Cystic fibrosis in Saudi Arabia

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Abstract. Cystic fibrosis (CF) is generally believed to be rare or nonexistent in Saudi Arabia. The aim of this report is to document the occurrence of CF in Saudi Arabia. Thirteen Saudi children were diagnosed as having CF, evidenced by typical clinical features and elevated sweat chloride concentrations (>60 mmol/l). Duration of symptoms prior to diagnosis varied from 1 month-5 years (mean 23 months). The main clinical manifestations of the children were abdominal distension, failure to thrive, steatorrhoea, hepatomegaly, rectal prolapse and recurrent respiratory infections, often with Pseudomonas aeruginosa. In addition, eight patients with symptoms and a family history highly suggestive of CF, but without confirmatory sweat test results are presented. We hope that this report will increase the awareness of CF and ensure an earlier diagnosis of the disease in Saudi Arabia.

Key words: Cystic fibrosis – Meconium ileus – Sweat test

Introduction

Cystic fibrosis (CF) is the most common fatal genetic disease in the Caucasian population. The incidence of CF varies considerably in different parts of the world and among different ethnic groups. The incidence of CF is estimated to be 1:2,000 in Caucasians [11], 1:17,000 in American Blacks, and 1:93,000 in Orientals living in Hawaii [12]. There are 1,000-2,000 new patients with CF diagnosed each year in the USA with an estimated prevalence of approximately 33,000 patients with a population base of about 200 million. It has been stated that only about one third of all patients in the USA suffering from CF have been accurately diagnosed [6, 9].

The high infant mortality in developing countries is mainly due to malnutrition, diarrhoea and chest infections. The clinical features of these diseases are similar to those in patients suffering from CF. It is very probable that many infants and children who have CF will be misdiagnosed due to lack of proper diagnostic facilities and lack of clinical suspicion [10].

The incidence of CF among Arabs is estimated to range from extremely rare to as common as in Caucasian populations [7, 10]. The first Arab child with CF was reported from Lebanon [11]. Subsequently, more patients with CF have been reported from Iraq [1], Kuwait [2, 8], and Jordan [10]. The incidence of CF in Saudi Arabia is unknown, but is generally thought to be rare or nonexistent. The aim of this report is to draw attention to the occurrence of CF in Saudi Arabia.

Patients and methods

The medical records of seven referral centres in Saudi Arabia were reviewed for patients with CF in children less than 14 years of age over the past 10 years. The patients were divided into three groups:

Group 1

True CF patients with clinical symptoms of recurrent respiratory problems and/or evidence of malabsorption together with a sweat chloride concentration ≥ 60 mmol/l either by the original Gibson-Cooke method [5] or by ion specific chloride electrodes (Ionalyzer-Orion research skin electrode meter, Model 417, Orion Research Inc, Cambridge Mass. USA).

Group 2

Siblings of patients in group I, who had died with typical CF-like clinical features prior to the diagnosis of their index siblings, but for whom no sweat test had been performed.

Group 3

Children who had died or were lost to follow up with typical CF-like clinical features but without any confirmatory sweat test.

Results

A total of 21 patients were found. Thirteen patients were in the first group, 4 in the second, and 4 in the third group.

Group 1

Thirteen Saudi children fulfilled the criteria for the diagnosis of CF; two of them were brothers. The duration of symptoms prior to confirmed diagnosis ranged from 1 month–5 years of
Table 1. Highlights of cases in which parents are first degree cousins

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age at presentation</th>
<th>Age at diagnosis</th>
<th>Initial diagnosis</th>
<th>Siblings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2 weeks</td>
<td>3.5 months</td>
<td>Intractable diarrhoea</td>
<td>1 Sibling died with CF</td>
</tr>
<tr>
<td>3</td>
<td>4 months</td>
<td>5.5 years</td>
<td>Pyloric stenosis, Bartter syndrome</td>
<td>1 Sibling died with CF</td>
</tr>
<tr>
<td>4</td>
<td>18 months</td>
<td>3 years</td>
<td>Coeliac disease</td>
<td>Brother of CF patient (Case no. 3)</td>
</tr>
<tr>
<td>5</td>
<td>5 months</td>
<td>2 years</td>
<td>Pneumonia</td>
<td>1 Sibling died with meconium ileus</td>
</tr>
<tr>
<td>9</td>
<td>2 months</td>
<td>4 months</td>
<td>Pneumonia</td>
<td>Only child (expired)</td>
</tr>
<tr>
<td>11</td>
<td>3 months</td>
<td>7 months</td>
<td>Pneumonia</td>
<td>5 Siblings are alive and well</td>
</tr>
<tr>
<td>13</td>
<td>6 months</td>
<td>5.5 years</td>
<td>Glycogen storage disease</td>
<td>1 Sibling died with CF</td>
</tr>
</tbody>
</table>

The parents of 11 affected children were consanguinous. Seven pairs were first degree and 4 pairs were second degree cousins. Some details of cases in which parents are first degree cousins are shown in Table 1.

The clinical presentation of group I is shown in Fig. 1. The most common presenting problems were failure to thrive, recurrent chest infections and abdominal distention. One child (case 7) had meconium ileus. Seven children had *Pseudomonas aeruginosa* in their sputum culture at the time of diagnosis.

Eight children had frequent hospitalizations prior to the correct diagnosis. One patient (case 1) had an extensive medical evaluation including normal sweat chloride determinations and was subsequently referred to the Children's Hospital in Boston, Massachusetts, United States where CF was diagnosed. This family had a previous child who died at 3 months of age with abdominal distention, chronic diarrhoea, and failure to thrive. He was suspected of having pulmonary tuberculosis and was given anti-tuberculous therapy for 3 months prior to accurate diagnosis. The remaining patients had frequent hospitalization with recurrent chest infections, features of malabsorption or both before a diagnosis of CF was made. The clinical features at presentation in this group of CF patients were divided into respiratory (5 cases), gastrointestinal (3 cases) and both (5 cases). One child (case 9) expired at 3.5 years of age from recurrent chest infections and failure to thrive.

### Group 2

Four children fulfilled the criteria set for this group. They all died with features highly suggestive of CF, but without confirmatory sweat test. All deaths occurred in the first 3 months of life. One child (sibling to case 5) died with meconium ileus (Table 1).

### Group 3

Four other patients with symptoms very suggestive of CF were found but their diagnosis was not proven.

### Discussion

The focus of this report is to document that the CF gene is present in Saudi Arabia, and probably more prevalent than has been previously thought. The exact incidence and prevalence of CF in Saudi Arabia is not known. We speculate that the majority of patients suffering from CF in Saudi Arabia are undiagnosed, and die in infancy or early childhood. This is supported by the observation that in seven reported families, four siblings died with CF-like symptoms within their 1st year of life.

For many patients, the diagnosis was significantly delayed, often due to repeated false negative sweat chloride determinations. Sweat chloride determination remains the single most conclusive investigation in the diagnosis of CF [3, 4]. It is not available in most medical centres in Saudi Arabia. To our knowledge most of the Saudi Arabian medical centres that do have the facilities to perform sweat chloride determinations do not have the laboratory personnel trained in proper specimen collection and analysis. Most errors in the determinations of sweat chloride levels are due to inadequate sweat collection, technical errors, and misinterpretation of results. The apparent low-frequency of diagnosed CF patients in Saudi Arabia could partly be due to lack of clinical suspicion and partly be due to technical errors in the determination of sweat chloride levels and lack of autopsy data.

CF is underdiagnosed in Saudi Arabia. A higher index of suspicion for an early diagnosis is needed. A comprehensive national program would be beneficial to increase awareness among general physicians and paediatricians to the occurrence and possible serious sequelae of CF in Saudi Arabia.