CYSTIC FIBROSIS IN MALAY CHILDREN - A REPORT OF THREE CASES

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ABSTRACT

Cystic fibrosis (CF) is a rare disease among Asians. Three Malay children with CF presenting with recurrent pulmonary symptoms, malabsorption and failure to thrive are reported. Problems in their management include availability of pancreatic enzymes, compliance to medications and climate factors.

Keywords: cystic fibrosis, Malay children

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INTRODUCTION

Cystic fibrosis (CF) is the most lethal inherited disease of Caucasians. It is rare among Asians and has not been reported in Malaysians. We report three Malay children with CF, two of whom are siblings. Problems of diagnosis and management of these patients are discussed.

CASE 1

A six-year-old Malay boy with a birth weight of 3.2kg was born to non-consanguinous parents. At the age of one week, he developed prolonged jaundice associated with hepatomegaly. There was no abdominal distension or difficulty in passing out meconium. Investigations were inconclusive but the jaundice resolved at three months. At two weeks, he developed persistent cough with copious sputum. His stools were bulky, oily and foul smelling. His eldest sibling died at six months of age after presenting with persistent hyponatremia soon after birth. There was no actual diagnosis made at his death.

When he was seen by a private paediatrician at three months of age, he was marasmic. His weight was 3.62 kg, length 55 cm, and head circumference 40 cm. All parameters were below the third centile for his age. He was tachypnoeic. He had a protuberant abdomen but no faecal mass was felt. Auscultation of the lungs revealed bilateral crepitations. The chest radiograph showed hyperinflated lung fields with generalised opacities which suggested bronchopneumonia. Investigations showed that the blood urea was 4.7 mmol/L, serum sodium 130 mmol/L, potassium 4.9 mmol/L and chloride 89 mmol/L. Mucoid *Pseudomonas aeruginosa* was cultured from the sputum. He responded to antibiotic therapy and intensive physiotherapy.

He was readmitted to the same hospital for another episode of chest infection at five months. *Pseudomonas aeruginosa* was again cultured from the sputum. He was hyponatremic with serum sodium of 120 mmol/L. A diagnosis of cystic fibrosis was entertained and he was referred to our clinic for confirmation. However, the facilities for sweat test was not available. He was referred to an Australian Hospital and the diagnosis was confirmed. The sweat sodium was 130 mmol/L and chloride was 80 mmol/L. The sodium mass was 0.428 gm. Pancrease for pancreatic replacement, oral and nebulised antibiotics and chest physiotherapy were prescribed. He improved and on returning to Malaysia, he continued his follow-up at our clinic. On follow-up, his growth and lung functions were monitored. He was advised regarding his pancreatic replacement and acute exacerbations of chest symptoms were treated aggressively.

At present, he requires 15-20 capsules of Cotazyme Forte a day taken with meals. He passes normal stools, once a day. He had an episode of meconium ileus equivalent which resolved with intravenous fluids and laxatives. Since his diagnosis, he has had chest infections which we treated aggressively. The pattern of organisms varied from *Staphylococcal aureus, Klebsiella pneumonia* and *Pseudomonas aeruginosa.* The most recent chest radiographs showed hyperinflation of both lung fields with peribronchial thickening, but there were no bronchiectatic changes. Clinically, he did have bilateral crepitations when he had acute chest infections. Regarding his long-term respiratory therapy, he is on long-term antibiotics, consisting of nebulised gentamicin 80 mg twice a day and oral ciprofloxacin 250 mg twice a day alternately for three weeks' duration. Chest physiotherapy is done at home. For the past one year, he had been admitted three times for acute exacerbations of chest infection. His growth has not been satisfactory with all parameters, height and weight, below the third centile. He was advised on his diet to ensure adequate calorie intake. He is now in standard one and has no problems adjusting to normal school.

CASE 2

A four-year-old Malay girl presented with recurrent cough with copious sputum and fever since eight months of age. Her stools were foul smelling and bulky. She was repeatedly admitted to another hospital for treatment of pneumonia. She had poor weight gain and was small for her age. She had a normal delivery with birth weight of 3 kg. There was no delay in passage of meconium. Her parents are non-consanguinous. On examination, she was small for her age. She had clubbing of the fingers but was not cyanosed. There were crepitations of both lung fields. Her abdomen was protuberant but there was no organomegaly. Her sweat sodium was 127 mmol/L and chloride was 110 mmol/L.

On admission, *Pseudomonas aeruginosa* was cultured from the sputum. The chest radiographs showed peribronchial thickening, hyperinflated lung fields and bronchiectatic lesions which were further confirmed on CT scan. At present, she requires 20 capsules of Cotazyme Forte a day to control her pancreatic insufficiency. Her chest infections were treated with intensive physiotherapy, long-term antibiotics and pancreatic replacements. Although she is gaining weight, her present height and weight are still below the third centile.

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CASE 3

At the time of admission of Case 2, her youngest sibling who was then two months old, was also investigated for similar presentations. Her delivery was normal, the birth weight being 2.5 kg. She too had no delay in passing out meconium. She had had recurrent cough with copious sputum since five weeks of age. She had foul smelling bulky stool with evidence of failure to thrive and poor muscle bulk. Her abdomen was protuberant. Auscultation of both lung fields revealed scattered crepitations. Her sweat sodium was 120 mmol/L and chloride was 72 mmol/L. Stools for fat globules were positive. Her chest infections were treated with intensive physiotherapy and intravenous antibiotics according to her sputum culture and sensitivity. *Staphylococcus aureus* infections, *Acinetobacter* and *Pseudomonas aeruginosa* had been grown from her sputum. Presently, she is on Cotazyme Forte 10-12 capsules/day with meals. Her chest symptoms are under control and she is steadily gaining weight. Developmentally, she is normal.

DISCUSSION

CF is the most common potentially lethal genetic disorder of the white population. It is an autosomal recessive disorder. It is less prevalent in other ethnic groups. Reports of CF in Asians are few. Goodchild et al reported three Asian children from the West Midlands and he estimated incidence of CF in Asians to be approximately 1:10,000[1].

The three Malay children presented during infancy with recurrent chest infections, pancreatic insufficiency and failure to thrive. The earliest diagnosis was made in the third case at two months of age. The second case was diagnosed late which caused her to have established lung damage.

The diagnosis of CF is based on analysis of sweat. Samples of sweat analysis should weigh at least 100 mg and a value greater than 60 meq of chloride is diagnostic of CF. The lack of facilities for sweat testing delayed the diagnosis in the first case. However, with the availability of the *macroduct* technique[2] in our laboratory, the diagnosis of CF in the latter cases were quickly confirmed.

The locus of cystic fibrosis gene is located on the long arm of chromosome 7. Seventy percent of them have deletion of Phenylalanine at codon 508. To date, 300 mutations have been reported in the literature[3]. Schwarz et al found that three of the six patients in the Lancashire Pakistani families carried the delta F508 mutations; all were homozygotes. The presence of the CF mutations other than delta F508 may have contributed to the difference of clinical phenotypes in the Asian groups studied. It is known that delta F508 appears to be the one with the worst prognosis with early presentations, pancreatic insufficiency and rapid deterioration of the pulmonary function. In the other 30%, the pulmonary disease can be mild. Genetic studies will be done in the future to determine the type of mutation in the two families.

The mainstay of therapy is to delay the progression of the pulmonary disease and to control the malabsorption problems by pancreatic supplements, prompt treatment of chest infections and intensive physiotherapy. The treatment is individualised, especially with the choice of antibiotics. Our problem in managing these children is acquiring the pancreatic supplements since it is not available locally. All three patients obtained their pancreatic enzymes from Australia. In the first case, expenses were borne by parents, while the other two siblings were sponsored by the parents' employers. The Cotazyme bill is approximately RM5000 a year per person. As the children grow, the requirement for enzymes would increase. In the future, they will face more problems as they become adolescents.

Religious considerations were taken into account in prescribing pancreatic enzymes, which are of porcine origin, in Muslim families. Consent was obtained from parents before pancreatic enzymes were prescribed. Other problems include the climatic factors. Hot spells resulted in the first case experiencing episodes of 'heat stroke' and hyponatremia. Sufficient intake of salt in the diet and salt supplements need to be advised. Compliance has been poor in the second family and the full regime of therapy is not easy implemented.

In summary, the management of CF children in a tropical and developing country has to take into consideration environmental, cultural, religious, dietary and economic issues that are peculiar to this part of the world.

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