Journal of Microbiology, Immunology and Infection (2014) 47, 358–361

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CASE REPORT

Cystic fibrosis: Experience in one institution

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Received 14 September 2011; received in revised form 17 December 2011; accepted 11 May 2012
Available online 16 September 2012

KEYWORDS
Cystic fibrosis;
Cystic fibrosis transmembrane conductance regulator gene (CFTR gene);
Taiwan

Cystic fibrosis (CF) is one of the most common autosomal recessive inherited disorders among Caucasians. Comparatively, it is considered to be a rare disease among Asians. To date, only a few cases of Taiwanese CF have been published. We report four CF cases from three families. Case 1 was the first report of CF associated with a homozygosity for the CF transmembrane conductance regulator gene (CFTR gene) mutation 3849+10kb C->T in a Taiwanese patient. Cases 2 and 3 had heterozygous c. 1898+5 G->T and heterozygous p. I1023R (novel mutation) for the CFTR gene mutation. Case 4 was homozygous for the CFTR gene mutation R553X being reported in 2005 and complicated with cor pulmonale. These four patients had received 300 mg bid aerosolized tobramycin treatment every other month.

Introduction

Cystic fibrosis (CF), an epithelial cell transport disorder caused by mutations of the CF transmembrane conductance regulator (CFTR) gene, is an autosomal recessive inherited disorder of exocrine gland function, involving multiple organ systems. CF is uncommon in Africa and Asia, with a reported frequency of 1 in 350,000 in Japan.[1] Previous studies reported that CF is quite rare among Taiwanese, and until now, only 10 Taiwanese patients with CF (from eight different families) have been reported.[2,3] However, we believe that the rate of CF is underestimated in Taiwan, and that this may be due to our clinicians seldom believing it to be one of the differential diagnoses.

Case reports

Case 1

The patient was a 20-year-old female who had frequent diarrhea and sinusitis with purulent nasal discharge and

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1684-1182/$36
http://dx.doi.org/10.1016/j.jmii.2012.06.005

nasal polyps before she was 13 years of age. Repeated hospitalizations because of pneumonia with *Pseudomonas aeruginosa* (*P. aeruginosa*) infection and bronchiectasis with acute exacerbation were noted. In addition, secondary amenorrhea 4 years ago and acute pancreatitis 2 years before were also noted.

Tracing back her family history, the patient had one healthy younger brother, but her older sister had died at 4 months old with pneumonia, and her younger sister, who had panbronchiolitis and bronchiectasis with recurrent *P. aeruginosa* pneumonia, also expired at 16 years old due to bronchiectasis and pneumothorax.

Her chest roentgenogram demonstrated hyperinflation, interstitial pneumonitis with emphysema and tramline appearance. High-resolution computed tomography showed peribronchial thickening and bronchiectasis throughout both lungs.

According to her clinical features, laboratory findings and family history, CF was highly suspected. DNA analysis was performed by direct sequencing of genomic DNA to screen the entire CFTR gene and homozygosity for the CFTR gene mutation 3849+10kb C->T was identified.

The patient's mother and younger brother were heterozygous for the CFTR gene mutation 3849+10kb C->T (Fig. 1) and there were no clinical manifestations. Their father did not receive DNA analysis. Nevertheless, because the patient was homozygous for the CFTR gene mutation 3849+10kb C->T, we consider that her father must be the carrier of the heterozygous 3849+10kb C->T gene mutation too. Furthermore, although her younger sister had a negative sweat chloride test, we still highly suspect that she had CF and was homozygous for the CFTR gene mutation 3849+10kb C->T, because the gene mutation of 3849+10kb C>T is found in patients with a normal sweat chloride test.

Case 2

The patient, a 17-year-old boy with clubbing fingers, was the first child of unrelated, healthy, native Taiwanese parents. He had nasal obstruction and recurrent sinusitis since early childhood and had received functional endoscopic sinus surgery (FESS) at 14 years of age. A persistent night cough was noted since he was 2 months old, which became productive and progressively worse since he was 8 years old. He was repeatedly hospitalized due to frequent bronchiolitis and pneumonia since early childhood. *P. aeruginosa* pneumonia and methicillin resistant *Staphylococcus aureus* (MRSA) pneumonia were proven by sputum cultures numerous times. There were six pneumothorax attacks since the age of 12 and pleurodesis at 15 years of age. His chest roentgenogram showed diffused bronchiectasis. Pulmonary function tests revealed: FEV1 = 1.12 L (37%), FVC = 2.05 L (56%), FEV1/FVC = 54%, FEF $_{25-75\%}$ = 10% and TLC = 3.3 L (73%). The flow-volume curve scooped out with a reduced flow-volume slope and low flows.

CF was suspected due to recurrent *P. aeruginosa* pneumonia and pneumothorax and was confirmed by gene analysis with heterozygous c. 1898+5 G->T and heterozygous p. I1023R mutation (novel mutation) at the age of 16 years. His mother had a heterozygous mutation in p. I1023R and his father had a heterozygous mutation in c. 1898+5 G->T (Fig. 2). The patient became bed-ridden and oxygen dependent at 16 years of age. After receiving tobramycin 300 mg bid every other month, he could walk by himself and oxygen was needed occasionally when sleeping at night.

Case 3

The patient, a 16-year-old boy, was the younger brother of Case 2. He also had recurrent sinusitis and nasal obstruction with progressing severity since 5 years of age and had received FESS at the age of 14. A dry cough had been noted since he was 12 years old, which became productive and progressively worse at 13 years of age. Recurrent *P. aeruginosa* pneumonia was also noted. His chest roentgenogram demonstrated diffused bronchiectasis. Pulmonary function tests revealed FEV1 = 2.35 L (61%), FVC = 2.87 L (64%), FEV1/FVC = 82%, FEF $_{25-75\%}$ = 55% and TLC = 4.12 L (80%). The slope of flow-volume curve was increased.

CF was suspected and also confirmed by DNA analysis, with heterozygous c. 1898+5 G->T and heterozygous p. I1023R mutations (Fig. 2). In addition, due to intermittent abdominal pain and heartburn sensation, a further survey of the abdomen revealed gastroesophageal reflux, a duodenal polyp and a hepatic hyperechoic lesion (16.7 × 7.0 × 7.4 mm).

Case 4

An 8-year-old boy had chronic diarrhea and a failure to thrive from the age of 2 months. He was also repeatedly hospitalized because of pneumonia with *P. aeruginosa* and

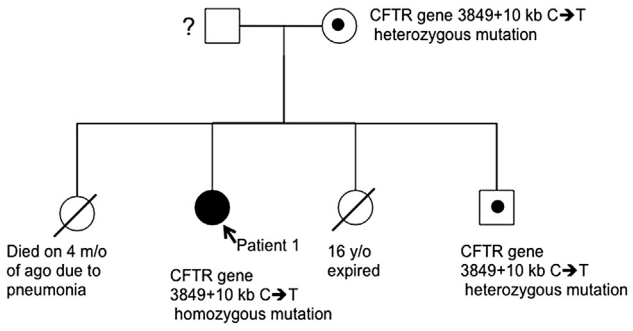

Figure 1. The pedigree of patient 1.

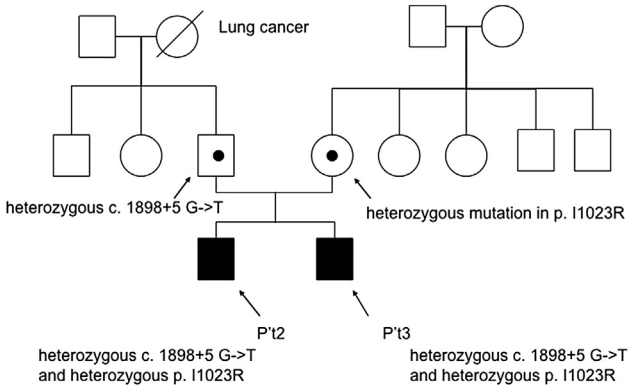

Figure 2. The pedigree of patients 2 & 3.