Introduction

McKittrick–Wheelock syndrome is a rare disorder caused by fluid and electrolyte hypersecretion from a rectal tumour. The most frequently reported tumours are villous adenomas [1–5].

The main clinical features of McKittrick–Wheelock syndrome are dehydration, mucous diarrhoea and symptoms of hyponatremia (headache, nausea, weakness, muscle cramps, lethargy and seizures) and hypokalemia (fatigue, paraesthesias, cramps, ileus, vomiting, hypotension, cardiac arrhythmias and electrocardiographic changes) [4,6]. Both cyclic adenosine monophosphate (cAMP) and prostaglandin E2 have been implicated as possible secretagogue compounds in the pathogenesis of this syndrome [3]. Laboratory findings typically reveal metabolic acidosis, prerenal azotaemia, hypoosmotic hyponatremia, hypochloremia and hypokalemia [1–3].

McKittrick–Wheelock syndrome should always be considered when severe hyponatremia and hypokalemia are accompanied by watery diarrhoea. Early diagnosis is essential to commence the appropriate symptomatic therapy directed towards life-threatening electrolyte disturbances, and causal treatment can be undertaken. Indomethacin as a prostaglandin inhibitor has been used with success in controlling the volume of rectal effluent in some patients with secretory villous adenomas [3]; however, a complete recovery can be expected only after the removal of the tumour [1].

Case report

A 57-year-old white man was admitted to hospital at 03:00 hours on 30 September 2005 because of diarrhoea, malaise, muscle cramps and dehydration. Diarrhoea seemed to start soon after the patient started taking amoxicillin tablets prescribed one week earlier because of a sore throat. Post-antimicrobial diarrhoea was the presumed diagnosis. A careful medical history collected during the patient’s stay in the hospital revealed that he had been suffering from watery diarrhoea for approximately 2 years. In the past week the diarrhoea had worsened and he felt progressive malaise and cramps in his legs. Two years earlier a rectal neoplasm was diagnosed by rectosigmoidoscopy and radical tumour surgery was proposed. The patient refused surgery so a pathological examination was not conducted. Except for chronic diarrhoea, he was otherwise healthy. The patient neither smoked tobacco nor drank alcohol. He took no drugs. There was no history of behaviour disturbances, melena, abdominal pain, rash, cough, exposure to tuberculosis or contact with animals. There was no family history of colorectal neoplasia either. There was no known exposure to toxic substances.

Soon after admission to the hospital the patient had seizures that were stopped with diazepam. As the patient was soporous with irregular respiration he was transferred to the intensive care unit. On examination, the patient was dehydrated, with shallow but regular respiration and depressed deep-tendon reflexes. His tympanic temperature was 36.2°C, pulse was 82 and respiration 24. Blood pressure was 140/75 mmHg. The Glasgow coma score was 5 and the APACHE II score was 33. Chest and cardiac examinations were unremarkable. The abdomen was meteoristic with hastened peristaltic waves. Rectal examination revealed a hypotonic anal sphincter, and on the right side of the rectum was a firm, painless, pedunculated tumour with an uneven surface. There was also abundant bloody mucous rectal discharge.
Laboratory tests revealed a leukocyte count of $24.7 \times 10^9$/l (neutrophils 91%, monocytes 3% and lymphocytes 5%). The red blood cell count was $5.4 \times 10^{12}$/l, haemoglobin was 162 g/l and platelets were $413 \times 10^9$/l. The erythrocyte sedimentation rate was 32 per hour. C-reactive protein was 4.4 mg/l and fibrinogen was 3.73 g/l. Prothrombin and partial-thromboplastin times were normal. Serum concentrations of glucose, ionized calcium and magnesium were normal. Total bilirubin, aminotransferases, lactate dehydrogenase, amylase and alkaline phosphatase were all normal. There were no abnormalities on serum protein electrophoresis.

The blood level of sodium was 93 mmol/l, potassium 2.7 mmol/l, chloride 63 mmol/l, urea nitrogen 38.2 mmol/l, creatinine 688 mmol/l and the phosphorus level was 2.59 mmol/l. The anion gap was 16.9 mmol/l. Calculated serum osmolality was 231 mOsm/kg and measured osmolality was 192 mOsm/kg. Osmolality of the urine was 288 mOsm/kg (normal level: 100–900 mOsm). The urine level of sodium was 10 mmol/l, potassium 10.7 mmol/l and chloride was 10 mmol/l. The urine anion gap was $+10.7 \text{ mmol/l}$.

Arterial blood gas analysis revealed metabolic acidosis (pH 7.31, blood oxygen saturation 98.9%, partial pressure carbon dioxide 26.7 mmHg, partial pressure oxygen 147 mmHg, hydrogen carbonate ion 13.1 mmol/l, base excess $-11.7 \text{ mmol/l}$). Urinalysis revealed microhaematuria. Urine pH was 5.0 and specific gravity was 1.008.

_Clostridium difficile_ toxin A in stool samples was not confirmed and stool cultures were negative. Toxicological work-up was negative. Serum levels of thyroid-stimulating hormone and cortisole were normal. Electrocardiogram was normal. Chest radiography showed no abnormalities. An electroencephalogram taken on admission was irregular, with diffuse background slowing.

Fluid replacement was started immediately after admission with isotonic saline. A central venous catheter was inserted in order to monitor the central venous pressure. After laboratory data were obtained a hypertonic saline infusion was added. The quantity and the rate of infusion were calculated in order to correct the serum sodium concentration at an hourly rate of 1–2 mmol/l for the first few hours. The sodium serum concentration was monitored hourly. Potassium supplementation was also started. When the patient was rehydrated (central venous pressure reached $+7 \text{ cmH}_2\text{O}$) and the serum sodium level reached 111 mmol/l, isotonic saline was continued. The patient's condition significantly improved, he was mildly lethargic but easily arousable. The new goal was to increase the serum sodium concentration by 5 mmol/l over the next 24 h. The mucose bloody rectal discharge did not abate. During his stay in the intensive care unit his blood pressure was normal, a normal urine output was established, and the state of consciousness was improved. Metabolic acidosis was corrected and laboratory signs of renal failure started to decline. After the clinical diagnosis was made, the patient was transferred to the department of gastroenterology of another hospital for long-term management. Tumour resection was carried out and the pathological diagnosis was adenocarcinoma.

**Discussion**

_Hyponatremia_ (serum sodium level less than 134 mmol/l) is a common electrolyte disturbance, especially in critical care patients. Its high prevalence and potential neurological sequelae make a logical and rigorous differential diagnosis mandatory before therapeutic intervention [7]. The manifestations of hypotonic hyponatremia are largely related to dysfunction of the central nervous system, and they are more conspicuous when the decrease in the serum sodium concentration is large or rapid [6]. Complications of severe and rapidly evolving hyponatremia include seizures, coma, permanent brain damage, respiratory arrest, and brain-stem herniation and death. On the other hand, improper therapy could also result in severe neurological sequelae. Although rare, osmotic demyelination is serious and can develop one to several days after aggressive treatment of hyponatremia. Shrinkage of the brain triggers demyelination of pontine and extrapontine neurons that can cause neurological dysfunction, including quadriplegia, pseudobulbar palsy, seizures, coma and even death. Hepatic failure, potassium depletion and malnutrition increase the risk of this complication [6]. Depletion of potassium accompanies many of these disorders and contributes to hyponatremia, because the sodium concentration is determined by the ratio of the ‘exchangeable’ portions of the body’s sodium and potassium content to total body water [6,8].

Laboratory data on our patient revealed metabolic acidosis, prerenal azotaemia, severe hypoosmotic hyponatremia, hypokalemia and hypochloremia. Pseudohyponatremia was ruled out because of hypotonicity, and neither hypetriglyceridemia nor paraproteinemia was present. There were no clinical and laboratory signs of hypothyroidism or hyperaldosteronism. According to the laboratory parameters, patient’s history and clinical examination, it was obvious that a hypersecretory rectal tumour caused all the symptoms and abnormalities. It is a very rare but known complication of villous adenoma, described for the first time 50 years ago [2–5,9]. Reaching the right diagnosis is not always as easy as in this case, and a complete colonoscopy is always mandatory. Therefore, in the case of a triade of prerenal failure, electrolyte disorder and chronic diarrhoea, the existence of an intestinal adenoma should always be considered [4].
The fluid and electrolyte hypersecretion in McKittrick–Wheelock syndrome results from the elevated adenylate cyclase, cAMP and prostaglandin E2 content of the mucosa [10,11]. The prostaglandin E2 levels were threefold higher in the rectal effluent of these patients than in patients with infectious diarrhoea [12]. Both cAMP and prostaglandin E2 inhibit sodium absorption, increasing the secretion of chloride and water and therefore causing the depletion of electrolytes and water. As non-steroidal anti-inflammatory drugs inhibit cyclooxygenase enzyme and the secretion of cAMP, treatment with indomethacin could markedly reduce the effects of secretagogues as was shown in several cases [3,12]. However, surgical removal is the only satisfactory treatment both to prevent the carcinoma formation and to stop the fluid and electrolyte loss. To our knowledge, this is the first report of McKittrick–Wheelock syndrome caused by rectal adenocarcinoma.

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Conflict of interest
None declared.

Authors’ contributions
Drs Lepur, Klinar and Mise were the primary physicians involved in the care of the patient during his initial presentation at the hospital. Dr Lepur was primarily responsible for collecting data and writing the manuscript. The other authors contributed to, reviewed and revised the article, and all approved the final version of the manuscript.

References