



GENETIC EXAMINATION OF CHILDREN SUFFERING FROM CYSTIC FIBROSIS

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ABSTRACT

CFTR protein (cystic fibrosis trans membrane conductance regulator) is expressed in multiple epithelial tissues, including upper and lower respiratory tracts, pancreas, sweat glands and gastrointestinal tract. More than 800 mutations and 100 polymorphic variants of DNA sequences were identified in patients with CF (Cystic fibrosis) and CFTR- diseases. In this study, genetic CFTR analysis of the children suffering from chronic lung disease (cystic fibrosis) is presented. They are treated and regularly controlled at the Pediatric hospital Sarajevo. CFTR analysis was done in 9 cases, 4 boys (44.4%) and 5 girls (55.55%). There are 3 children (33.3%) in the age group 1 to 3 years, 1 child (11.1%) in the age group 3 to 6 years, 3 children (33.3%) in the age group 6 to 9 years and 2 children (22.2%) in the age group 9 to 12 years. Genetic analysis was conducted at the Medical center for molecular biology, School of Medicine, Ljubljana. PCR method with PAGE and direct sequestration on ABI PRISM 31 was applied. The majority of children (7 children, i.e. 77.77%) had CFTR mutation $\Delta F 508$ whilst one child had G542X mutation and one child R 1174 mutation. The purpose of this study is to emphasize the need for CFTR gene identification in the institutes of our country.

KEY WORDS: cystic fibrosis, CFTR gene, children who suffer from cystic fibrosis

INTRODUCTION

Cystic fibrosis (CF) is a complex gene syndrome revealed by dysfunction of all exocrine glands. It is defined by mutations of CFTR gene (cystic fibrosis transmembrane conductance regulator), which result in the production of hyper-viscous mucus and chloride malabsorption in the sweat glands' ducts (1, 2, 3). It is inherited as autosomal recessive trait, with gene locus for cystic fibrosis mapped at 7q31. The most frequent mutation is $\Delta F 508$ that is found in approximately 70% of affected children. The mutation of CF gene is connected to deletion of three pairs of bases, which results in shift of phenylalanine residue to the position 508 of the mature protein (4, 5). The diagnosis of cystic fibrosis is established according to the criteria that can be divided into 2 groups (6). Group A - clinical criteria: typical pulmonary clinical features, typical gastrointestinal clinical features and positive family history of cystic fibrosis in close relatives. Group B- laboratory criteria: Chloride concentration in the sweat and CFTR mutation. At least one criterion from each group is necessary for conclusive diagnosis. The treatment is symptomatic and supportive, until the introduction of gene therapy which means replacement of mutated CFTR gene with functional one.

SUBJECTS AND METHODS

In this study we present the results of genetic analysis of 9 children, in the age between 1 and 12 years, who suffer from cystic fibrosis. They are treated and monitored at the Pulmological department of the Pediatric Hospital Sarajevo. The diagnosis was established by repeated broncho-obstructions, X-ray examinations of the lungs, measurements of the enzyme activities in the duodenal secretions and measurement of chloride content in the sweat, which was above 100 mmol/l in

all cases. The genetic analysis was realized using PCR based method, with PAGE and direct sequestration on ABI PRISM 31 Genetic Analyzer at the Medical center for molecular biology, School of Medicine, Ljubljana.

RESULTS

In the Table 1. the results are presented for nine children, 4 girls and 5 boys 1-12 years of age, who suffer from cystic fibrosis. In 7 cases (77.77%) $\Delta F 508$ mutation of CFTR gene was identified. In the age group 3-6 years one G542X mutation was identified, while one R1174 mutation was identified in a girl from the age group 9-12 years.

DISCUSSION

Cystic fibrosis is a chronic, multisystem disorder, most frequently characterized by pulmonary manifestations. Due to the modern supportive care, about half of the patients live to the age of 20 and about 25% of the patients survive until 30 years of age (6). In our patients, the diagnosis of cystic fibrosis established based on clinical features and sweat test. The sweat test is the most important and standard diagnostic procedure (7).

CONCLUSION

1. The diagnosis of cystic fibrosis was confirmed by genetic analysis, which is especially important in the case of atypical and mild forms of cystic fibrosis.
2. In the future, cystic fibrosis will be cured when an adequate way of replacement of the defective CFTR gene with intact gene is found and an ideal vector for safe and efficient entrance of CFTR gene into the cell is discovered.

AGE	No.	MALE	FEMALE	CFTR GENE
1-3 YEARS	3 (33.3 %)	1	2	$\Delta F 508$
3-6 YEARS	1 (11.1 %)	1	0	G542X
6-9 YEARS	3 (33.3 %)	2	1	$\Delta F 508$
9-12 YEARS	2 (22.2 %)	1	1	$\Delta F 508$ R 1174
TOTAL	9 (100 %)	5	4	$\Delta F 508$ (77.77 %)

TABLE 1. CFTR mutations in children with cystic fibrosis

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