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THE CASE OF PSEUDO-BARTTER'S SYNDROME: AN ATYPICAL PRESENTATION OF CYSTIC FIBROSIS

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Summary. *A 72-day-old infant with the beginning at the basic disease, cystic fibrosis, was presented with Pseudo-Bartter's syndrome. The disease began with coughing, diarrhoae, vomiting and weakness. Investigations serum of electrolytes showed hyponatremia (110mmol/L) and hypokalemic, hypochloremic metabolic alcalosis (serum potassium 2.6mmol/l; chloride 63.1mmol/l; bicarbonate 43mmol/L and pCO_2 47.3mmol/l).*

Key words: *Pseudo-Bartter's syndrome, cystic fibrosis.*

Introduction

Pseudo-Bartter's syndrome is a rare syndrome of electrolyte depletion, alcalosis and persistent failure to thrive. Hypokalaemic metabolic alkalosis, encountered in a variety of diseases without renal tubular pathology, will ultimately be corrected once the underlying disease is identified and treated. Any corrective fluid and electrolyte supplementation will therefore be a part of the basic disease treatment. Pseudo-Bartter's syndrome can be differentiated from Bartter's syndrome where sweat electrolyte loss is normal and the electrolyte disturbance is due to detective renal electrolyte handling.

Case history

A 72-day-old female, born to nonconsanguineous parents was hospitalized with a cough (which had persisted for the previous 10 days). There had been no prior respiratory symptomatology. The pregnancy was normal. Perinatal course had been uncomplicated. There was no history of administration of drugs. The baby weighed 3350gr and she was 51 cm lonh. It was on breast feeds, and it was apparently normal up to 62 days of life. Three day before being admitted to hospita,l she developed frequent loose stools, non bilious vomiting, abdominal distension and failure to thrive.

Examination and investigation

On examination, the child weighed 4.6 kg with length of 55cm and head circumference of 37 cm (which was 50thcentil for the age). The patient's initial vital signs were as followling: body temperature was 37.2 °C, respiratory rate was 30 breaths per minute, pulse rate was 150 beats per minute and oxygen saturation on the room air was 92%. She was dehydrated with no facial dysmorfism and had no localizing signs on neurological examination. The systemic examination was otherwise normal.

After admission, the haemogram revealed the following: white blood cell count was $14x10^3$ cells per μL with 42.4% neutrophils, 39.4% lymphocytes, 18.2% monocytes and platelet count was $488x10^3$ cells per μL, haemoglobin 14.8 g per dL, red cell count was $5.38x10^6$ per μL and haematocrit 50.2%. Sedimentation rate, C reactive protein level, glucose, aspartat and alanin aminotransferase, total bilirubin, urea nitrogen and creatinin levels were within the normal range. The serum electrolytes level was: sodium 110mmol/l (normal range 135-147), potassium 2,6mmol/l (normal range 4.1-5.6), chloride 63,1mmol/l ((normal range 96-106), bicarbonate 43mmol/l (normal range 18-22mmol/l), pH was 7,56; pCO_2 was 47.3mmol/l; anion GAP was 22.1mmol/l and BE (excess of base) + 20. Urine analyses were normal.

Additional investigations

Subsequently, the patient underwent cardiac investigation, ruling out any underling heart disease. Electrocardiography showed signs of hipokalaemia (flattening of T waves, depressed ST segments). Abdominal ultrasonography (liver, spleen, adrenal glands and kidneys) was normal. Chest radiography was normal. Naso-pharyngeal aspirates culture showed growth of Enterobacter species. Klebsiella was isolated in stool culture. Haemoculture was sterile. Hemoculture showed no growth.

Sweat testing revealed a sweat sodium of 110 and 81,6 mmol/L. DNA analysis at a later date identified delta F508 mutation heterozygosity (father is heterozygous for delta F508 mutation, in mother no determined any mutation).

Clinical course

On the third day, the respiratory rate increased to 60-70 breaths per minute. The child was agitated. Pulse oximetry showed oxygen saturation 80% on room air. White cell account increased to 28 x 10^3/µL. She had inter-coastal retractions. Auscultatory findings included prolonged expiration, wheezy and inspiratory crackles.

Child was maintained on supportive care, potassium and sodium supplements, dietary advice (formula feeds 200 ml/kg/day), oxygen therapy and antibiotic with clinical and biochemical improvement. Electrolytes values on 83rd day of age (after 10 days of admission) were serum sodium 140.1mmol/L, potassium 4.29mmol/L, bicarbonate 32mmol/l, pH 7.46 and pCO_2 42mmol/L.

The level of serum electrolytes was normalized during the hospitalisation. Despite streneuous efforts to maintain caloric intake, weight gain remained suboptimal (lost 400gr; figure 1). When intercurrent illness resolved, it was recognized that the child had persistent borderline hypokalaemia, hyponatremia and alkalosis. A diagnosis of Psudo-Bartter's syndrome was made. Following the

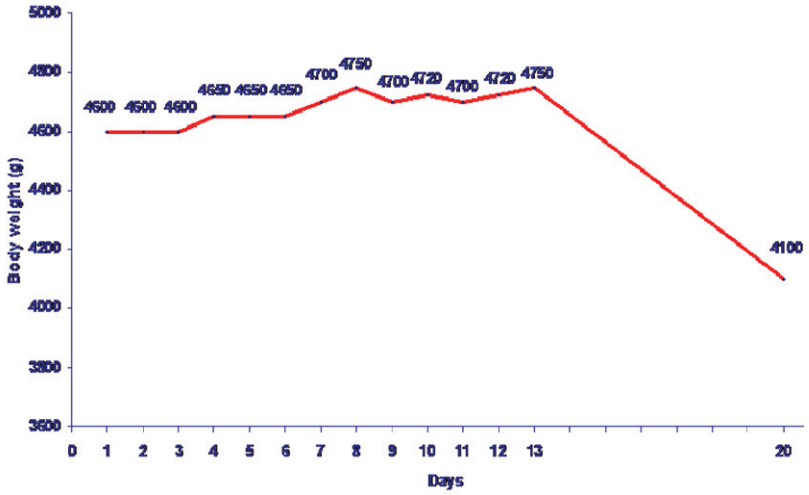

Fig. 1. Body weight during the hospitalization

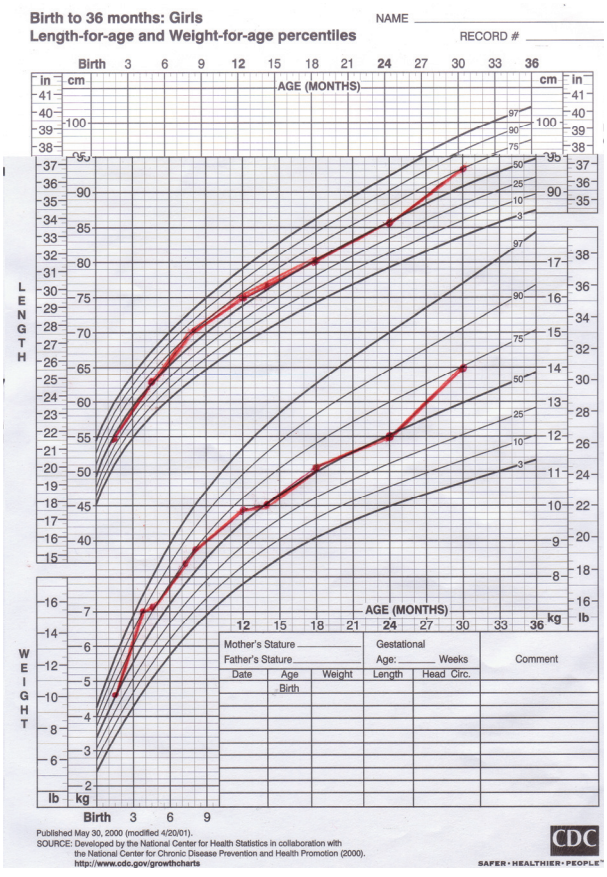

Fig. 2. The weight and length up to 30 months of life

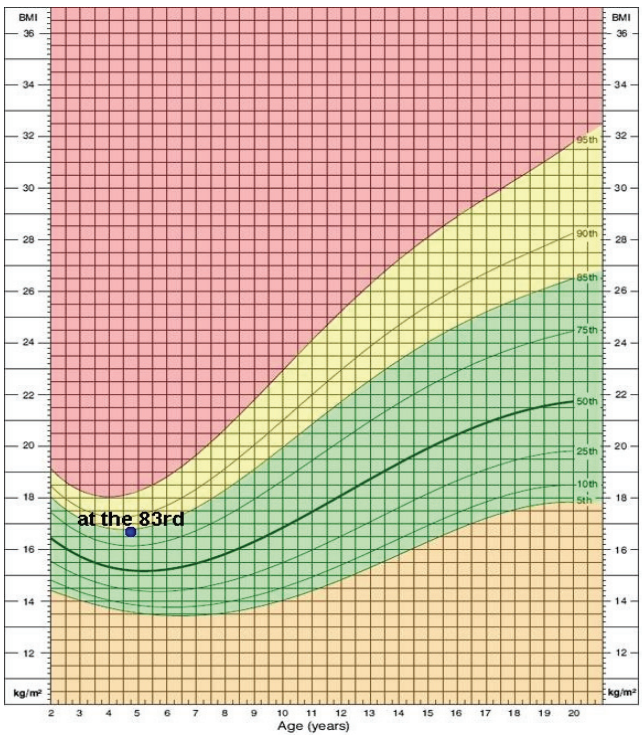

Fig. 3. Body mass index (4 years 9/12 months)

introduction of 2mmol/kg/day of sodium supplements, her weight gain dramatically improved at the initial rate of 30-50gr/day. Figure 2 shows the increase of weight and length up to 30 months of life. Figure 3 shows BMI 16,6 responding to 83thcentil (4 years 9/12 month)

Discussion

Cystic fibrosis (CF) is an autosomal recessive multisistemic disease affecting 1 in 2500 newborns among Caucasians (though rare among Orientals, 1: 90 000). The disease was described first by Anderson in 1938 as 'cystic fibrosis of the pancreas' to the point of the pancreatic exocrine function. In 1953 Di Sant'Agnese et al (….) demonstrated that excessive salt loss occurs in the sweat of CF patients. This finding led to the use of sweat electrolytes measurement as a diagnostic tool. The major clinical characteristics of CF are pancreatic insufficiency and progressive lung disease, caused by thick and dehydrated airway mucus frequently infected with *Pseudomonas* and *Staphylococcus*, leading to respiratory failure and CF mortality. In addition, most males are infertile, due to congenital bilateral absence of the vas deferens (1).

Cystic fibrosis is typically present in infancy with combinations of a failure to thrive and steatorrhoea and respiratory symptoms. Pseudo Bartter's syndrome is a rare atypical presentation of cystic fibrosis with electrolyte depletion, alkalosis and persistent failure to thrive (2). Investigations of serum electrolytes in our patient showed hyponatremia (110mmol/L) and hypokalemic hypochloremic metabolic alcalosis (serum potassium 2,6 mmol/l; chloride 63,1mmol/l; bicarbonate 43mmol/L and pCO_2 47,3mmol/l).

Pseudo Bartter's syndrome is often difficult to distinguish from Bartter 's syndrome. Three phenotypes of Bartter's syndrome have now been recognized: antenatal Bartter's syndrome, classical Bartter's syndrome and Gitelman's syndrome. Mutations in several renal tubule transport protein have been shown to be responsible for these syndromes. The onset may be during the neonatal period, infancy or childhood. Antenatal features include polyhydramnios (increased water in the uterus) and premature delivery. Polyuria is also seen later in life. Other clinical features are a failure to thrive, characteristic faces with thin, triangular face, prominent forehead, large eyes, protruding ears, drooping mouth, strabismus, sensorineural deafness, convulsions and increased susceptibility to infections (3, 4). The history of anamnesis of the Bartter's syndrome in our patient was not evident and clinically the above characteristics of the Bartter's syndrome were not proved.

Bartter syndrome is an inherited renal tubular disorder characterized by hypokalemia, hypochloremic metabolic alkalosis, hyperreninemia, hyper-prostaglandinism, normal blood pressure, with an increased urinary loss of sodium, chloride, potassium, calcium and prostaglandins (4, 5, 6).

Other differential diagnoses are Gitleman's syndrome characterized by hypomagnesemia, hypocalciuria, psudohyperaldosteronism (hypertension with no evidence of increased secretion of mineralocorticoids) and Psudo-Bartter syndrome due to an administration of high doses of prostaglandin E1. Patients with Gitleman's syndrome do not have symptoms throughout their infancy and preschool years other than some febrile seizures, a common disturbance in this age group. The Gitleman's syndrome present during adolescence or adulthood with dominant features like fatigue, weakness, hypocalciuria, hipomagnesiamia with hypermagnesuria and normal prostaglandin production (6,7,8). Our patient was an infant and had no hipomagnesiamia with hypermagnesuria and hypocalciuria.

Conclusion

Nutritional requirements in cystic fibrosis will differ depending on: age, sex, efficacy of small intestinal absorption, respiratory status and activity levels. Improved nutrition benefits growth, respiratory muscle strength and immunological status. A normal nutritional status and the growth rate are achievable goals for the majority of patients. Nutritional intervention should begin as soon as the diagnosis is made in order to prevent or resolve malnutrition. The recent publication of nutritional management guidelines in the UK (9), Europe (10) and the USA (11) will help to improve dietary treatment, standardize practice and hopefully lead to further improvements in morbidity and mortality.

Early diagnosis and prompt treatment of cystic fibrosis reduce long-term morbidity and promote psychological and social adaptation to the condition.

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SLUČAJ PSEUDO-BARTTER-OVOG SINDROMA - ATIPIČNA PREZENTACIJA CISTIČNE FIBROZE

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Kratak sadržaj: *Prikazuje se odojče uzrasta 72 dana kod koga je osnovna bolest, cistična fibroza, počela u vidu Pseudo-Barterovog sindroma. Bolest je počela kašljem, prolivom, povraćanjem i slabošću. Analize serumskih elektrolita pokazivali su hiponatremiju (110mmol/l) i hiokalemijsku hipohleremijsku metaboličku alkalozu (serumski K 2,6 mmol/l, hloridi 63mmol/l, bikarbonati 43 mmol/l i ukupni pCO_2 47,3mmol/l).*

Ključne reči: *Pseudo-Barterov sindrom, cistična fibroza*