

## Pseudo-Bartter syndrome as an initial presentation of cystic fibrosis

### Síndrome de pseudo-Bartter como apresentação inicial de fibrose quística

Catarina Maia<sup>1</sup>, Ana Garrido<sup>1</sup>, Isabel Carvalho<sup>1</sup>, Helena Pinto<sup>2</sup>, Luísa Guedes Vaz<sup>2</sup>, Graça Ferreira<sup>1</sup>

<sup>1</sup> Department of Paediatrics, Centro Hospitalar de Vila Nova de Gaia / Espinho, EPE. Vila Nova de Gaia, Portugal

<sup>2</sup> Department of Paediatrics, Centro Hospitalar de São João, EPE. Porto, Portugal

Received for publication: 08/07/2014

Accepted in revised form: 07/11/2014

#### ■ ABSTRACT

**Introduction:** The clinical manifestations of cystic fibrosis may involve multiple organs. Although the most commonly affected systems are respiratory and gastrointestinal ones, it can present as an acid-base and electrolyte imbalance called pseudo-Bartter syndrome. **Case Report:** We present a case of a 4-month-old boy that presented in our hospital in mid-August with complaints of anorexia and irritability for two weeks. There had been no previous history of respiratory or gastrointestinal symptoms. His parents and remaining family were healthy. Physical examination showed an irritable child with moderate dehydration. No other abnormalities were recorded. Laboratory tests on admission revealed hyponatremic hypochloremic dehydration and metabolic alkalosis. Further investigation showed a high sweat chloride concentration (109mEq/L and 103mEq/L) and a genetic profile confirmed the diagnosis of delF508/delF508 cystic fibrosis. **Conclusion:** The authors describe this case to remind that the diagnosis of cystic fibrosis should be always considered in any infant with metabolic alkalosis and hyponatremic hypochloremic dehydration, whether or not there are associated pulmonary and/or gastrointestinal symptoms typical for cystic fibrosis. Early diagnosis is essential in improving the prognosis and long-term survival of these children.

**Key-Words:** Children; cystic fibrosis; dehydration; metabolic alkalosis; pseudo-Bartter syndrome.

#### ■ RESUMO

**Introdução:** A fibrose quística é uma doença autossômica recessiva que pode envolver múltiplos sistemas. Apesar de tipicamente se manifestar por sintomas respiratórios e/ou gastrointestinais, o possível envolvimento de outros órgãos, nomeadamente com alterações do equilíbrio ácido-base e hidro-electrolítico (denominado síndrome de Pseudo-Bartter), não pode ser esquecido. **Caso Clínico:** Os autores apresentam o caso de um lactente, sexo masculino, 4 meses de idade, admitido por recusa alimentar parcial com 2 semanas de evolução, associada a sensação materna de irritabilidade. Sem história prévia de sintomas respiratórios ou digestivos. Sem antecedentes familiares relevantes. Ao exame apresentava-se prostrado, embora hemodinamicamente estável, com sinais de desidratação moderada. O estudo complementar

realizado na admissão mostrou hiponatremia ligeira, associada a alcalose metabólica hipoclorêmica. No decurso da investigação etiológica foi realizado teste de suor que se revelou positivo (109mEq/L e 103mEq/L) e estudo genético que mostrou a mutação F508del em homozigotia no gene CFTR, o que confirmou o diagnóstico de fibrose quística. **Conclusão:** Este caso pretende relembrar que, perante uma criança com alcalose metabólica hipoclorêmica e desidratação hiponatrêmica, deve ser considerado o diagnóstico de fibrose quística mesmo na ausência de queixas respiratórias ou gastrointestinais. O diagnóstico precoce da doença é fundamental na melhoria do prognóstico e da sobrevivência a longo prazo destas crianças.

**Palavras-Chave:** Alcalose metabólica; criança; desidratação; fibrose quística; síndrome de pseudo-Bartter.

## INTRODUCTION

Cystic fibrosis (CF) is an autosomal recessive condition caused by a large number of mutations of the cystic fibrosis transmembrane regulator gene (CFTR) on chromosome 7. It is the most common, serious, inherited disease in Caucasians and affects multiple organ systems. Although it primarily affects the respiratory and gastrointestinal systems, it can also involve other organs and cause electrolyte and acid base disturbances, such as hypokalaemia, hyponatremia, hypochloremia and metabolic alkalosis, called pseudo-Bartter syndrome. This presentation is most common in children under the age of 6 months<sup>1,2</sup> and should not be forgotten. A case of pseudo-Bartter syndrome as an initial presentation of CF is described.

## CASE REPORT

In mid-August, a 4-month-old boy came to our hospital with complaints of anorexia and irritability for two weeks. He weighed 5320g and had lost 400g of body weight recently. His mother denied fever, vomiting, diarrhoea, cough or any other symptom. He was born at full term and was small for gestational age, but the prenatal, perinatal and postnatal periods progressed uneventfully. There had been no previous history of respiratory or gastrointestinal symptoms. His parents and remaining family were healthy. Initial physical examination revealed an irritable child with moderate dehydration. His vital signs were: blood pressure 91/65mmHg, pulse rate 155 beats/min, respiratory rate 25 breaths/min and temperature 36.6 °C. No other physical abnormalities were noted. Laboratory tests on admission revealed haemoglobin of

15.4g/dL with a blood cell count (WBC) of 12830/uL (36.2% neutrophils and 51.4% lymphocytes), sodium 128 mEq/L, potassium 3.75mEq/L, chloride 77.4mEq/L, urea 40mg/dL and creatinine 0.47mg/dL. Additional laboratory studies included a venous blood gas which demonstrated metabolic alkalosis: pH of 7.6, pCO<sub>2</sub> 31mmHg, pO<sub>2</sub> 57mmHg, base excess 8.9mmol/L and bicarbonate 30.4mmol/L. Urinalysis showed: pH 5, specific gravity 1.025 and no ketones, blood, protein or glucose. Urinary chloride level was not measured in the first stage. The serum levels of aldosterone, calcium, phosphorus and magnesium were normal. He required intravenous fluid therapy with clinical improvement and resolution of electrolyte abnormalities. Further investigation revealed a high sweat chloride concentration (109mEq/L and 103mEq/L) and the genetic profile confirmed the suspected diagnosis of cystic fibrosis with F508del homozygosity for the CFTR gene.

## DISCUSSION

The clinical manifestations of CF may involve multiple organs. Although the most commonly affected systems are respiratory and digestive ones, it can present as an acid-base and electrolyte imbalance, such as hyponatremia and metabolic alkalosis, called pseudo-Bartter syndrome. Multiple inter-related factors have been incriminated in its pathophysiology. The volume of sweat in CF patients is different from that in healthy people<sup>3</sup>. Although the production of primary sweat is relatively normal in CF patients<sup>4</sup>, the dysfunctional CFTR in the sweat duct results in excessive sodium and chloride loss in the final one<sup>3,4</sup>, resulting in the telltale sign of “salty taste”. This

loss in sodium chloride is more pronounced in hot weather where the rate of sweat production is higher<sup>3-5</sup>, leading to massive sodium chloride loss which results in significant extracellular volume contraction and secondary hyperaldosteronism<sup>1,6-12</sup>. The pathophysiology of metabolic alkalosis includes: volume depletion leading to a relatively high bicarbonate level in the contracted extracellular volume<sup>1,6,7,13</sup>, and low extracellular chloride leading to increased reabsorption of bicarbonate to replace the lost extracellular anions (chloride and bicarbonate)<sup>1,7</sup>. In addition, the extracellular volume depletion leads to decreased filtered load of bicarbonate in the urine due to low glomerular filtration rate<sup>1,6</sup>.

Hypochloremic metabolic alkalosis occurs in both Bartter and pseudo-Bartter syndromes<sup>10,11,13</sup>. The main difference between the two conditions is that urinary chloride losses in Bartter syndrome are high, while they are low in pseudo-Bartter syndrome (in CF the chloride losses are increased in sweat)<sup>14</sup>. In our case study, the urinary chloride level, the urinary sodium level and serum aldosterone were not measured in the first stage before the intravenous fluid therapy, so it is not possible to make conclusions. The patient came to the hospital in mid-August, the warmest month, with hyponatremic hypochloremic dehydration and metabolic alkalosis, which is consistent with the literature. Furthermore, he was 4-months-old and this mode of presentation is most common in children under the age of 6 months<sup>1,2</sup>. Older CF children probably compensate excess losses of sodium, chloride and potassium in sweat by increasing the rate of aldosterone secretion and the salt intake. However, the low salt contained in human milk is insufficient to compensate for the increased electrolyte losses with sweating in CF infants during the high environmental temperatures.

Previous isolated reports<sup>15</sup> have described the occurrence of salt depletion and metabolic alkalosis in infants with cystic fibrosis. Although the incidence of metabolic alkalosis as a primary feature of CF is unknown, the studies showed that pseudo-Bartter syndrome is quite common in children with CF. In 2002, Fustik *et al.*<sup>16</sup> reviewed the records of children diagnosed as having CF before the age of 12 months in a 10-year period. The prevalence of metabolic alkalosis in association with low serum electrolyte concentrations in an infant CF population in their

region was 16.5%. This is nearly similar to what was reported from other countries. Pseudo-Bartter syndrome was found in 16.3% of CF patients reported by Dahabreh and Najada<sup>17</sup>, from Jordan, and in 12% of CF patients reported by Yalcin *et al.*, from Turkey<sup>18</sup>. A study from Spain showed that the occurrence of pseudo-Bartter syndrome as a presentation of CF was 16.8%<sup>19</sup>. According to the authors' knowledge, there are no other reported cases of this presentation of CF in Portugal.

In conclusion, the diagnosis of CF should be seriously considered in any infant with metabolic alkalosis and hyoelectrolytemia, mostly during warmer months, whether or not there are associated pulmonary and/or gastrointestinal symptoms typical of CF.

**Conflict of interest statement:** None declared.

## References

- Bates CM, Baum M, Quigley R. Cystic fibrosis presenting with hypokalemia and metabolic alkalosis in a previously healthy adolescent. *J Am Soc Nephrol* 1997; 8(2):352-355.
- Sojo A, Rodriguez-Soriano J, Vitoria JC, Vazquez C, Ariceta G, Villate A. Chloride deficiency as a presentation or complication of cystic fibrosis. *Eur J Pediatr* 1994; 153(11):825-828.
- Bijman J. Transport processes in the eccrine sweat gland. *Kidney Int Suppl* 1987; 21:5109-112.
- Quinton PM. Physiology of sweat secretion. *Kidney Int Suppl* 1987; 21:5102-108.
- Ruddy R, Anolik R, Scanlin TF. Hypoelectrolytemia as a presentation and complication of cystic fibrosis. *Clin Pediatr (Phila)* 1982; 21(6):367-369.
- Ozçelik U, Göçmen A, Kiper N, Coşkun T, Yılmaz E, Ozgüç M. Sodium chloride deficiency in cystic fibrosis patients. *Eur J Pediatr* 1994; 153(11):829-831.
- Halperin ML, Goldstein MB, Halperin ML. *Fluid, Electrolyte and Acid-Base Physiology: A Problem-Based Approach*, 3rd ed. Philadelphia: WB Saunders, 1999.
- Fustik S, Pop-Jordanova N, Slaveska N, Koceva S, Efremov G. Metabolic alkalosis with hypoelectrolytemia in infants with cystic fibrosis. *Pediatr Int* 2002; 44(3):289-292.
- Oztürk Y, Soylu OB, Arslan N. Prevalence and clinical features of cystic fibrosis with pseudo-Bartter syndrome. *Ann Trop Paediatr* 2006; 26(2):155.
- Sauter R, Will M, Helwig H. Schwere Hyponatriämie als diagnoseweisendes Symptom der cystischen Fibrose [Severe hyponatremia as diagnostic symptom of cystic fibrosis]. *Klin Pädiatr* 1997; 209(6):361-363.
- Yalcin E, Kiper N, Doğru D, Ozçelik U, Aslan AT. Clinical features and treatment approaches in cystic fibrosis with pseudo-Bartter syndrome. *Ann Trop Paediatr* 2005; 25(2):119-124.
- Forsyth JS, Gillies DR, Wilson SG. Cystic fibrosis presenting with chronic electrolyte depletion, metabolic alkalosis and hyperaldosteronism. *Scott Med J* 1982; 27(4):333-335.
- Kennedy JD, Dinwiddie R, Daman-Willems C, Dillon MJ, Matthew DJ. Pseudo-Bartter's syndrome in cystic fibrosis. *Arch Dis Child* 1990; 65(7):786-787.
- Marah MA. Pseudo-Bartter as an initial presentation of cystic fibrosis. A case report and review of the literature. *East Mediterr Health J* 2010; 16(6):699-701.

15. Beckerman RC, Taussig LM. Hypoelectrolytemia and metabolic alkalosis in infants with cystic fibrosis. *Pediatrics* 1979; 63(4): 580-583.
16. Fustik S, Jordanova N, Slaveska N, Koceva S, Efremov G. Metabolic alkalosis with hypoelectrolytemia in infants with cystic fibrosis. *Pediatr Int* 2002; 44(3): 289-292.
17. Dahabreh MM, Najada AS. Pseudo-Bartter syndrome, pattern and correlation with other cystic fibrosis features. *Saudi J Kidney Dis Transpl* 2013; 24(2): 292-296.
18. Yalcin E, Kiper N, Dogru D, Ozcelik U, Aslan AT. Clinical features and treatment approaches in cystic fibrosis with pseudo-Bartter syndrome. *Ann Trop Paediatr* 2005; 25(2):119-124.
19. Ballesteros Y, Hernandez MI, Rojo P, *et al.* Hyponatremic dehydration as a presentation of cystic fibrosis. *Pediatr Emerg Care* 2007; 22(11):725-727.

**Correspondence to:**

Dr.<sup>a</sup> Catarina Maia

Department of Pediatrics, Centro Hospitalar de Vila Nova de Gaia / Espinho, EPE

Rua Dr. Francisco Sá Carneiro, Mafamude

4400-129 Vila Nova de Gaia, Portugal.

E-mail: catarinammaia@gmail.com