(P-62)

PTPN11, *SOS1*, and *BRAF* Gene Mutation Spectrum in RASopathies in Molecular Diagnosis

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RASopathy is a group of clinically defined medical genetic syndromes that are caused by germline mutations in genes encoding the Ras/mitogen-activated protein kinase (MAPK) pathway components or regulators. Noonan, LEOPARD, cardio-phasio-cutaneous, Costello, Legius syndrome, and neurofibromatosis type 1 are included in this group. The aim of this study was to evaluate the *PTPN11*, *SOS1*, and *BRAF* gene mutation spectrum of 70 patients with molecular diagnosis upon the prediagnosis of CFC and Noonan syndrome in RASopathy spectrum between 2008 and 2016 in Ege University Medical Faculty Medical Genetics Department.

Sequence analysis was performed on all coding exons and flanking intronic regions of the *PTPN11* gene, exons 6, 7, 8, 10, and 16 of *SOS1* gene, and exons 6, 11, 12, 14, and 15 of *BRAF* gene in 403 cases referred with prediagnosis of RASopathy between 2010 and 2016. Sanger sequencing analysis method was used for sequence analysis.

Mutations were detected in seventy of the cases (17%). In 63 cases, 28 different mutations were detected in the *PTPN11* gene. The frequency rates of *PTPN11* mutation in this study were as follows: p.N308D (26%), p.Y63C (6%), p.I282V (5%), p.M504V (5%), p.T468M (5%), and p.Y62D (5%). In 4 cases, 3 different mutations were detected in the *SOS1* gene. Mutations were identified as p.R522K, p.I600V, and p.E846K. In 3 cases, 3 different mutations were detected in the *BRAF* gene. Mutations were identified as p.E501K, p.N581D, and p.A481E.

In our study, we presented the largest RASopathy mutation spectrum in Turkey to date and we demonstrated that the mutation spectrum is also highly heterogeneous in these clinically heterogeneous group diseases.

FREE COMMUNICATIONS

(FC-01)

Impact of *CYP21A2* Gene Mutations on Clinical Management of Congenital Adrenal Hyperplasia

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Congenital adrenal hyperplasia (CAH) is a defect of cortisol biosynthesis. The most common cause of CAH is 21-hydroxylase deficiency (21-OHD) caused by *CYP21A2* gene mutations. 21-hydroxylase activity is correlated with different clinical presentations such as salt-wasting (SW), simple-virilizing (SV), and non-classical (NC) CAH. We aimed to determine the *CYP21A2* gene mutations and evaluate the genotype-phenotype correlation in 21-OHD patients to value the impact of these mutations for clinical management.

CYP21A2 gene mutation analysis with respect to common mutations P30L, IVS2, I172N, cluster E6, V281L,Q318X,R356W, Del 8-bp E3, P453S, R483P, L307 frameshift, large deletions, and conversions was performed by different methods namely RFLP, MLPA and reverse-hybridization, in 42 CAH patients from 38 families.

The mean age of the patients was 2.5 years. Ambiguous genitalia (45.2%) and vomiting/weight loss (23.8%) were the most common clinical presentations. 50% of the patients were in SW, 33.3% in SV, and 16.6% in NC forms. Mutations were found in 94% of 84 alleles. 88.1% of the patients had more than one mutations. 59.5% of the patients presented with homozygous genotype, whereas 28.6% were compound heterozygous. The most common mutations were IVS2 (22.6%), I172N (22.6%), Q318X (15.4%), and large deletions (14.2%). Q318X, large deletions, R356W, and cluster E6 mutations were more correlated to SW, I172N was more common in SV, and V281L was seen more frequently in NC.

Genotypes were well-correlated with phenotypes within clinical subtypes in most of the patients. The most common mutations were IVS2 and I172N in our study group. We believe that these data as well as others in the literature will serve for better genetic counseling in daily practice of CAH.