Cystic fibrosis presenting as diabetes insipidus unresponsive to desmopressin

S. Vande Velde, S. Van Biervliet, E. Robberecht

Cystic fibrosis centre, Ghent university Hospital, Ghent, Belgium.

Abstract

The diagnosis of cystic fibrosis (CF) can be confusing when only a part of the typical symptoms is present. In children, CF is usually suspected when dealing with chronic pulmonary symptoms (chronic productive cough, recurrent pneumonia or bronchiolitis). The pediatric gastroenterologist will exclude CF in all children with a meconium ileus, rectal prolaps or a poor weight gain. Atypical CF symptoms are hypochloremic alkalosis, recurrent pancreatitis and increased appetite to compensate for the pancreatic insufficiency. This case report shows how a diagnosis can be delayed when you are mislead by atypical symptoms. It shows the importance of looking in napkins and argues for the inclusion of CF in the differential diagnosis of polyuria in infants. (Acta gastroenterol. belg., **2007**, 70, **300-301**).

Short report

The diagnosis of cystic fibrosis (CF) can be confusing when only a part of the typical symptoms is present. In children, CF is usually suspected when dealing with chronic pulmonary symptoms (chronic productive cough, recurrent pneumonia or bronchiolitis). The pediatric gastroenterologist will exclude CF in all children with a meconium ileus, rectal prolaps or a poor weight gain. Atypical CF symptoms are hypochloremic alkalosis (1), recurrent pancreatitis (2) and increased appetite to compensate for the pancreatic insufficiency. This case report shows how a diagnosis can be delayed when you are mislead by atypical symptoms. It shows the importance of looking in napkins and argues for the inclusion of CF in the differential diagnosis of polyuria in infants.

A 4 month old girl was seen by her pediatrician because of polyuria and poor weight gain. The stools were described as normal loose infant stools. The weight evolution declined from percentile 50 at birth to percentile 10. The height evolution was on percentile 25. The parents offered on demand, a standard infant formula of which she drank 250 ml/kg/day whereas the normal intake for an infant is 120 ml/kg/day (+/- 20ml). Laboratory investigations revealed normal blood count, electrolyte and protein concentrations. Urinary osmolality was 40 mOsm/kg (normal value 50-1200 mOsm/kg). After an overnight fast (8.5 hours) the urinary osmolality was 299 mOsm/kg (normal value after 12 h fluid restriction > 850 mOsm/kg). Intranasal administration of 1 µg desmopressin resulted in a decreased diuresis but the maximum urinary concentration was only 434 mOsm/kg. Serum antidiuretic hormone concentration was 7.9 pg/mL (normal value < 8 pg/mL). An intravenous desmopressin test was performed, after normalising the intake to 150 ml/kg/day during one day. A dose of 0.2 U/kg desmopressin was administered intravenously followed by the measurement of serum and urine osmolality every hour for a period of 4 hours. The urinary concentration increased from 150 mosm/kg to a maximum of 603 mosm/kg after 2 hours, when the expected value is more than 900 mosm/kg. The ratio serum osmolality to urine osmolality was below 1 in the beginning of the test but above 1 at the end when she developed also an hypernatremia (Na 148 mmol/L). Since there was only a partial response the diagnosis of a partial nephrogenic diabetes insipidus was suggested (3).

Fig. 1.

There were no mutations in the arginine vasopressin receptor 2 gene encoding for the X-linked nephrogenic diabetes insipidus nor in the aquaporin-2 gene encoding for autosomal recessive nephrogenic diabetes insipidus (4).

She was treated with a low sodium, low protein diet. The girl received an infant formula on demand. This resulted in an intake of at least 1,25 L a day and she was given an extra night feeding. At the age of 5 months the

Corresponding author : Dr S. Van Biervliet, M.D., UZ Gent, De Pintelaan 185, B-9000 Gent. E-mail : stephanie.vanbiervliet@ugent.be.

Submission date : 18.05.2007
Acceptance date : 28.05.2007

meals were diversified with fruits and vegetables. She was hospitalised for intravenous fluid administration (100 ml/kg/d = basal fluid needs of an infant) when oral intake decreased due to illness. Height followed percentile 25 and weight percentile 10. During the follow up, blood count, electrolytes (sodium, potassium, chloride, calcium, magnesium, bicarbonate and phosphor), albumin and total protein remained normal.

At the age of 2 years, she achieved continence and her mother noticed shiny orange jelly stools (Fig. 1), interpreted before as urine stains in the diaper. The aspect of the stools suggested the presence of steatorrhoea. Pancreatic insufficiency was confirmed by a fecal elastase of < 15 IU/g faeces. The serum cholesterol was 93 mg/dL (112-200), vitamin A was 19.8 µg/dL (normal 20-43) and vitamin E 0.28 mg/dL (0.3-0.9). There was a normal vitamin D concentration and coagulation was also normal. The diagnosis of cystic fibrosis was confirmed by a positive sweat test (93 mmol/L) and genetic analysis (ΔF508/DF508). She did not have any respiratory symptoms at the time of the diagnosis.

The girl was treated with pancreatic enzyme replacement therapy and the appetite normalised. The ability to concentrate returned. Urinary osmolality after overnight fast was 905 mOsm/kg.

Discussion

Differential diagnosis of infants with increased intake of formula with poor weight gain should include malabsorption syndromes even if diarrhoea is not one of the presenting symptoms. A voracious appetite in CF infants can compensate for the gastrointestinal nutrient losses due to pancreatic insufficiency. This baby drank more than 250 ml/kg/day of an infant formula containing 67 kcal, 1.4 g protein and 17 mg of sodium in 100 ml. In this way she managed after an initial decline, to gain weight following percentile 25 for a length on percentile 10. However, this resulted in an increased fluid intake with increased diuresis. It led to a wash-out of the corticomedullary gradient and secondary urinary concentration problems. This aspect of the history was very misleading.

At the time of continence training the importance of the steatorrhea became clear and the diagnosis of CF was confirmed by sweat test and genetic analysis. Once the child was treated with pancreatic enzyme replacement therapy the appetite normalised and the ability to concentrate returned. CF patients are advised to increase their caloric intake to 130% of RDA and to use ad libitum salt in their food (5). In infants it is especially in warm weather conditions sometimes necessary to give salt supplements (5). It was not easy to convince the parents to increase the caloric density and salt intake due to contradiction with the earlier given advice. The decrease in appetite caused also a lot of stress during the meal times since decreased appetite resulted in the past in a rapid weight loss.

Although, diabetes insipidus is described as a cause of abnormal sweat tests (6,7,8) the possibility of missing the diagnosis of CF should be kept in mind. A positive sweat test is CF until proven otherwise. There are some conditions where permanent or reversible sweat test disturbances are described. Reversible disturbances are observed in failure to thrive conditions (anorexia, celiac disease, malnutrition, neglect...), endocrine diseases (hypothyroidism, hypoparathyroidism, pseudohypoaldosteronism) and renal diseases (nephrogenic diabetes insipidus, nephrosis) (9).

References

1. VANDE VELDE S., VERLOO P., VAN BIERVLIET S., ROBBERECHT E. Heroin withdrawal leads to metabolic alkalosis in an infant with cystic fibrosis. *Eur. J. Pediatr.*, 2007, **166** : 75-76.
2. VANDERBRUGGEN K., DEWAELE K., VAN BIERVLIET S., VAN DER CRUYSSEN G., ROBBERECHT E. Cystic fibrosis : an unusual cause of chronic pancreatitis. *Acta gastroenterologica Belgica*, 2003, **66** : 260-262.
3. ZERBE R.L., ROBERTSON G.L. A comparison of plasma vasopressin measurements with a standard indirect test in the differential diagnosis of polyuria. *N. Engl. J. Med.*, 1981, **305** : 1539-1546.
4. FUJIWARA T.M., BICHET D.G. Molecular biology of hereditary diabetes insipidus. *J. Am. Soc. Nephrol.*, 2005, **16** : 2836-2846.
5. SINAASAPPEL M., STERN M., LITTLEWOOD J., WOLFE S., STEINKAMP G., HEIJERMAN H.G., ROBBERECHT E., DORING G. Nutrition in patients with cystic fibrosis : a European Consensus. *J. Cyst. Fibros.*, 2002 , **1** : 51-75.
6. ROSENSTEIN B.J., LANGBAUM T.S. Misdiagnosis of cystic fibrosis. Need for continuing follow-up and reevaluation. *Clin. Pediatr.*, 1987, **26** : 78-82.
7. DOHERTY-FULLER E., COPELAND K.C. Sweat tests in patients with diabetes insipidus. *Clin. Pediatr.*, 1988, **27** : 330-332
8. SPIGELBLATT L., ROSENFELD R. False-positive sweat tests. *J. Pediatr.*, 1981, **99** : 1001-1003.
9. BEAUCHAMP M., LANDS L.C. Sweat-testing : a review of current technical requirements. *Pediatr. Pulmonol.*, 2005, **39** : 507-11.