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The frequency of MEFV gene mutation in patients admitted to hospital with preliminary diagnosis of familian mediterranean fever who undergone a prior appendectomy

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Abstract. – OBJECTIVES, Familial mediterranean fever (FMF) is an autosomal recessive disease characterized by recurrent and self-limiting fever, peritonitis, arthritis, synovitis, pleuritis, carditis, and erysipelas-like lesions. The aim of this study was to investigate the frequency of the MEFV gene mutation in patients who admitted to hospital with preliminary diagnosis FMF and who had undergone a prior appendectomy.

PATIENTS AND METHODS, We retrospectively reviewed the files of 52 patients between the ages of 7-18 who admitted to hospital with preliminary diagnosis of FMF and who had undergone a prior appendectomy. Age, gender and the MEFV gene mutations were included in the data. The 12 known, common MEFV gene mutations [E148Q, P369S, F479L, M680I (G/C), M680I (G/A), I692del, M694V, M694I, K695R, V726A, A744S, R761H] were investigated in the patients.

RESULTS, Of these 52 cases, 29 (55.8%) were female and 23 (44.2%) were male. Their mean age was 12.1± 3.1 years (range 7-18 yr). MEFV gene mutation was detected in 31/52 cases (59.6%). In this study was found an high frequency of the MEFV gene mutation in patients admitted to hospital with a preliminary diagnosis FMF who had undergone a prior appendectomy. MEFV gene mutations were M694V 16/41 (39%), E148Q 13/41 (31%), M680I 6/41 (15%), V726A 4/41 (10%) and R761H 2/41 (5%). Other genes mutations were F479L, M680I (G/A), I692del, M694I, K695R and A744S.

CONCLUSION, There are too much indications of unnecessary appendectomy in MEFV gene mutation carriers. In MEFV gene mutation carriers the frequency of appendicitis can be higher than the normal population. A more detailed and extensive study should be done about it.

Key Words:

Familial Mediterranean fever, FMF, MEFV gene mutation, Diagnosis Appendectomy.

Introduction

Familial mediterranean fever (FMF) is an autosomal recessive disease characterized by recurrent and self-limiting fever, peritonitis, arthritis, synovitis, pleuritis, carditis, and erysipelas-like lesions[1]. On 16 chromosome, pyrin gene mutation has been found to cause disease[2]. FMF is common in Jews, Armenians, Turks, Kurds and Arabs also less common in Greeks and Italians[1]. The incidence of FMF is 1/1000 and carrier frequency is 20% in Turkey. The frequency of MEFV gene mutations was 74% in patients diagnosed as FMF[3].

Abdominal pain is an important reason for recourse to emergency services in children[4]. In children older than two years, the prevalence of abdominal pain has been reported to 8.1% and prevalence of acute abdominal pain has been reported as 5.1%[5]. Nowadays, FMF have the highest rate of incorrect diagnosis of appendicitis as the most common reason for unnecessary surgery[4,5]. Because of early diagnosis of acute appendicitis is very important for appendectomy before perforation occurred, surgeons often decide an indication for early and unnecessary appendectomy. Rate of acute appendicitis perforation is around 16-20% in the early period depending on misdiagnosis and delay in diagnosis. Despite developments in diagnostic and surgical techniques, there is no reduction in the rate of perforated appendicitis and unnecessary appendectomy but deaths due to acute appendicitis significantly decreased[6,7].

Severe abdominal pain seen in patients with FMF during an attack is usually with fever, increased erythrocyte sedimentation rate and C-reac-

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tive protein (CRP), and leukocytosis. So, it is very difficult to make a distinction between abdominal pain of FMF and acute appendicitis. Therefore, these patients are often underwent appendectomy with an incorrect surgical indication[8].

The aim of this study was to investigate the frequency of the MEFV gene mutation in patients admitted to hospital with preliminary diagnosis FMF who had undergone a prior appendectomy.

Patients and Methods

We retrospectively reviewed the files of 52 patients between the ages of 7-18 who admitted to hospital with preliminary diagnosis of FMF and who had undergone a prior appendectomy in Dicle University Medical School, Diyarbakir, Turkey, between 2008-2010 years. Age, gender and the MEFV gene mutations were included in the data. The 12 known, common MEFV gene mutations [E148Q, P369S, F479L, M680I (G/C), M680I (G/A), I692del, M694V, M694I, K695R, V726A, A744S, R761H] were investigated in the patients. Genomic DNA was extracted from 3 mL of whole blood, obtained from the patients according to standard procedures. The patients were studied using a reverse-hybridization, test strip-based assay (FMF StripAssay, Vienna Lab Labordiagnostika, GmbH, Austria) in Dicle University Medical School Laboratory.

Statistical Analysis

MEFV gene mutations are given as number and percentage. The mean age of the patients is presented mean ± standard deviation (SD).

Results

Of these 52 cases, 29 (55.8%) were female and 23 (44.2%) were male. Their mean age was 12.1± 3.1 years (range 7-18 years). MEFV gene mutation was detected in 31/52 cases (59.6%). MEFV gene mutations were M694V 16/41 (39%), E148Q 13/41 (31%), M680I 6/41 (15%), V726A 4/41 (10%) and R761H 2/41 (5%). Other genes mutations were F479L, M680I (G/A), I692del, M694I, K695R and A744S were found at all in the patients who had undergone a prior appendectomy (Table I).

Discussion

Whether too much indication of unnecessary appendectomy is considered in MEFV gene mutation carriers is not known exactly. Or may be in MEFV gene mutation carriers the prevalence of appendicitis is higher than the normal population. There are limited studies on this topic.

Because of FMF patients have the similar clinical and laboratory findings with acute appendicitis, FMF patients are often exposed to unnecessary surgical interventions. Samli et al[9] found that 10.7% (16) cases of 159 FMF patients had appendectomy and 5.7% (9) cases had the other surgical intervention. Lidar et al[10] found that appendectomy rate in patients with FMF gene was in 60%. In a nationwide multicenter study evaluating 2838 Turkish FMF patients the frequency of appendectomy was found as 19%[11]. But in those studies the Authors did not investigate if these appendectomies were necessary or unnecessary. Ciftci et al[12] found

Table I. Types of MEFV gene mutation in 31 cases (59.6%) where MEFV gene mutation was detected.

Individuals with mutations in one allele			Individuals with homozygous or compound heterozygous mutation		
Genotype	**n**	**%**	**Genotype**	**n**	**%**
E148Q	Wt 9	29.0	E148Q M694V	2	6.5
M680I (G/C)	Wt 2	6.5	E148Q P369S	2	6.5
M694V	Wt 4	12.9	M680I (G/C) M694V	1	3.2
R761H	Wt 2	6.5	M694V V726A	2	6.5
V726A	Wt 2	6.5	M694V M680I	1	3.2
			M680I (G/C) M680I (G/C)	1	3.2
			M694V M694V	3	9.7
Total	**19**	**61.4**	**Total**	**12**	**38.6**

that intestinal obstructions may occur in 3% of patients with FMF who had not undergone a prior laparotomy. Although the MEFV gene mutation prevalence is around 20% in Turks[13], in our research the MEFV gene mutation prevalence was 59.6% (31/52) in patients who had undergone a prior appendectomy.

Samlı et al[9] found that types of MEFV gene mutation was M694V 40.5% (17), E148Q 9 21.4% (9), M680I 7.1% (3), V726A 7.1% (3) and R761H 1 2.4% (1). Other gene mutations M694I, F479L, A744S, and P369S were found in the patients who had undergone a prior surgical interventions. In our study similar results were found in the patients who had undergone a prior appendectomy. Samlı et al found types of MEFV gene mutation 28.6% (6) homozygous mutation, 33.3% (7) double-allele mutation and 38.1% (8) heterozygous mutation in the 21 patients who had undergone a prior abdominal surgery. In our investigation types of MEFV gene mutation 13% (4/31), homozygous mutation, 26% (8/31) double-allele mutation and 61% (19/31) heterozygote mutation were found in the patients who had undergone a prior appendectomy.

In conclusion, there are too much indication of unnecessary appendectomy in MEFV gene mutation carriers. In MEFV gene mutation carriers the frequency of appendicitis can be higher than the normal population. We think that a more detailed and extensive study should be done about it.

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