Short Reports

Anomalous Sweat Chloride Levels in Cystic Fibrosis During Antibiotic Therapy

It is becoming increasingly common to confirm the diagnosis of cystic fibrosis by using a skin chloride electrode, and estimation of the sodium content of sweat is now often omitted.

The following case report concerns a child with proven cystic fibrosis in whom raised sweat sodium but normal sweat chloride levels were obtained while the baby was receiving cloxacillin.

Possible explanations for the findings are discussed and attention is drawn to their implications in relation to screening programmes for cystic fibrosis.

Method

Sweat was collected on to sodium chloride free Whatman No. 40 filter paper squares (3·5 cm) after conventional pilocarpine iontophoresis using the EMI sweat unit.* The sweat was eluted with 2·0 ml deionized water. 100 mg of sweat was accepted as the minimum weight for analysis as suggested by Varley (1967). Sodium was estimated by flame photometry and chloride by a modified Schales and Schales technique.

The mean and normal range for sweat electrolytes at this hospital are as follows: sodium: mean 21·1 mEq/l., range 5-45 mEq/l. (n = 56); chloride: mean 13·6 mEq/l., range 2-40 mEq/l. (n = 55).

Case Report

The infant was delivered by caesarean section after a pregnancy complicated by pre-eclamptic toxemia, birthweight 2·3 kg. She was the youngest of three sibs, one of whom has diabetes mellitus. On two occasions in the early months of life she was admitted to an isolation hospital with suspected gastroenteritis, and at the age of 10 months presented with a history of recurrent respiratory infections and persistent stridor. Her chest x-ray was normal and a diagnosis of congenital laryngeal stridor was made. The stridor gradually subsided over the next 14 months.

She was referred again at the age of 3 years with rectal prolapse and a history of passing loose, bulky, grey stools. Coeliac disease was suspected and she was admitted for observation. There was no pot belly or muscle wasting and she was discharged after a few days as her stools were thought to be normal. A total faecal fat excretion of 43·2 g over a 5-day period was recorded at this time, but no further action was taken.

The rectal prolapse remained troublesome for the next 12 months.

She was next referred at the age of 9 years to the chest clinic with a 3-month history of cough. A chest x-ray then showed increased lung markings and fibrosis in the right upper zone. Breathing exercises were started and antibiotics advised during the winter months. She

REFERENCES


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EMI—Electromedical Supplies (Greenham) Ltd.

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Short Reports

TABLE

Sweat Electrolytes

<table>
<thead>
<tr>
<th>Date</th>
<th>Weight of Sweat (mg)</th>
<th>Sodium (mEq/L)</th>
<th>Chloride (mEq/L)</th>
<th>Method</th>
<th>Place</th>
<th>Antibiotic Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>21.10.70</td>
<td>25</td>
<td>29</td>
<td>19</td>
<td>Iontophoresis</td>
<td>Nevill Hall Hospital</td>
<td>Nil (cloxacillin discontinued 8.10.70)</td>
</tr>
<tr>
<td>28.10.70</td>
<td>66</td>
<td>106</td>
<td>12</td>
<td>Iontophoresis</td>
<td>Nevill Hall Hospital</td>
<td>Cloxacillin 125 mg 6-hourly (begun 24.10.70)</td>
</tr>
<tr>
<td>30.10.70</td>
<td>258</td>
<td>103</td>
<td>5</td>
<td>Iontophoresis</td>
<td>Nevill Hall Hospital</td>
<td>Cloxacillin 500 mg 6-hourly</td>
</tr>
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<td>4.11.70</td>
<td>77</td>
<td>113</td>
<td>8</td>
<td>Iontophoresis</td>
<td>Nevill Hall Hospital</td>
<td>Ampicillin 500 mg 6-hourly</td>
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<tr>
<td>11.11.70</td>
<td>108</td>
<td>99</td>
<td>6</td>
<td>Skin chloride</td>
<td>East Glamorgan Hospital</td>
<td>Nil (previous antibiotic stopped 24.11.70)</td>
</tr>
<tr>
<td>17.11.70</td>
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<td>—</td>
<td>14.5</td>
<td>Iontophoresis</td>
<td>Nevill Hall Hospital</td>
<td>No antibiotics</td>
</tr>
<tr>
<td>25.11.70</td>
<td>70</td>
<td>107</td>
<td>150</td>
<td>Skin chloride</td>
<td>East Glamorgan Hospital</td>
<td></td>
</tr>
<tr>
<td>26.11.70</td>
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<td>—</td>
<td>150</td>
<td>Skin chloride</td>
<td>Llandough Hospital</td>
<td></td>
</tr>
<tr>
<td>5.12.70</td>
<td>159</td>
<td>85</td>
<td>75</td>
<td>Iontophoresis</td>
<td>Nevill Hall Hospital</td>
<td>Carbenicillin 500 mg 6-hourly (begun 27.11.70)</td>
</tr>
</tbody>
</table>

did not improve over the next 2 years and was admitted to the regional chest hospital in July 1970, at the age of 11 years, with suspected bronchiectasis. When she was first seen by one of us (A.D.G.) in October 1970, she was febrile (temperature 38 °C), dyspnoeic, slightly jaundiced, and many spider naevi were visible. The sputum was frankly purulent, her fingers clubbed, there was moderate intercostal insuction, and crepitations were audible over the whole chest. The abdomen was distended and both liver and spleen were palpably enlarged. A clinical diagnosis of cystic fibrosis was made and sweat tests arranged. The quantities of sweat obtained initially were low. On 29 October 1970 she was transferred to this hospital for further investigation. The results were as follows: Hb 11·6 g, ESR 76 mm, WBC 6900/mm³ (73% polymorphs), sputum cultured a coagulate positive staphylococcus and _H. influenzae_. Bone age normal. Faecal fat excretion over 3 days 8·6 g as stearic acid/24 hours. Plasma proteins 7·3 g/100 ml, albumin 5 g/100 ml, IgG 2200 mg/100 ml, IgA > 500 mg/100 ml, IgM 190 mg/100 ml. Total bilirubin 1·0 mg/100 ml, SGOT 112 RF units/ml, SGPT 44RF units/ml, LDH 420 BB units/ml. The results of several sweat tests are shown in the Table. She was treated with various antibiotics (see Table), inhalations, and physiotherapy, and discharged 1 month later, by which time she had improved though crepitations persisted at the left base.

She was readmitted on 2 further occasions with exacerbations of her chest infection and during the latter suffered a massive haemoptysis and died 13 February 1971, at the age of 11 years 8 months.

Necropsy revealed saccular bronchiectasis of the right upper lobe, haemorrhagic consolidation of both lower lobes, and purulent secretion in the bronchi. There was moderate ascites, and the liver, which weighed 1360 g, was grossly nodular and tawny green in colour. The pancreas was of fibrous fatty structure with small cysts containing thick mucinous secretions. Histologically the pancreas showed the typical features of cystic fibrosis and sections of the liver revealed fibrosis of the portal tracts, the bile ducts being dilated with dark bile.

**Discussion**

Altogether 9 sweat tests were performed on this child and the results are summarized in the Table. The weight of sweat obtained in the initial test, on 21 October 1970, was small and the results therefore questionable, but in the following 5 tests a markedly raised sodium concentration in the presence of a normal chloride level was consistently demonstrated.

Apparent disproportionate rise of the sodium content of sweat might occur if the sample is contaminated with sodium containing dusting powders which have been applied to the skin. This possibility can be excluded in the present case as care was taken to cleanse the skin thoroughly before the test, and in any event it would fail to explain the concurrent low chloride levels unless it was assumed either that the child did not have cystic fibrosis, or that she had, but without sweat gland involvement. Both these assumptions are invalid, as the diagnosis of cystic fibrosis was confirmed at necropsy and involvement of the sweat glands shown by subsequent sweat tests at this and other hospitals.

The possibility of a temporary laboratory error in chloride assessment has to be considered, but it is unlikely as the low level was also confirmed at another hospital using a skin chloride electrode.

All the low sweat chloride levels were recorded during a period when the child was receiving cloxacillin sodium, and when this drug was dis-
continued the discrepancy between sodium and chloride levels disappeared. It was not possible to see whether reintroduction of cloxacillin would reproduce the sweat anomaly in the present case as the organisms in the sputum had become resistant to this antibiotic, and death occurred shortly afterwards.

Although the sweat abnormality might be due to as yet unknown factors, the temporal association with cloxacillin administration suggests a causative relation, and it is tempting to speculate that the anomaly was produced by the substitution of the cloxacillin radicle for the chloride ion in the sweat during the period of therapy.

While it is possible that these findings are peculiar to this case, until further study has been undertaken it is suggested that the results of sweat tests in children with suspected cystic fibrosis be reviewed in the light of any antibiotic therapy which they may be receiving; this applies especially where a sweat chloride only is assessed, as in screening programmes utilizing a skin chloride electrode.

Summary

A case is reported of a child with proven cystic fibrosis in whom normal sweat chloride levels were obtained during treatment with cloxacillin. The possible explanations for this finding and its implications in relation to the use of a skin chloride electrode in screening programmes for cystic fibrosis are discussed.

The authors thank Dr. P. Bray and Mr. R. Christopher-Prosser for arranging sweat tests at Llandough and East Glamorgan Hospitals.

Reference


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Transient Neonatal Hyperglycaemia, Hyperlipidaemia, and Hypermethioninaemia

In 1969 Gentz and Cornblath reviewed the literature regarding neonatal hyperglycaemia. In the 30 cases of transient diabetes of the newborn no abnormality in amino acid metabolism has been reported. A case is described here in which an abnormality in amino acid metabolism was found.

Case Report

The pregnancy was the mother's first and had been uneventful apart from a urinary tract infection. The patient was born at 40 weeks' gestation after an assisted breech delivery, birthweight 1·84 kg, head circumference 32 cm. Striking physical features included minimal subcutaneous tissue, a 'wizened' face, a flat abdomen, and thin 'matchstick' extremities.

The baby's weight gain was inadequate and on the 22nd day of life glucosuria (12·6 g/24 hr) was detected. The 24-hour urine collection contained 6·6 mg homocystine and 1 mg cystine, but no ketones. Venous blood withdrawn 4 hours after a feed was noted to be milky and turbid in character. The concentrations of the various blood constituents are shown in the Table. In arterialized capillary blood the pH was 7·35, the Pco₂ 36 mm Hg, and the standard bicarbonate 20 mEq/l.

A few hours after the blood samples were taken the baby had 5 generalized convulsions. He was treated with chloralhydrate orally and with insulin and 5% dextrose in 0·45% saline intravenously. The blood sugar level after intravenous injection of 2 units crystalline insulin fell from 440 mg to 290 mg/100 ml in 30 minutes. Two units of insulin were given later and the next day the baby's condition had much improved.

On an intake of 660 ml of a proprietary milk (SMA, Wyeth) per day, crystalline insulin (2 units) was given if the sugar content of the ureine voided around 6 a.m. or 6 p.m. was 2% according to the Clinitest tablet method. On the 28th day of life homocystine could not be detected in the 24-hour urine collection. During the third week of insulin treatment glucosuria occurred only occasionally and when a blood sugar of 28 mg/100 ml was obtained the insulin therapy was discontinued. By this time he had received a total of 64 units of insulin in 21 days.

At 2 months' the baby weighed 3·5 kg and was discharged from hospital. When seen again at 3, 6, and 9 months of age, the infant's behaviour was that of a normal baby with a good motor development. The weight curve was around the 10th centile and the height curve slightly below the 3rd centile. The oral glucose tolerance tests became normal (Fig.).

Methods

Amino acids and ketones. Plasma was deproteinized with 3%, sulphosalicylic acid solution and evaporated to dryness, excess acid was neutralized with sodium hydroxide, and norleucine was added as an internal standard. Samples were analysed on a modified Technicon Amino Acid Analyser using the standard 22-hours chromatogram buffer gradient.

Urine amino acid patterns were developed with the standard butanol/acetic acid/water and phenol/ammonia/
Anomalous sweat chloride levels in cystic fibrosis during antibiotic therapy.
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