A Chinese Pediatric cystic fibrosis patient with the c.1624G>T, p. Gly542x / c.223C>T, p. Arg75x genotype

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Abstract

In conclusion, we present this case in order to complement CFTR gene mutations data of Chinese children with cystic fibrosis and improve clinicians' understanding of this disease in China. Besides, with the development of molecular biology technology, gene detection was expected to play an important role in the early diagnosis, early treatment, and prognosis improvement of the disease.

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To the Editor,

We read with great interest the article entitled "A systematic review of the clinical and genetic characteristics of Chinese patients with cystic fibrosis" by Ruihe Shi and colleagues (year 2020, volume 55, issue 11). The authors reported that common CFTR gene mutations, such as c.1624G>T, c.1652G>A, c.350G>A, had not been reported in China [1].

Here, we report a case of a Chinese CF child with gene mutations of 1624G>T, p. Gly542x (heterozygous mutation, paternal) and c.223C>T, p. Arg75x (heterozygous mutation, maternal) (Figure 1). This 5-year-old female patient presented with chronic cough, expectoration, wheezing, and growth retardation since the age of 3. Due to recurrent pulmonary infection and repeated dyspnea, she was hospitalized approximately 2 times every year. During her first admission to our hospital when she was 33-month-old, sputum culture was positive for Pseudomonas aeruginosa. On the 9th day of hospitalization, she suffered from abdominal distension and weakened bowel sounds, and failure to pass flatus or bowel movements for 3 days without obvious peritonitis. Abdominal CT showed that the colon was narrow, part of the colon wall was thickened; liver density was generally decreased. The surgery was performed given the diagnosis of Hirschsprung's disease. Human whole exome sequencing was conducted by Beijing Quanpu Medical Laboratory on the 23rd day of admission. On 13th April 2022, during her third admission to our hospital when she was 46-month-old due to aggravated cough and wheezing, along with the gene mutations of 1624G>T, p. Gly542x and c.223C>T, p. Arg75x, the diagnosis of cystic fibrosis was made. Sputum and bronchoalveolar lavage fluid cultures were consistently positive for Pseudomonas aeruginosa, aztreonam was administered for anti-infection. Serum vitamin examination did not show lipo-soluble vitamins deficiency at that time. Since inhaled tobramycin was not available in our country, her discharge medications were oral cefixime, azithromycin, and inhaled hypertonic saline.

During the most recent admission, she presented with malnutrition (weight <25th centile) and chronic diarrhea. Serum vitamin examination showed lipo-soluble vitamins deficiency, consequently, she needed supplementation of lipo-soluble vitamins and pancreatic enzyme replacement therapy. Increased secretions were seen under bronchoscopy. Sputum culture was positive for both Staphylococcus aureus and Pseudomonas

aeruginosa, while bronchoalveolar lavage fluid culture was only positive for Staphylococcus aureus. Linezolid plus piperacillin-tazobactam were prescribed according to drug sensitivity results for anti-bacterial treatment this time.

Mutations in CFTR, the gene encoding the epithelial ion channel that normally transports chloride and bicarbonate, lead to impaired mucus hydration and clearance [2]. Despite the high morbidity in Caucasian, it is still a rare disease in China. At present, about 200 CF patients have been reported in China, however, no population-based prevalence was calculated [3]. Recent study revealed that the prevalence of Chinese CF ranged from 1/153,825 to 1/110,127 [4]. The most common CFTR gene mutations in Chinese CF patients, which presented with c.2909G-A, are different from those in Caucasian patients[1]. However, the child in our report carried a common gene mutation among Caucasian patients but rare among Chinese patients. By searching the CFTR2 database (http://www.cftr2.org), we found that there were only 4 patients with this variant combination in the CFTR2 database and this variant combination may able to cause pancreatic insufficiency. She experienced colostomy due to neonatal megacolon, and surgery for meconium ileus. Although her clinical manifestations were typical for CF, without sufficient understanding of this disease and newborn screening, the age at CF diagnosis is relatively older. Sweat detection is an important and accurate method for detecting CF,in which the chloride ion concentration is usually higher than 60 mmol/L, however, we did not find an institution that could perform this test during her first admission in our hospital.

The population-specific genetic spectrum of CF is still unknown, and CF prevalence would be significantly underestimated in Chinese if using the Caucasian-specific screening panel. Thus, recent study recommended the 53 pathogenic/likely-pathogenic variants as CF screening panel for Chinese population, especially the six variants with high allele frequencies: G970D (c.2909G>A), D979A (c.2936A>C), M469V (c.1405A>G), G622D (c.1865G>A), L88X (c.263T>G), and 1898+5G->T (c.1766+5G>T), which could also be used in clinical diagnosis process [4]. Besides, in a most recent systematic review of gene mutations of Chinese CF patients, c.1624G>T was not reported as well[5]. To our knowledge, this is the first report of c.1624G>T mutation among Chinese patients with CF and this gene mutation would be a complementary for Chinese-specific screening panel.

In conclusion, we present this case in order to complement CFTR gene mutations data of Chinese children with cystic fibrosis and improve clinicians' understanding of this disease in China. Besides, with the development of molecular biology technology, gene detection was expected to play an important role in the early diagnosis, early treatment, and prognosis improvement of the disease.

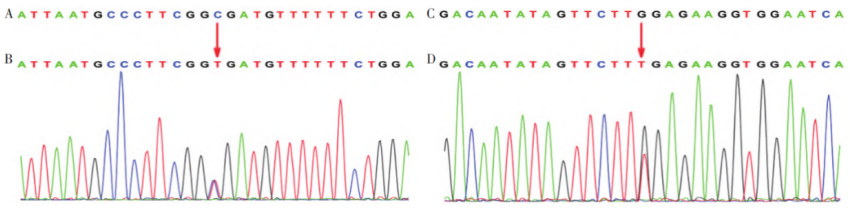

Figure 1 results of genetic testing of this patient (A: Standard DNA sequence; B: index case c.223C>T, p. Arg75x, heterozygous mutation, maternal; C: Standard DNA sequence; D: 1624G>T, p. Gly542x, heterozygous mutation, paternal)

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Conflict of interests:

The authors declare that they have no conflict of interests.