CASE 2

UNEXPLAINED HYPOKALEMIA

Caucasian female, 36 years old, admitted March 01 2016

MC: weakness, inability to move

PMH:

- Unremarkable, except one pregnancy with caesarian section at 22-23 weeks of gestation due to premature placental abruption
- Patient denies diabetes, food restriction, usage of antibiotics, diuretics, laxatives and any herbal products
- Family history is also unremarkable

History of present illness:

- February 22 2016 after physical exercise she felt low extremities muscle tension and hip muscle pain, which regressed spontaneously in two days. However three days later she developed low grade fever, thirst, dry mouth, progressive muscle weakness and numbness
- Next night she was unable to be up and about, fell of her bed, and for 6 hours lay on the floor without movement. She denies loss of awareness, but reports single episode of vomiting and headache

- February 29 she was admitted to the infectious disease hospital, suspected with meningitis
- She was conscious, alert, RR 24 per minute, BP 120/70 mm Hg, HR 88 per minute
- Neurological exam did not reveal any meningeal signs but confirmed tetraparsesis
- Work-up:
  - Moderate leukocytosis with normal differential count
  - Thrombocytosis
  - Mild hyperglycemia
  - High CK level with normal CK-MB
  - Anti-CMV and Anti-EBV IgG positive, anti-CMV and anti-EBV IgM negative
  - LP: liquor colorless, transparent, protein 4.2 g/L, cytosis 1/3, glucose 4.5 mmol/L
  - Chest and paranasal sinuses X-Ray unremarkable
- The diagnosis of meningitis was ruled out. Patient was suspected with Guillain-Barre syndrome and referred to our hospital

At admission to ER:

- Conscious, alert. Body temperature 36.4°C, RR 18 per minute, pulse regular 90 per minute, BP 120/80 mm Hg, SpO^2 98% (room air)
- Well nourished, skin dry, normally coloured, no oedema or palpable peripheral lymph nodes. HEENT and neck otherwise normal. Lungs: no dullness to percussion, any rhonchi, wheezes or rubs. Heart: regular rhythm, no murmur. Abdomen soft, non-tender, bowel sounds normal. Liver +1 cm below rib arch, non-painful, spleen and kidneys not felt. Urination is free, urine colourless
- Neurologic exam: no meningeal signs; pupils round, D=S, normal photoreaction; tetraparesis, upper limbs – grade 2, lower limbs - grade 1, muscle tone and power decreased; tendon reflexes depressed, D=S; feet signs negative; no dysaesthesia.

Point-of-care work-up in the ER:

- Moderate leukocytosis with normal differential count
- Severe hypokalemia
- CK even higher than before with normal CK-MB
- Slightly elevated aminotransferases
- Mild hyperglycemia
- Other blood chemistry tests within normal range
- Urinalysis: low specific gravity and moderate proteinuria and leukocyturia
- ECG: atrial fibrillation with regular rhythm 2:1, 95 bites per minute, QT interval elongation
- Brain and spinal MRI did not confirm demyelinating lesions

❑ Diagnosis of Guillain-Barre syndrome was not confirmed.

Treatment and further work-up in ICU:

- Due to severe hypokalemia with atrial fibrillation patient was admitted to ICU and started on intravenous potassium chloride infusions 40 mEq/h, and heparin
- Urethral catheter was placed; urine output reached 7000 ml/day
- Under treatment in next 4 days her serum potassium gradually elevated to normal range, ECG showed sinus rhythm, muscle weakness partially resolved; urine output became 3500 ml/day
- However :
  - CK and aminotransferases were still growing
  - Myoglobin was elevated
  - Glucose and WBC count became normal, Hb level slightly decreased
  - Procalcitonin test, coagulation tests, thyroid hormones and aldosterone - within normal range
  - Infectious screening, including RPR-test for Treponema Pallidum, HBsAg, anti-HCV and anti-HIV-antibodies, PCR for VEB, CMV, HSV type 1 and 2 was negative
  - Chest X-Ray was otherwise normal, abdomen and kidney ultrasound unremarkable.

	WBC x10^9/L	Hв (g/dL)	Plt x10^9/L	ESR mm/h
February 29	20.1	15.1	517	21
March 1	25.1	13.0	279	25
March 4	9.6	9.9	314	15

	February 29	March 1	March 4
Potassium mmol/L		1.4	3.5
CK U/L	1836	2730	31782
CK-MB U/L [%]	63 [3.3]	68.9 [2.5]	
AlAT U/L		39	143
AsAT U/L		60	342
Glucose mmol/L	9.6	7.7	5.2
Urea µmol/L	6.6	6.3	
Creatinine µmol/L	94	97	
Total Bilirubin µmol/L		10	
Total Protein g/L		71.4	
Lactate mmol/L		3.5	1.2
Sodium mmol/L		134	137
Chloride mmol/L		112	115
Calcium ionized mmol/L		1.31	1.20
Magnesium mmol/L		0.74	
Bicarbonate mmol/L		16.1	18.4
pH		7.25	7.33
Osmolality mOsm/kg		276.7	278.2
Myoglobin µg/L			1710

	Color	SG	pH	Protein g/L	Glucose mmol/L	WBC hpf	RBC hpf	Casts hpf	Urobilin µmol/L	Crystals
March 2	Light yellow	1010	7.0	1.0	abs	50-70	abs	abs	abs	abs

Diagnostic considerations and final diagnosis:

- At that point nephrologist was invited to see the patient and search for polyuria and hypokalemia cause
- Given patients history, presence of acidosis, normal sodium and magnesium levels, normal thyroid hormones level and normal blood pressure, the most often causes of hypokalemia were ruled out:
  - Excessive sweating
  - Diarrhea
  - Starvation
  - Milk-alkali syndrome
  - Drug-induced potassium losses
  - Hyperaldosteronism, hyperreninemia
  - Bartter, Gitelman's and Liddle syndromes
  - Thyrotoxicosis
- Pseudohypokalemia was also ruled out as leucocytosis was not that prominent and patient had multiple symptoms of true hypokalemia

- Additional history taking revealed that since adolescence the patient used to consume Coca-Cola about 2 L per day (and more) every day, without any signs and symptoms but thirst and stools 2-3 times a day
- At the onset of present illness her thirst increased and she consumed as much as 5 L per day, mostly Coca-Cola and water
- That led us to the diagnosis of hypokalemia with myopathy, rhabdomyolysis, atrial fibrillation and hypokalemic nephropathy due to excessive Coca-Cola consumption
- We presume that she had chronic hypokalemia with asymptomatic myopathy for a long time
- Physical exercise triggered rhabdomyolysis with fever, inflammatory response and exaggeration of hypokalemia with typical symptoms like paralysis, arrhythmia and polyuria
- She most probably also had hypokalemic nephropathy long before, as the duration of Coca-Cola consumption exceed 20 years

Further treatment and follow-up:

- Patient was discharged from ICU and treated with oral potassium formulations in nephrology unit for next 8 days
- Her neurological symptoms completely resolved, serum potassium was normal as well as enzymes and blood count, but her urinalysis still showed low specific gravity and mild proteinuria
- She was discharged after totally 2 weeks of hospital stay and advised to avoid Coca-Cola consumption
- Three month later at out-patient consult she was doing well, no complains, taking no medications
- Her serum potassium is quite normal; however her urine specific gravity is still low – 1012-1013.

	WBC x10⁹/L	Hв (g/dL)	Plt x10⁹/L	ESR mm/h
February 29	20.1	15.1	517	21
March 1	25.1	13.0	279	25
March 4	9.6	9.9	314	15
March 14	8.9	13.5	263	24

	February 29	March 1	March 4	March 14
Potassium mmol/L		1.4	3.5	4.5
CK U/L	1836	2730	31782	235
CK-MB U/L [%]	63 [3.3]	68.9 [2.5]		
AlAT U/L		39	143	16
AsAT U/L		60	342	36
Glucose mmol/L	9.6	7.7	5.2	4.6
Urea µmol/L	6.6	6.3		3.7 [
Creatinine µmol/L	94	97		75
Total Bilirubin µmol/L		10		
Total Protein g/L		71.4		
Lactate mmol/L		3.5	1.2	
Sodium mmol/L		134	137	138
Chloride mmol/L		112	115	105
Calcium ionized mmol/L		1.31	1.20	
Magnesium mmol/L		0.74		
Bicarbonate mmol/L		16.1	18.4	
pH		7.25	7.33	7.36
Osmolality mOsm/kg		276.7	278.2	
Myoglobin µg/L			1710	

	Color	SG	pH	Protein g/L	Glucose mmol/L	WBC hpf	RBC hpf	Casts hpf	Urobilin µmol/L	Crystals
March 2	Light yellow	1010	7.0	1.0	abs	50-70	abs	abs	abs	abs
March 14	Light yellow	1010	7.0	0.2	abs	0-1	abs	abs	abs	abs

- First case of hypokalemia, associated with heavy Coca-Cola consumption, was described in 1994
- Since that time a number of case reports came up, describing patients who drank large volumes of Coca-Cola and developed a severe degree of hypokalemia and paralysis
- The first interpretation of this phenomenon postulated that Coca-Cola contains large amount of caffeine, which enhances the shift of potassium from extracellular space into cells, and increase renal excretion of potassium via renin release, β-adrenergic stimulation and hyperventilation with alkalosis
- Other explanations refer to several mechanisms, all of which may play a role simultaneously:
  - Cola contains large amount of fructose, which is absorbed in limited quantities (only about 40% as compared to glucose) in the small intestine, therefore, unabsorbed fructose pass into the colon, causing an osmotic diarrhea and chronic potassium depletion
  - Elevated glucose levels secondary to excessive cola consumption lead to osmotic diuresis, resulting in the urinary loss of potassium
  - Hyperinsulinemia subsequent to hyperglycemia causes intracellular migration of potassium
  - Inadequate dietary potassium is supposed to play a role as well - Cola contains small amount of potassium, and as the appetite in persons, constantly consuming Cola, is lowered by fructose intake, lack of balanced diet and lack of consumption of fruits or other dietary ingredients rich in potassium lead to insufficient repletion of potassium, along with excessive potassium losses