Case Report

Surreptitious hyperkalaemia and its complications

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Abstract
Surreptitious hyperkalaemia is not a common problem, particularly in patients not yet dialysis dependent. We encountered a patient who baffled her physicians and their consultants, who nonetheless proposed life-saving treatments and novel explanations. However, according to the maxim that common things are common and rare things are rare, we solved the problem by focusing on the accompanying anion.

Keywords: dialysis; hyperkalaemia; Munchausen syndrome; potassium citrate; surreptitious

Introduction
Hyperkalaemia is a medical emergency known to all physicians and drilled into all nephrology trainees and their trainers. Generally, the problem is ‘our fault’. Sometimes, we are quite innocent and instead, unknown, unpredictable and unfathomable powers are responsible. We encountered such a patient.

Case report
The patient is a 50-year-old woman, who first developed hyperkalaemic episodes 3 years earlier in 2005. At the time, her serum creatinine was 2.5 mg/dl and she was not oliguric. She had a prior history of difficulty to control hypertension and had undergone uninephrectomy years earlier because of a ‘small contracted’ kidney. Her family history was unremarkable. She is married and her spouse reported that the patient was compliant and denied any surreptitious ingestions (drugs or other preparations). The patient and her spouse were counselled about bananas, chocolate, nuts, dates and other high-potassium foods.

The patient reported sensing the presence of hyperkalaemia in that she would develop muscle stiffness, paraesthesias, and then complete paralysis. Initially, her primary physicians attributed the hyperkalaemia to inhibitors of the renin–angiotensin system that she ingested for her hypertension. Plasma renin (activity) was measured at 17.2 µU/ml and aldosterone was 139 pg/ml, both normal for the reference laboratory. Her creatinine clearance was measured at ~50 ml/min, and her 24-h potassium excretion was 82 mmol/l. With symptoms, her serum potassium ranged between 7 and 9 mmol/l. During a paralytic episode in April 2006, her potassium rose from 7.2 to 8.1 mmol/l within 12 h under observation, despite intensive treatment with saline, frusemide, bicarbonate, glucose and insulin. Her physicians elected to perform periodic haemodialysis for potassium removal since high-dose diuretic therapy and a polystyrene exchange resin (Resonium®) did not influence the hyperkalaemic episodes or their frequency. Dialysis at this stage was solely used to treat hyperkalaemia.

A few months later, at the beginning of a dialysis session for hyperkalaemia, the potassium level had been 6.9 mmol/l. One hour later, the potassium level rose to 7.5 mmol/l and the patient developed a cardiac arrest. The arrest event resulted in the placement of a cardiac defibrillator. An arteriovenous fistula was also placed. During the summer of 2006, the patient appeared two to three times weekly with life-threatening hyperkalaemia, while her physicians tried to perform dialysis on a ‘demand basis’. Not until a regular schedule of three to four dialysis treatments per week had been established did the episodes become less frequent (every 1–2 weeks), although they remained unpredictable. Oddly, towards the end of 2006, a 4-week rhythm in the events appeared and the occurrence of hyperkalaemia became more predictable. The events occurred about every 28th day, plus or minus 1 day.

Initially, the primary physicians considered the diagnosis of periodic hyperkalaemic paralysis, although several aspects of the clinical course did not fit this diagnosis. Consultation was obtained and the coding regions of SCN4A and KCNJ2 were sequenced, but revealed no mutations. Admissions because of profound hyperkalaemia continued despite relatively preserved renal function. For instance, an admission in January 2007 featured the afore-mentioned

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Acid–base status was regularly determined during the hyperkalaemic episodes; however, an anticipated metabolic acidosis was never encountered. For instance, during a hospital admission in November 2006 at which time her potassium ranged from 5.1 to 7.28 mmol/l, her arterial pH was 7.44, PaCO₂ 39 mmHg, PaO₂ 74 mmHg and HCO₃⁻ 26 mmol/l. Other laboratory values were haemoglobin 13.4 g/dl and haematocrit 39 vol%; the white cell count, calcium and magnesium values were normal. The events continued throughout 2007. In October 2007, the patient was admitted because her defibrillator had discharged. The review of the device record yielded ventricular tachycardia and ventricular fibrillation, as well as nine episodes of nonsustained ventricular tachycardia.

The primary physicians were impressed by the 28-day rhythm of the hyperkalaemic episodes. They therefore performed a gynaecological assessment with the idea that the oestrogen–progesterone hormonal axis could be involved in her clinical picture. The patient was noted to have secondary amenorrhoea, since a hysterectomy had been performed earlier; however, her ovaries were intact. A monthly oestrogen peak (>300 ng/l) was measured. Several ovarian cysts were found up to 3 cm in diameter. The gynaecologist determined that the patient was actually premenopausal and recommended either ovariectomy or gonadotropin releasing hormone (GnRh) therapy with goserelin. Goserelin is a GnRh analogue that results in decreased release of the endogenous hormone. This treatment did lower her oestrogen levels, but the hyperkalaemia then appeared more frequently than earlier (once or twice per week) and was again unpredictable.

A psychiatric evaluation was conducted in December 2007. The psychiatrist determined that the patient was fully oriented. The presence of disturbed thought processes, altered reality testing or psychoses, could not be determined. However, the psychiatrist did remark on indications of dissociative symptoms and intrusions. The psychiatric diagnoses were post-traumatic stress syndrome, presumably because of or related to the hyperkalaemic episodes and their consequences, depression and panic disorder. A treatment with citalopram 40 mg was recommended.

In the summer of 2008, the hyperkalaemic episodes recurred at increasing frequency so that by August a bi-monthly hospital visit was the rule. By this time, her renal function had deteriorated to a creatinine value of ~4 mmol/l (eGFR <15 ml/min) so that chronic dialysis treatments had begun. At the most recent episode, the patient vomited while dialysis was being initiated. The vomit potassium concentration was 190 mmol/l, the chloride concentration was 114 mmol/l and the sodium concentration was 48 mmol/l. The hydrogen ion concentration was not determined. However, the citrate concentration was reported at >5 g/l. Each citrate binds three potassium ions, which makes citrate the highly likely accompanying anion in this case. The patient has not divulged precisely what she was doing, but did consent to begin psychiatric care.

**Discussion**

Hyperkalaemia is a life-threatening condition that evokes fear and respect amongst all clinicians. Death can come unexpectedly, and above all rapidly. Nephrologists are particularly attuned since their patients are at the greatest risk and because they have a definitive life-saving treatment when conservative modalities fail. The body’s capacity for potassium is immense. The current intake in acculturated societies is ~1 mmol/kg/day [1]. Experts argue that the intake was far greater in an earlier era before acculturation took place [1,2]. Indeed, in certain societies the intake is substantially greater [2]. About 300 mmol potassium as the chloride salt was necessary to significantly increase potassium concentrations in healthy American volunteers [3]. In patients with diminished renal function or in patients ingesting drugs or agents that interfere with potassium excretion, life-threatening hyperkalaemia commonly occurs. Problems generally reside with dietary indiscretion or therapeutic misadventures. We encountered a vexing patient with recurrent, unexplained bouts of hyperkalaemia that did not fit the clinical paradigm of decreased renal function or decreased excretory capacity from drugs, disease or extraneous factors. During the course of her illness, the patient’s kidney function declined. She had been uninephrectomized earlier. No biopsy was possible, and we are uncertain as to what cause(s) were responsible for the decline in function. A literature perusal of surreptitious hyperkalaemia produced relatively few reports, although the condition is surely more common [4,5]. We present this patient to draw attention to a possible psychiatric origin.

We considered any and all possible causes of endogenous paroxysmal hyperkalaemia in this patient. Hyperkalaemic periodic paralysis was ruled out on clinical and molecular grounds. Muscle disease appeared extremely unlikely since creatine kinase and myoglobin concentrations were invariably normal. We then considered the possibility that potassium might come from erythron. Erythrocytes store much potassium and could release it quickly. Haemolytic anaemia from antibodies, haemolysis from malaria parasites and paroxysmal haemoglobinuria are examples. Erythrocytes are ‘retired’ via an apoptotic process called eryptosis [6,7]. Eryptosis is paralleled by cell shrinkage due to potassium exit, a possible source of elevated extracellular potassium [8]. A further hallmark of eryptosis is cell membrane scrambling with phosphatidyl serine exposure at the cell surface. We exposed normal human erythrocytes from volunteers to the patient’s serum harvested before or after haemodialysis. As illustrated in Figure 1A and B, exposure to predialytic but not to postdialytic patient serum was followed by a significant decrease of erythrocyte forward scatter, reflecting cell shrinkage. In contrast to predialytic patient serum, serum from a healthy volunteer did not significantly decrease forward scatter. These data support the notion that the patient harboured an eryptosis-inducing factor and suggest that this factor can be removed by dialysis.

Annexin-V binding was then utilized to identify phosphatidyl serine-exposing erythrocytes. As illustrated in Figure 2A and B, treatment of erythrocytes with predialytic but not with postdialytic patient serum was followed by a significant increase in annexin-V binding. Again,
serum from healthy volunteers did not significantly increase annexin-V binding. Thus, the patient’s predialytic serum contained a factor(s) promoting eryptosis. Dialysis removed the factor(s). We have not identified the dialyzable component. Eryptosis could be triggered by a wide variety of factors and clinical disorders [9] including renal insufficiency [10] and haemolytic uraemic syndrome [11]. The fact that the patient exhibited eryptosis that was influenced by dialysis is highly intriguing, and could provide an explanation for the anaemia despite a rather enhanced reticulocyte count (Table 1).

The eryptosis could, however, not explain her massive pe-

Table 1. Patient blood data are given

| Parameter/dates | 11.12.06 | 8.1.07  | 12.2.07 | 21.2.07 | 3.3.08 | 7.4.08 |
|-----------------|----------|---------|---------|---------|--------|--------|
| Leukocytes (/nl) | 8.91     | 5.95    | 6.7     | 8.11    | 4.3    | 4      |
| Erys (/pl)      | 3.75     | 4.06    | 4.39    | 4.13    | 2.8    | 3.7    |
| Hb (g/dl)       | 11.9     | 12.6    | 13.5    | 12.9    | 10.9   | 10.9   |
| PCV (%)         | 35.9     | 37.3    | 40.9    | 38.1    | 25.8   | 32.6   |
| MCV (fl)        | 95.7     | 91.9    | 93.2    | 92.3    | 91     | 89     |
| MCH (pg)        | 31.7     | 31      | 30.8    | 31.2    | 31     | 30     |
| Thrombo (/nl)   | 246      | 260     | 271     | 282     | 242    | 293    |
| Hypochr. Erys (%)| 0.2      | 0.2     | 0.1     | 0.1     | 0.1    | 0.1    |
| RET-He (pg)     | 34.4     | 33.2    | 34.3    | 34.6    | 33.5   | 28.7   |
| Retics (%)      | 2.7      | 3.2     | 3.3     | 3       | 1.66   | 1.58   |
| Creatinine (mg/dl) | 1.34  | 1.45    | 1.49    | 1.49    | 3.4    | 4.9    |
| Urea (mg/dl)    | 56       | 20      | 39      | 54      | 87     |        |
| K+ (mM)         | 4.6      | 4.5     | >8.0    | 6.3     | 3.1    |        |
| Ca2+ (mM)       | 2.19     | 2.12    | 2.26    | 2.38    | 2.2    | 2.2    |
| PO4 3- (mM)     | 0.84     | 0.94    | 0.55    | 0.54    | 1      | 1.6    |

Dates are in day/month/year.
Hb = haemoglobin, PCV = packed cell volume, MCV = mean corpuscular haemoglobin and RET-He = reticulocyte haemoglobin.

might be a candidate. Our patient answered our question for us when her stomach contents were analysed.

Our patient suffered from a form of Munchausen’s syndrome, named after the famous Baron who told fantastic stories. In Munchausen’s syndrome, the affected person exaggerates or creates symptoms of illnesses in themselves in order to gain investigation, treatment, attention, sympathy and comfort from medical personnel [12]. In some extremes, people with Munchausen’s syndrome are highly knowledgeable about the practice of medicine, and are able to produce symptoms that result in multiple unnecessary operations or procedures. Our patient was surely aware that hyperkalaemia is life threatening and a highly effective way to garner attention of physicians. Her defibrillator discharges are documentation for that conclusion. She was clearly responsible for numerous treatments. In her case, the treatments were not unnecessary, but rather saved her life on numerous occasions.

Potassium citrate, shown in Figure 3, is rapidly absorbed when given by mouth and is excreted in the urine as the carbonate. The compound is commonly used to treat recurrent kidney stones, particularly those containing uric acid, to reduce the pain and frequency of micturition when the urine is very acidic, and to treat hypokalaemia. Potassium citrate is also present in many soft drinks as a buffering agent. It has been successfully used experimentally to alleviate the course of experimental chronic renal disease [13]. Hyperkalaemia can occur in patients ingesting large amounts, even if renal function is relatively preserved [14]. Furthermore, two other cases of potassium citrate-induced
hyperkalaemia were cited in that report, both in patients >70 years [15,16].

We believe the patient ingested Kalinor Brause®, effervescent tablets that are dissolved in water as a fizzy drink. Each tablet contains 2.057 g citric acid, 2.17 g hydrated potassium citrate, 2 g potassium bicarbonate and 2.049 g potassium citrate. The total potassium content per tablet amounts to 40 mmol. Interestingly, in Germany Kalinor Brause® can be obtained in any pharmacy without a prescription. We did not observe notable disturbances in the acid–base balance in this patient. The citrate ion is catabolized to three bicarbonates, and a metabolic alkalosis would be expected. However, the Kalinor Brause® effervescent tablet also contains citric acid. This compound may have masked metabolic alkalosis. Nonetheless, citric acid would be expected to increase the anion gap until the citrate is metabolized [17].

Conflict of interest statement. None declared.

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