Abstract

Familial Mediterranean fever (FMF, OMIM 249100) is the most common hereditary fever, resulting from mutations in *MEFV*. FMF is characterized by episodic febrile attacks and polyserositis. Renal AA-amyloidosis is a major complication, which often leads to end-stage renal disease in untreated patients. The data about the renal AA-amyloidosis secondary to FMF are scarce in North African countries and non-existent in Algeria. We aimed to investigate the *MEFV* mutations associated with this complication in an Algerian patient cohort. Molecular analysis included 28 unrelated Algerian FMF patients with ascertained amyloidosis, 23 of them were symptomatic and 5 were asymptomatic. For this study, a group of 20 FMF patients without renal amyloidosis were selected as controls according to their age, disease onset and disease duration. The mutations were detected by sequencing exon 10 of *MEFV*. A total of 87.5% (49/56) mutant alleles were identified in 27/28 analyzed patients; p.M694I was predominant and appeared with an allele frequency of 62.5%, followed by p.M694V (17.85%), p.M680I (5.35%) and p.I692Del (1.78%). Remarkably, only p.M694I mutation was observed among the asymptomatic patients. The M694I/M694I genotype, identified in 14/27 (52%) patients, was significantly associated with the development of amyloidosis compared to group of controls ($p = 0.022$). This study did not link the M694V/M694V genotype to the renal complication despite the fact that it has been observed only in the patients with amyloidosis (3/27; 11%) ($p = 0.349$). The association of other identified genotypes to this complication was statistically insignificant. The progression of amyloidosis led to end-stage renal disease in 14 patients with 6 deaths. This study shows that p.M694I homozygosity is a potential genetic risk factor for the development of renal AA-amyloidosis in Algerian FMF patients.