Exceptional Case

Over-expression of colonic K⁺ channels associated with severe potassium secretory diarrhoea after haemorrhagic shock

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Abstract

A 67-year-old woman with end-stage renal disease (ESRD) was referred with chronic diarrhoea, severe hypokalaemia and recurrent colonic pseudo-obstructions following haemorrhagic shock. The cause of secretory diarrhoea was uncertain, but an ileostomy identified the colon as the source of the watery diarrhoea and potassium (K⁺) losses, and symptoms only resolved after colectomy. Immunohistochemistry of the colon revealed over-expression of high conductance K⁺ (BK) channel protein in surface colonocytes and crypt cells compared with controls and other patients with ESRD. We hypothesize that colonic ischaemia during haemorrhagic shock led to increased BK channel expression and thus enhanced colonic K⁺ and water secretion, resulting in severe hypokalaemia and colonic pseudo-obstruction.

Keywords: colonic K⁺ channel; colonic K⁺ secretion; ischaemic colitis; secretory diarrhoea

Background

Maintenance of potassium (K⁺) homeostasis is essential for survival. In patients with end-stage renal disease (ESRD), increased colonic K⁺ secretion probably helps to regulate plasma K⁺ concentration as urinary K⁺ excretion declines [1]. Compared to control patients, normokalaemic patients with ESRD exhibit significant increases in distal colonic K⁺ secretion, apical K⁺ permeability and apical BK channel expression [1,2]. We report here an unusual case of K⁺ secretory diarrhoea complicated by profound hypokalaemia and colonic pseudo-obstruction (CPO) following haemorrhagic shock and ischaemic colitis in a patient with ESRD, and discuss a possible pathophysiological mechanism to account for the clinical picture.

Case report

A 67-year-old woman was referred to our gastroenterology unit in September 2003 with severe watery diarrhoea, hypokalaemia and recurrent CPO. Her past medical history included atrial fibrillation, aortic stenosis and ESRD requiring haemodialysis since 1994. A renal biopsy in 1991 had shown interstitial fibrosis, arteriosclerosis and glomerulosclerosis with hyalinosis. During a dialysis session in March 2003, while over-anticoagulated with heparin, she suddenly developed severe haemorrhagic shock secondary to haematoma after mild trauma to her buttock. She was treated in intensive care by massive red cell transfusion, continuous adrenaline and mechanical ventilation. Three weeks later, she developed acute CPO that was treated initially with subcutaneous neostigmine, but then began with profuse watery diarrhoea, severe hypokalaemia and recurrent CPO despite repeated colonic decompression, high levels of oral (40 mmol/day) and intravenous (133 mmol/day) K⁺ supplementation, and use of a K⁺ rich solution (4 mmol/L) during haemodialysis.

When transferred to our care, the abdomen was distended and tympanic. Investigations revealed serum Na⁺ 138 mmol/L, K⁺ 2 mmol/L, Cl⁻ 107 mmol/L, HCO₃⁻ 18 mmol/L, Ca²⁺ 2.77 mmol/L, creatinine 399 μmol/L, total protein 56 g/L and albumin 29 g/L. The blood count was normal. Serum levels of immunoglobulin, TSH, vitamin B₁₂, folate, vitamin D, PTH and PTH-related peptide, VIP and serotonin were normal. Serum gastrin level was 715 pg/mL (normal value <60 pg/mL), as expected in ESRD. Computerized tomography of the abdomen showed colonic distension with air-fluid levels, but no mechanical obstruction (Figure 1). Stool examinations were negative. A 3-day stool collection revealed a mean stool output of 982 g/day (dry weight 2%), osmolality 290 mmol/L,
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Na$^+$ 16 mmol/day (11 mmol/L), K$^+$ 205 mmol/day (143 mmol/L), Cl$^-$ 124 mmol/day (86 mmol/L) and fat 10 g/day. Gastroscopy, colonoscopy, small bowel contrast radiology and gastric, duodenal and colonic biopsies, were normal. The usual causes of secretory diarrhoea were excluded.

Treatment with anti-diarrhoeal drugs (loperamide, enkephalinase inhibitors, omeprazole, somatostatin analogue) was ineffective. Ileostomy was performed in April 2004 to locate the origin of the secretory diarrhoea. The stoma output was 1 L/day, containing 16 mmol K$^+$ and 131 mmol Na$^+$. Profound hypokalaemia and CPO persisted, indicating that the diarrhoea and K$^+$ losses originated from the colon. Laparoscopic colectomy in July 2004 revealed marked colonic dilatation with wall thickening. Histology showed submucosal fibrosis with persistent myenteric plexi and ganglion cells in the right colon, consistent with an earlier ischaemic colitis. Immunostaining using a specific antibody to the high conductance (BK) K$^+$ channel $\alpha$-subunit revealed massive over-expression of BK channel protein along colonic crypt axes (Figure 2). Following colectomy, plasma K$^+$ concentrations returned to normal without K$^+$ supplementation. The patient’s general condition improved steadily and she was discharged 3 months later.

Discussion

Our patient with ESRD was unusual in that she developed chronic severe secretory diarrhoea, persistent hypokalaemia and recurrent CPO following life-threatening haemorrhagic shock. The outstanding feature of the diarrhoea was its very high K$^+$ content, resulting in a daily stool K$^+$ output more than 20-fold greater than normal, and a diverting ileostomy identified the colon as the source of the persistently high intestinal K$^+$ losses. Profuse watery diarrhoea driven by enhanced colonic K$^+$ secretion has recently been reported in another patient with CPO in whom stool weight and K$^+$ output were directly related, suggesting that massively increased colonic K$^+$ secretion could be a novel cause of secretory diarrhoea [3]. Similar to our patient, colectomy has also been used to successfully treat intractable severe diarrhoea and hypokalaemia in patients with microscopic colitis [4,5]. The novel feature of our case from the standpoint of understanding the mechanism of the persistent hypokalaemia was the massive over-expression of colonic apical BK channels. The level of BK channel expression was far greater than the elevated levels previously demonstrated in ESRD patients without diarrhoea or hypokalaemia [2], who nevertheless exhibit enhanced distal colonic K$^+$ secretion compared with controls [1]. Interestingly, channel-inducing factor (CHIF) has been proposed as a K$^+$ channel regulator in the colon and kidney, and a 250% increase in colonic CHIF mRNA expression has been reported in rats after ischaemic injury and reperfusion [6]. Thus, in our patient, it is conceivable that intestinal ischaemia during haemorrhagic shock led to increased expression of both colonic CHIF and apical BK channels, inducing severe K$^+$ secretory diarrhoea and the clinical picture of profound hypokalaemia and CPO.
Conflict of interest statement. None declared.

References


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