 19 patients (12.8%), 5 to10 years: 17 patients (11.4%) and longer than10 years duration: 112 patients (75.2%).

In our study, when 148 patients have been screened for genetic mutations, the most frequently seen mutations are M694V, M680I, R202Q and E148Q, respectively. The most common genotype is M694V/M694V mutation and this mutation has been found in 37 patients (25%). In 25 patients M694V heterozygous have been found (16.8%). The third frequent mutation is M694V/M680I/R202Q and has been found in 13 patients (8.7%).

When patients have been evaluated for mutations with amyloidosis development, in 23 of 148 patients amyloidosis have been developed. 10patients with amyloidosis have M694V homozygous mutations and this is 27% of all M69V homozygous patients. Amyloidosis has developed in five M694V heterozygous patients (20%). The both of the two patients who carry the homozygous E148Q mutations have developed amyloidosis.

Discussion: Genetic mutations of 148 patients participating in the study were identified. The genetic mutations of the patients were investigated in terms of severity, clinical features, age at onset, age of diagnosis, level of colchicine used in treatment, treatment response to disease, disease activity score and development of amyloidosis.

In our study, the distribution of the frequency of mutations is consistent with other similar studies performed in Turkey. When the age of diagnosis was evaluated, it was determined that the patient group with the lowest mean age of diagnosis, except for the only patient carrying M694V / P369S, was also seen to carry the homozygous M694V mutation. This result suggests that the disease is more severe in this group and therefore the diagnosis is made earlier. When genetic mutations were evaluated for amyloidosis, 10 of the patients who were diagnosed with amyloidosis with renal biopsy had M694V homozygote mutation, and M694V / M680I, M694V / M680I / R202Q V726A-heterozygote had amyloidosis in one patient. for each mutation. The majority of the group that developed amyloidosis was carrying the M694V mutation homozygously and heterozygously.

As a result, it has been shown that genetic mutations carried by patients affect the clinical course of the disease. In our study, we found that patients with M694V mutation had a significantly higher rate of exacerbation, higher drug doses for treatment, and a close relationship with amyloidosis, as compared to patients with other mutations

Key words : Familial Mediterranean Fever, Amyloidosis, Genotype-Phenotype

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