Acute Dehydration, Hyponatremia, Hypochloremia and Metabolic Alkalosis: a manifestation of CF?

Marija Dimitrovska-Ivanova MD, Irena Nikolova MD
Marija Karagjozova MD, Luiza Doneva MD
Department of Pediatrics
Clinical Hospital Stip
University “Goce Delcev” Stip
Macedonia

Case Presentation

- 6 months old male. Born after normal pregnancy and delivery.
- 4 days prior to admission - reduced appetite, fatigue, nausea progressing into refusal of food and liquids.
- On examination:

  37,4^{C,}, HR – 160/min, BP – 90/60 mmHg, SaO2 – 98%.

  pale, perioral cyanosis, signs of dehydration: dry tongue, reduced turgor and elasticity of the skin, sunken fontanelle, mild hypotonia.

- Rest of the physical examination - normal.

Laboratory tests

- Na = 126 mmol/l, K = 2.8 mmol/l, Cl = 68 mmol/l
- Urea = 9.1mmol/l, Creatinine = 50.5 umol/l
- Urine positive for ketones.
- pH = 7.61; BE = 14.6 mmol/l, HCO3 = 37,2 mmol/l.
- Chest X ray and abdominal ultrasound - normal

Question 1

1. What can be the reasons for the acute dehydration in this patient?

A. Vomiting

B. Diarrhea

C. Hyperventilation

D. Increased sweating and refusing food and liquids

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Question 2

2. Which of the following conditions is not associated with metabolic alkalosis with hypokalemia?

A. Potassium-losing nephropathy

B. Cystic fibrosis

C. Pyloric stenosis

D. Bartter’s syndrome

E. Acute kidney injury

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Hypokalemia - Differential diagnosis

A. **Potassium losing nephropathy** – molecular hereditary disorder of the function of the ion channels of the renal tubules.

- ***Antenatal*** *Bartter Syndrome*: fetal polyuria, premature birth, postnatal severe dehydration, hypercalciuria and nephrocalcinosis.

- *Gitelman Syndrome*: in **late childhood and adolescence**. Mutation of a gene responsible for NaCl co-transport of the distal tubule. It is characterized by muscle weakness or tetany, hypokalemia and hypomagnesaemia.

Hypokalemia - Differential diagnosis

B. **CF**: CFTR dysfunction in the sweat ducts resulting in excessive chloride and sodium losses, especially in warm weather. Hypokalemia is secondary to renal potassium wasting, volume contraction and chloride depletion.

C. **Pyloric stenosis**: Excessive bilious vomiting after feeds at age 4-8 weeks. Hypokalemia is secondary to vomiting, dehydration, volume contraction, chloride depletion and renal potassium wasting.

D. **Bartter Syndrome**: Age 2 - 5 years, characterized by polyuria, hypokalemia and growth retardation. It is a genetic defect of the chloride duct in the thick ascending limb of Henle's loop and distal convoluted tubules.

E. **Acute Kidney Injury** – Hypokalemia usually accompanied with metabolic acidosis.

Question 3

3. What is the **most probable** cause of alkalosis in this child?

A. Hyperventilation

B. Hypochloremia

C. Loss of acid in the stool

D. Loss of acid in the urine

E. Intoxication with alkaline food

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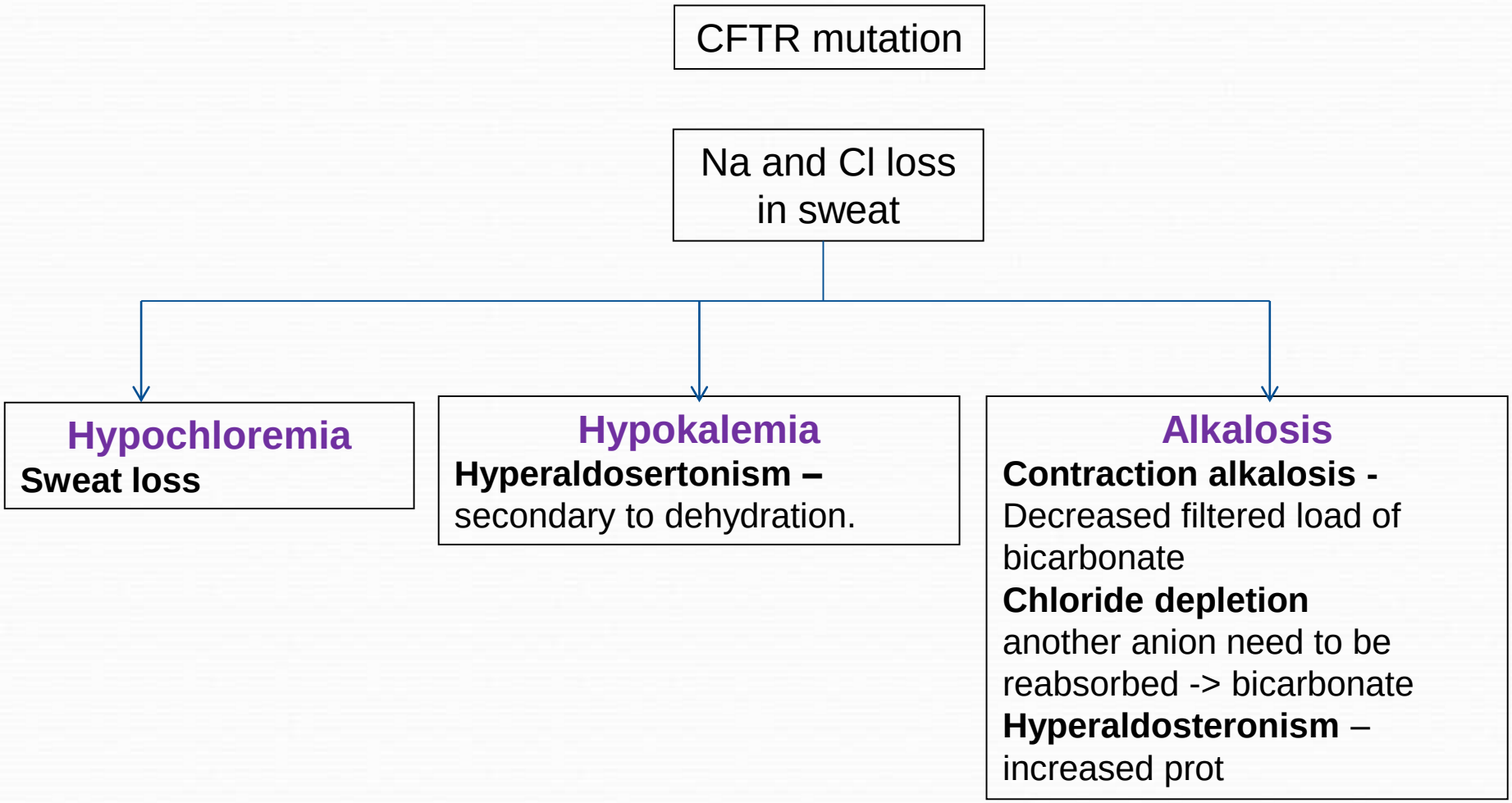
Case presentation - continue

- Sweat test - Chloride - 124 mmol/L.
- CFTR mutations panel - F508/del (c.1521_1523delCTT) on one allele, second allele not found in the panel
- CFTR gene sequencing - pending

The mechanism of electrolyte abnormalities in this child



Question 4

4. How would you treat this child?

A. Correct hyponatremia with hypertonic 3% NaCl

B. Parenteral bolous rehydration with 0,9% NaCl, followed by maintenance fluid.

C. Correct hypokalemia with oral administration of 7,4% solution of KCl

D. Forced diuresis to increase urinary bicarbonate secretion

E. All of the above

Question 4

4. How would you treat this child?

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First report of acute hypoelectrolytemia and metabolic alkalosis in CF

Heat Prostration in fibrocystic disease of the pancreas and other conditions

KESSLER & DOROTHY ANDERSEN Pediatrics 1951

- During the heat wave in NY in 1948
- 7 children presented with vomiting, dehydration, hypoelectrolytemia and metabolic alkalosis, some with seizures
- They were considered to be doing well prior to the acute onset and diagnosed afterwards

Literature review

Acute hypoelectrolytemia and metabolic alkalosis can be the **initial presentation of CF**, during warm weather or in areas with hot climate, in previously healthy:

- Infants (*Beckerman et al 1979, Salvatore et al 2004, Ballestero et al 2006*)
- Children (*Leoni et al 1995, Epaud et al 2005*)
- Adults (*Bates et al 1997, Priou-Guesdon et al 2010*)

Question 5

5. In infants with CF having CFTR mutation on only one allele, what other investigation can be done?

A. Repeat sweat tests

B. Examination of the pancreatic function

C. CFTR gene sequencing

D. CFTR functional tests (NPD, ICM)

E. All of the above

Question 5

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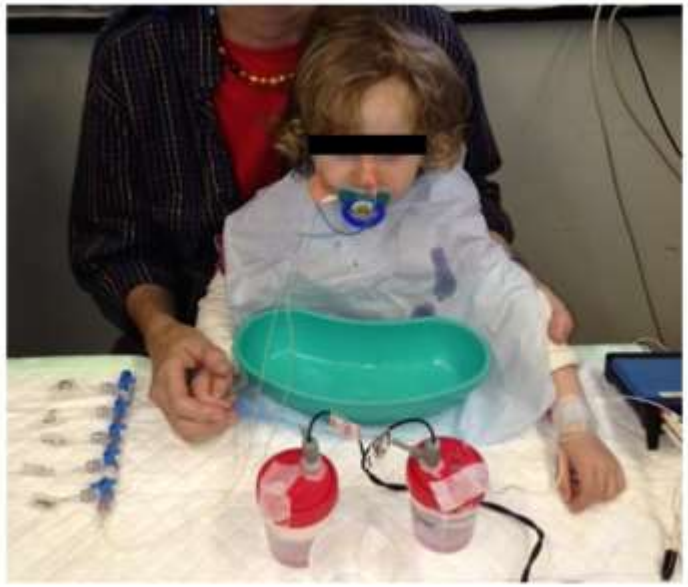
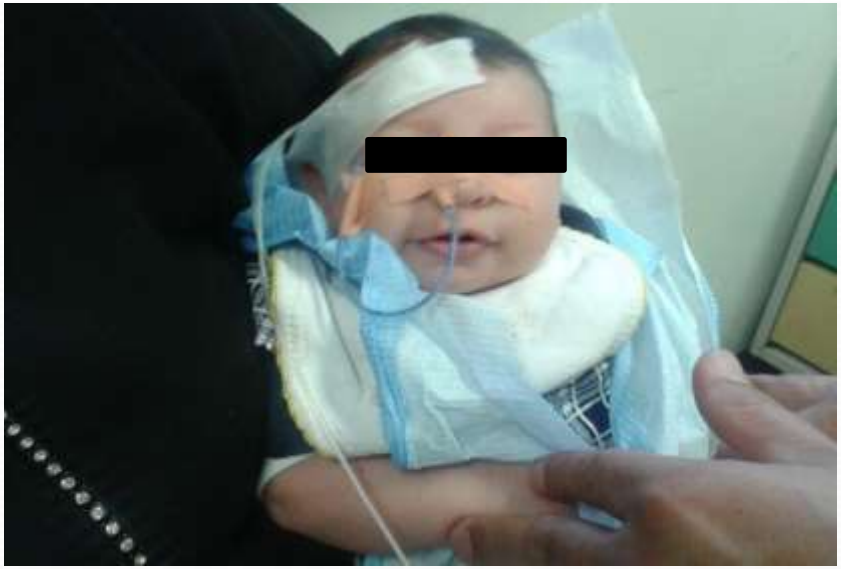
Pancreatic function in CF

- Secretin pancreosymin challenge test – reduced secretion of pancreatic lipase, trypsin chymotrypsin and HCO3.
- Activity of pancreatic chymotrypsin can be examined indirectly with PABA test.
- Activity of pancreatic lipase and co-lipase is examined by measuring fat in the stool.
- Fecal elastase (EL1)- it remains intact during its intestinal transition and its fecal concentrations reflects the pancreatic exocrine secretory capacity .

NPD in infants suspected with CF

- Measures Na and Cl transport in nasal surface epithelial cells.





NPD in infants suspected with CF

- Young children and infants may require some degree of sedation. The risks of the modified infant NPD protocol appear minimal. Careful infant positioning, smaller catheter size, and lower flow rates should minimize the risk of direct aspiration from the nasopharynx.
- The doses of amiloride and isoprenaline are each well below the pharmacologically active concentrations.

Southern et al. **A modified technique for measurement of nasal transepithelial potential difference in infants. J Pediatr**. 2001; 139: 353–358

K. De Boeck et al. **New clinical diagnostic procedures for cystic fibrosis in Europe, J. of Cystic Fibrosis** Volume 10 Suppl 2 (2011) S53-S66

ICM in infants suspected with CF

The advantages of ICM include:

- easy accessibility of intestinal tissue at any age, allowing its use in CF children identified by newborn screening;
- no or minimal tissue destruction or remodeling triggered by bacterial or viral infections;
- its ability to detect very low amounts of functionally active CFTR.

ICM in infants suspected with CF

- ICM can be performed without sedation.
- Further reference data will help to establish the ICM test in the diagnostic workup of individuals in whom the diagnosis of CF is difficult.

K. De Boeck et al. **New clinical diagnostic procedures for cystic fibrosis in Europe**, J. of Cystic Fibrosis Volume 10 Suppl 2 (2011) S53-S66

Summary

The occurrence of acute hyponatremic/ hypochloremic dehydration and metabolic alkalosis, especially in the summer period, without visible additional fluid loss in childhood, should lead to think of cystic fibrosis.