THE FREQUENCY OF MEFV GENE MUTATIONS IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE PATIENTS

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Objectives:

Autosomal dominant polycystic kidney disease (ADPKD) is the most common of the inherited renal cystic diseases and effectuates 10% of the end stage renal disease (ESRD) population (1). Familial Mediterranean fever (FMF) is an autoinflammatory disease characterized by recurrent attacks of polyserositis and fever which has an autosomal recessive inheritance (2). ADPKD is one of the most common Mendelian disorders and also, the most common inherited kidney disease, with an incidence of 1 in 400-1000. ADPKD is caused by PKD1 and PKD2 gene mutations in 85% and 15% of the cases respectively (3).
PKD1 gene of ADPKD is identified in chromosome 16p13.3 and 46 exons, likewise FMF is caused by mutations in the MEFV gene which is located on the same chromosome region 16p13.3, but slightly different 2, 10 exons (3,4). The episodes of fever and abdominal pain/tenderness in ADPKD patients are generally believed to be arised from the renal and urinary complications. However, these symptoms may be the sign of serous inflammation in patients with ADPKD and FMF. And these individuals may have increased frequency of MEFV gene mutations carriage in risk groups. Therefore, we aimed to evaluate the frequency of MEFV gene mutations in ADPKD patients with abdominal pain, tenderness, fever or arthritis attacks who may have coexistence of FMF.

Methods:

Twenty-four ADPKD patients with the medical history of recurring and self-limited episodes of fever, abdominal pain and arthritis with inflammation, of one or several serous (peritoneum, pleura, pericardium, synovial or vaginal tunic of the testicle) attending consecutively to our nephrology and rheumatology departments were included in the study, and MEFV gene mutations were analyzed.

Results:

In this study, twenty-four ADPKD patients (male/female:14/10) were included. The mean age was 43.2 years. In 7 ADPKD patients, MEFV gene mutations were determined with 8 allelic variants. The allelic variants were heterogenous M694V (3/48, 6%), heterogenous E148Q (2/48, 4%), heterogenous V726A, heterogenous P369S, and compound heterogenous M680I (G/C). According to Tel-Hashomer criteria, three patients with higher than 1000 mg proteinuria had diagnosed as FMF and amyloidosis by endoscopic biopsies. Two of them were heterogenous M694V and one of them was compound heterogenous M680I (G/C). One of the 3 patients with amyloidosis (heterogenous M694V) had a successful living-donor renal transplantation (RTx) after a 5 years dialysis period at the age of 48 years. In the literature, a high frequency of MEFV carriers in the healthy Turkish population (20%) was reported. In the current study, we found the prevalence of total allelic MEFV variants to be the same in ADPKD patients (17%) compared with healthy Turkish subjects ($p > 0.05$).

Conclusions:

Although, there was no increase in frequency of MEFV gene mutations in ADPKD patients compared with the healthy controls in Turkish population three patients had diagnosed as FMF and amyloidosis. The ADPKD phenotype displays a significant variability that is widely influenced by the affected gene. *PKD1* patients have a median age at ESRD of 58 years (3), and about 2–5% of ADPKD patients present with an early and severe phenotype (5). There may be a coexistence of this two common genetic disorders, especially, MEFV gene mutations may play a specific or an occult role in the development of FMF related amyloidosis in ADPKD patients. In this regard, gene mutations, comorbidities, and/or other urological, renal complications (like amyloidosis) may constitute the severity and early manifestation of ADPKD. Further large trials are needed to show if the synchrony of these two disorders can simply be explained as incidental or not.

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