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## Education And Debate

# Lesson of the Week: Cystic fibrosis presenting as hyponatraemic heat exhaustion

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Cystic fibrosis is the commonest autosomal recessive disorder in Europe. It can present late with atypical features.<sup>1</sup> Mutations in a gene on chromosome 7 that regulates transmembrane conductance cause the disease.<sup>2</sup> Seventy two per cent of patients with cystic fibrosis are homozygous or heterozygous for eight mutations of the gene.<sup>3</sup> The primary defect is low permeability of cell membranes to chloride ions which affects fluid transport during secretion and absorption by epithelial cells.<sup>4</sup> We report a case of late presentation of cystic fibrosis in a man with the (del)F508 and R117H mutations.

## Case report

A 24 year old infantryman was referred after having collapsed twice with hyponatraemia in hot climates. He said that he sweated more than his colleagues in the heat and formed a crust of salt on his skin in hot climates. Before these episodes he had been generally well with no medical history.

In 1991 he was posted to Saudi Arabia, where he underwent heat acclimatisation, which culminated in running 4.8 km after two months. His water intake was greater than his colleagues' during the run. He collapsed immediately afterwards and was admitted to a civilian hospital with nausea, vomiting, dizziness, and muscle cramps. He was posturally hypotensive. Serum electrolyte concentrations were: sodium 116 mmol/l, potassium 2.68 mmol/l, and chloride 57 mmol/l. Liver function tests gave normal results; 1.8 l of urine were collected over 24 hours and urine and plasma osmolalities were 245 mmol/kg. Urinary sodium and potassium excretion was 32.4 mmol/l and 11.8 mmol/l respectively. He was given intravenous normal saline

with potassium replacement (3 l over 24 hours), and he made a complete recovery within 48 hours. He returned to a military hospital in the United Kingdom for investigation and underwent extensive biochemical screening, including a formal water deprivation study. The results were normal and diagnosis was deferred.

For the following year he carried out duties that entailed strenuous physical exercise in various temperate countries; he had no adverse effects. In July 1993 he was posted to Cyprus, where temperatures averaged 30–34°C. Acclimatisation protocols limited running to 2.5 km a day for the first two weeks. Ten days after arrival he was admitted to hospital with nausea, muscular cramps, and dizziness. On the day of admission he had not exercised. On examination he was posturally hypotensive. Biochemical investigations on admission showed the following serum concentrations: sodium 128 mmol/l, potassium 4.6 mmol/l, creatinine 310 mmol/l, and urea 40.2 mmol/l. He responded to intravenous saline and recovered within 24 hours. During this admission his serum cortisol concentration and response to a short tetracosactrin stimulation test were checked and found to be normal. At this point he was referred by JGD to this hospital for further investigation—in particular, an accurate assessment of sweat electrolyte concentrations.

He had a family history of infertility—both his brothers were infertile. He had not taken any drugs in the previous three years. He was a non-smoker and did not drink alcohol excessively. Clinical examination showed nothing abnormal, and extensive biochemical, haematological, and endocrine investigations gave normal results.

Pilocarpine induced iontophoresis was carried out twice.<sup>5</sup> The first time it gave a sweat sodium concentration of 81 mmol/l and a sweat chloride concentration of 102 mmol/l and the second time a sweat sodium concentration of 103 mmol/l and a sweat chloride concentration of 143 mmol/l. These results were raised, the ratio of sodium to chloride concentration being 0.8 and 0.7 respectively. Nasal potential difference was normal.<sup>6</sup>

Genetic testing for cystic fibrosis mutations showed that the patient carried the (del)F508 and R117H mutations. We then performed chest radiography and spirometry, both of which gave normal results; semen analysis, which showed a low volume (0.3 ml) and azoospermia; and a pancreolauryl test, which showed normal exocrine pancreatic function.

## Discussion

Our patient presented with hyponatraemic heat exhaustion at the age of 24. To our knowledge, this is the first time that an adult has had cystic fibrosis diagnosed with this presentation. The diagnosis was confirmed by sodium and chloride concentrations in sweat and by genotyping. His pancreas and lungs were functioning normally, but he was azoospermic.

Patients with cystic fibrosis are adversely affected by high temperatures. Excessive sweating leads to massive sodium loss with vascular collapse; coma may result, especially when combined with an intake of unsalted water. Laboratory investigations show hyponatraemia, hypokalaemic alkalosis, and dehydration.<sup>7</sup> The management of hyponatraemia is discussed by Sant'Agnes.<sup>8</sup> Sodium and chloride concentrations in sweat and their ratio fulfilled the criteria for cystic fibrosis in adults in our patient.<sup>9</sup>

The clinical features of patients who are heterozygous for the (del)F508 mutation have been described.<sup>3</sup>

Patients who are heterozygous for the R117H mutation are older at presentation than those with other genotypes. Eighty seven per cent of patients with the R117/(del)F508 genotype have a normally functioning pancreas, compared with 0.5-9% of patients with other genotypes. The lungs are not usually affected in such patients; the extent of the dysfunction varies widely and may occur late.<sup>10</sup> Our patient will be followed up regularly for signs of lung disease.

The patient has been restricted to service in temperate climates. All patients with cystic fibrosis who are visiting hot climates or undertaking vigorous exercise should receive regular salt supplementation. We conclude that patients who present with a history of heat exhaustion and hyponatraemia warrant further investigation as cystic fibrosis may be the underlying diagnosis.

We thank Dr W E A Wood of Greenwich District Hospital for carrying out the sweat tests in our patient.

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