Abstract

Objective: To study the clinical spectrum of Chinese Noonan syndrome and perform the mutational analysis of Protein-Tyrosine Phosphatase, Non-receptor 11 (PTPN11) among them. Method: Fifty-one unrelated Noonan patients and their parents were enrolled according to a modified inclusion scoring system. In addition, Noonan-like syndromes including 2 cases of Cardio-faciocutaneous (CFC) syndrome and 1 Costello patient were tested for PTPN11 mutation. Results: Thirty-nine sporadic and 12 familial cases of Noonan syndrome were ascertained clinically. Of these familial cases, maternal versus paternal transmission occurred at a ratio of 11:1. Thirty-two index cases and 9 familial cases were found to have mutations in PTPN11 gene. Heterozygous missense mutation of PTPN11 and recurrent mutation N308D (c.922A>G) constituted 62.7% and 28.1% respectively. Five novel mutations were reported. Genotype-phenotype correlation revealed that exon 3 and 13 mutations were significantly associated with typical faces (p<0.044). Exon 3/c.181G>A mutation was noted to present more prominent ectodermal features like sparse hair and eyebrows. No mutation of PTPN11 gene was identified in CFC and Costello patients. Conclusion: These results demonstrate the role of PTPN11 gene in the expression of the phenotype. However, other gene(s) may also be involved in the pathogenesis of Noonan phenotype. The mutational screening of PTPN11 is recommended to ascertain those affected parents with less obvious phenotype and Noonan syndrome associated with atypical features.

Keyword: Diagnostic scoring system; Genotype-Phenotype correlation; Missense mutation; Noonan syndrome; PTPN11 gene