Cystic fibrosis and renal tubular acidosis

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SUMMARY A case is reported of a child who was born to consanguineous parents and who had the clinical features of two autosomal recessive conditions—cystic fibrosis and distal renal tubular acidosis.

Cystic fibrosis affects 1 in 2000 infants and is the most common inherited disease among white races. The basic metabolic defect is unknown, although chromosome 7 has recently been identified as the site of the defective gene. Increased concentrations of sodium and chloride in the sweat are usually diagnostic of the condition and a defect of chloride reabsorption has been found. When renal function has been examined in cystic fibrosis defects in renal tubular handling of sodium have been found. These have not been associated with clinically recognised abnormalities of renal function.

In contrast, distal renal tubular acidosis is rare. Most cases are sporadic but it may occur in families. The primary defect in distal renal tubular acidosis is a defect in the acidification of urine caused by an inability to generate an adequate hydrogen ion gradient between the blood and tubule fluid. The nature of the cellular defect is unknown but may be a cellular metabolic defect. Similarly, the basic metabolic defect in patients with cystic fibrosis is unknown but the primary defect may be in ion transport.

We describe here the association of distal renal tubular acidosis and cystic fibrosis in the same patient.

Case report

The patient was a baby girl, the third child of healthy Asian parents of Pakistani origin, who were first cousins. Pregnancy was normal and the birth weight was 3050 g. Her immediate neonatal condition was satisfactory, although she had bilateral talipes equinovarus. There was no family history of either cystic fibrosis or renal tubular acidosis. She had a positive meconium screening test for cystic fibrosis (B M Meconium test) and a low faecal chymotrypsin concentration of less than 10 μg/g (normal range greater than 90 μg/g). A sweat test was arranged at 3 weeks of age, and on the 10th day she was discharged home.

At 13 days of age she was thought to have gastroenteritis and admitted to an infectious disease unit. She was wasted, dehydrated, and acidic with a pronounced disturbance of the serum concentrations of electrolytes: sodium 128 mmol/l, potassium 2-0 mmol/l, bicarbonate 7-4 mmol/l, urea 13-6 mmol/l, and creatinine 65 μmol/l. She was rehydrated with intravenous fluid and electrolyte replacement but failed to gain weight satisfactorily despite an adequate energy intake and dietary manipulations including a diet free of lactose and cows’ milk.

She was transferred to our hospital at 31 days of age for further investigation. The diagnosis of cystic fibrosis was supported by raised concentrations of electrolytes in sweat: sodium 99 mmol/l, and chloride 90 mmol/l, sweat weight – 205 mg) and further low faecal chymotrypsin concentrations. A repeat sweat test also gave abnormal results.

Although adequate oral feeds and electrolytes were given, she failed to gain weight and was dry skinned and dehydrated with pronounced loss of skin elasticity. The urine was not infected but was persistently alkaline (pH 7-5) despite a severe systemic acidosis (pH 7-15), suggesting the diagnosis of distal renal tubular acidosis. Further investigations showed persistent plasma electrolyte abnormalities: sodium 138 mmol/l, potassium 3-1 mmol/l, bicarbonate 10-3 mmol/l, creatinine 45 μmol/l, and a pH of 7-15. At this time urine electrolytes were: sodium 28 mmol/l, potassium 33 mmol/l, bicarbonate 12 mmol/l, creatinine 1-6 mmol/l, and a pH of 7-5. The fractional excretion of bicarbonate was 3-28. Other investigations done at this time were as follows: haemoglobin concentration 146 g/l; white cell count 11-6×10⁹/l; and platelets 244×10⁹/l with normal leucocyte morphology. Radiographs of skull and abdomen, and an intravenous pyelogram, were normal. There was no radiological or biochemical evidence of rickets.

The infant was treated with high energy feeds, pancreatic enzyme supplements, prophylactic flucloxacillin, vitamin supplements, and regular chest physiotherapy. The distal renal tubular acidosis was treated with regular oral electrolyte supplements adjusted according to the plasma electrolyte concentrations.
At the age of 7 years she is well and development is normal. Her height of 108·3 cm and weight of 16·4 kg (89% height for age, 70% weight for age, and 88% weight for height) both lie below the third centile. Her electrolyte concentrations are variable, but usually normal with daily oral supplements adjusted on regular electrolyte values. There is no evidence of rickets. The talipes equinovarus has responded to serial splinting and physiotherapy and she walks normally. Her chest radiograph is within normal limits with a Chrispin-Norman score of 3.

Discussion

Renal tubular acidosis is a syndrome characterised by systemic hyperchloraemic acidosis with inappropriately high urine pH, excessive urinary sodium bicarbonate excretion, and normal glomerular function. In the distal tubular type the urinary pH remains high during severe acidosis (blood pH less than 7·2). In contrast patients with proximal renal tubular acidosis can acidify their urine in severe acidosis, and the complex dysfunction of the proximal tubule characteristic of Fanconi’s syndrome is absent. Although there is bicarbonate wastage in distal renal tubular acidosis, it is usually less than 8% of the fraction of filtered bicarbonate, and the acidosis can be corrected with small amounts of sodium bicarbonate.

This child had an inappropriately alkaline urine in the presence of severe acidosis. There is no doubt that she also has cystic fibrosis. The association of these two inherited conditions in the same patient may be a chance finding illustrating the increased occurrence of complex metabolic problems in children of consanguineous marriages. Electrolyte disturbances from a number of causes are common in patients with cystic fibrosis and should be considered in such circumstances. Decreased electrolyte concentrations and profound alkalosis in patients with cystic fibrosis caused by chronic loss of sweat electrolytes and mild gastrointestinal disturbances have been reported. Decreased electrolyte concentrations caused by sweat losses in hot weather have been reported after the original observations by di Sant’Agnese et al. In addition to excessive losses both modern low solute milks and breast feeding may lead to an inadequate net electrolyte intake in the infant with cystic fibrosis.

Our patient was unusual because her reduced electrolytes were accompanied by severe acidosis with serum and urinary electrolytes compatible with a profound renal tubular disorder. Finally, in children with an inherited disorder whose parents are first cousins (as are 60% of the Asian population in our area) an additional recessive condition should be suspected if the clinical picture of a disorder is atypical or the response to treatment unsatisfactory.

References


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Diffuse nephrocalcinosis and idiopathic renal hypercalciuria

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SUMMARY A 12 year old boy presented with primary nocturnal enuresis. Investigation showed extensive bilateral nephrocalcinosis of no obvious or recognised cause. Persistent severe renal hypercalciuria was confirmed by an intravenous calcium infusion. Idiopathic hypercalciuria is not a common cause of nephrocalcinosis and has not previously been described in a child.
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