Tidsskriftet Tidsskrift for Den norske legeforening

A woman in her forties with chest pain and life-threatening bradycardia

EDUCATIONAL CASE REPORT

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A woman contacted the emergency medical communication centre in the morning with chest pain and dyspnoea. Her condition rapidly deteriorated and became life-threatening in less than an hour. In an urgent situation with combined respiratory and circulatory failure, it is essential to take a broad approach and not to tie oneself to the initial differential diagnosis.

The patient was a woman in her forties with known Crohn's disease, chronic pain and short bowel syndrome following repeated surgery for stenoses. Her remaining small bowel length was 170 cm, and she had also undergone resection of the sigmoid colon following spontaneous perforation. Her Crohn's disease had been highly refractory to treatment and had not responded to treatment with anti-tumour necrosis factor (TNF) agents or interleukin

inhibitors. She was now being treated with budesonide tablets 9 mg once daily, subcutaneous methotrexate 25 mg once weekly and intravenous vedolizumab 300 mg once every 8 weeks. She was also taking pain relief in the form of oxycodone tablets 30 mg in the early morning, 25 mg mid-morning and 30 mg in the evening, paracetamol tablets 1 g four times daily and amitriptyline tablets 25 mg once daily in the evening. She had several previous admissions for severe hypokalaemia secondary to short bowel syndrome and required high-dose potassium supplementation. At the time in question, she was taking potassium chloride tablets 4.5 g four times daily. She was also taking loperamide tablets 2 mg as required for loose stools and desogestrel 75 µg once daily for contraception.

The patient had been feeling increasingly unwell and nauseous for 2–3 days, but on the day of admission she had developed chest pain radiating to the left arm and dyspnoea. She then telephoned the local emergency medical communication centre. When the ambulance came, she had oxygen saturation of 88 %, pulse 34 bpm, blood pressure 98/51 mmHg and respiratory rate 24 breaths per minute. Her skin was pale and clammy, and her radial pulse was not palpable, but she was awake and talking in full sentences.

A pre-hospital ECG was taken, which was sent to the local hospital for interpretation (Figure 1). The ambulance team was informed that the patient had a probable ST-elevation myocardial infarction and that the plan should be to transport her to the university hospital if she was clinically stable. In the meantime, the patient's condition had declined. She developed bradycardia with a pulse of 17 bpm recorded on the ECG monitor, and her level of consciousness was decreasing. The ambulance team assessed that she was not stable enough to be transported to a centre for percutaneous coronary intervention (PCI), and therefore she was taken directly to the local hospital.

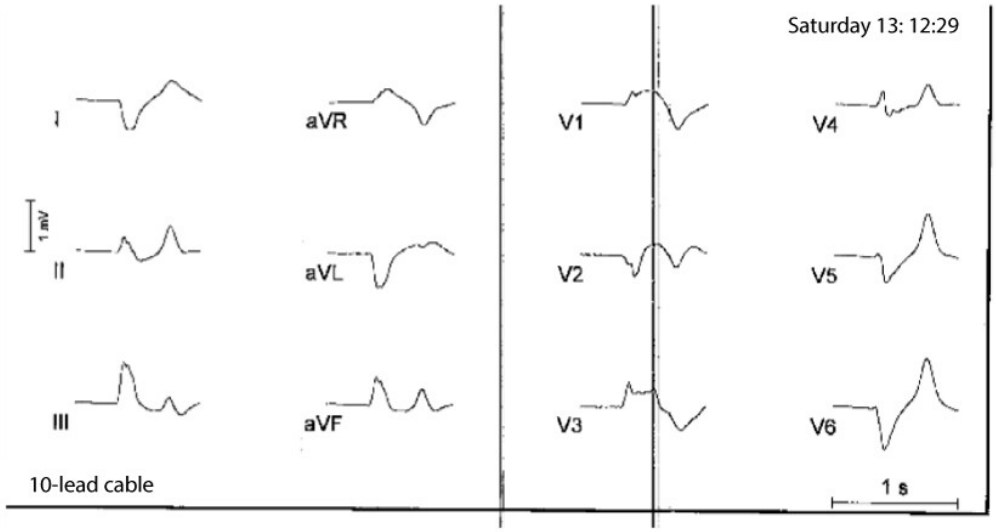

Figure 1 Pre-hospital ECG shows widened QRS complex with absent P waves. It is easy to misinterpret the QRS complex as an ST-elevation myocardial infarction due to ST elevation in V1–V3 and possible reciprocal changes in V5–V6.

In cases of ST-elevation myocardial infarction and a journey time to a PCI centre enabling treatment within 2 hours from the time of diagnosis, patients should be taken straight to a PCI centre without going via a local hospital (1). In

most cases, the transportation time will be longer, and the patient must also be stable enough to tolerate transportation. In this case, the patient was unstable, and therefore the ambulance went directly to the local hospital.

The patient arrived in the Emergency Department and was received by the medical team. She was cyanotic, had a respiratory rate of 8 breaths per minute and oxygen saturation of 75 % despite 12 litres of oxygen through a non-rebreather mask. It was noted that she was emptying the whole reservoir with every breath. Initially, her blood pressure was not measurable, with the best pulse being a weak pulse in the groin. She was no longer responsive and scored 6–7 on the Glasgow Coma Scale (GCS). ECG revealed severe bradycardia, a heart rate of 23 bpm, absent P waves and extreme widening of the QRS complex (Figure 2).

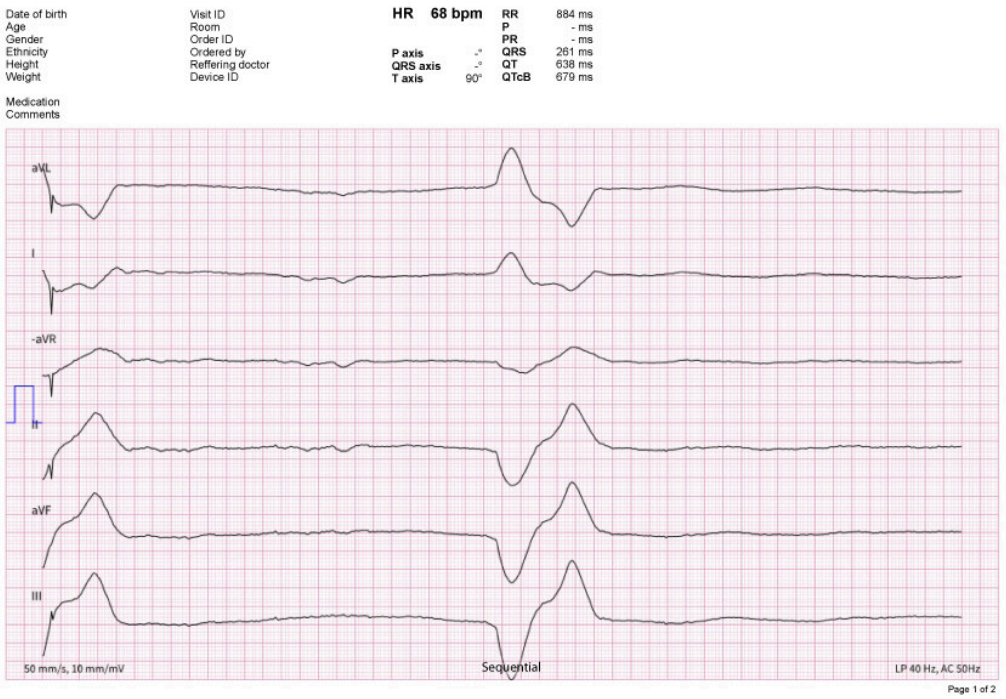

Figure 2 ECG taken on arrival in the Emergency Department. Severe bradycardia with heart rate of 23 bpm. Extreme widening of the QRS complex, with the T wave taking off directly from the R, which is referred to as sine wave. Propagation of electrical impulse through the ventricle has almost stopped. This is a pre-terminal rhythm unless action is taken immediately.

Focused echocardiography did not reveal decreased regional cardiac muscle motion (hypokinesia), reduced global function or any other signs of acute myocardial infarction. However, it did find clear flattening of the dividing wall between the right and left ventricles (septal flattening), which raised suspicion of increased right ventricular pressure, referred to as right heart strain.

Initially, there were three different aetiologies that could all potentially explain the patient's condition: myocardial infarction, pulmonary embolism and hyperkalaemia. Echocardiography should be performed if myocardial infarction is suspected and ECG findings are inconclusive. In this case, there was no evidence of acute myocardial infarction on echocardiography. Conversely, there were signs of right heart strain, which can be seen in cases of large pulmonary embolism.

Furthermore, the patient was a relatively young woman taking oral contraception who had respiratory failure and chest pain. Therefore, consideration was given to thrombolytic treatment as an emergency indication. However, she also had an ECG with sine-wave appearance and absence of P waves, which raised suspicion of abnormal potassium levels. Therefore, we decided *not* to administer thrombolytic treatment until we had information about electrolytes.

Following repeated attempts, it was not possible to insert peripheral venous catheters or take blood gases from the radial artery. Therefore, blood gases were taken from the femoral artery. Analysis found pH 7.22 (reference range 7.35–7.45), pCO_2 3.5 kPa (4.7–5.9), pO_2 8.6 kPa (11.0–14.4), base excess (BE) –15.9 mmol/L (–3 to 3), HCO_3^- 10.3 mmol/L (22–26), sodium 134 mmol/L (137–145), potassium 10.6 mmol/L (3.6–4.7), chloride 123 mmol/L (98–110), glucose 25 mmol/L (4.2–6.3), lactate 6.8 mmol/L (0.0–2.0). The patient's potassium levels were confirmed in a follow-up blood gas analysis.
Therefore, the patient had very severe hyperkalaemia. The first ECG changes seen with hyperkalaemia are high pointed T waves and shortened QT interval. Progressively, the QRS complex will widen, and loss of P wave may develop due to lack of impulse conduction through the atrium. In the most severe cases, there is a sine wave pattern on ECG, which typically occurs at potassium levels > 10 mmol/L. In these cases, the ST segment will have disappeared and ventricular impulse conduction almost completely stopped. This is a pre-terminal rhythm, which will be rapidly followed by asystole unless action is taken (2).

The patient received high-dose nebulised terbutaline 5 mg. At the same time, a triple lumen central venous catheter was inserted, as well as an arterial cannula in the groin. Once these lines had been established, 20 ml calcium gluconate (4.5 mmol calcium) was immediately administered intravenously. Within the space of a few minutes, the patient's pulse increased to 40 bpm and QRS width decreased.
It is absolutely essential to ensure good intravenous access in a critically ill patient. Failing to do so often leads to delayed diagnosis and treatment. Terbutaline is a beta-2 agonist that redistributes potassium into cells and thus reduces the amount of circulating potassium. It can also be administered via a nebuliser, so treatment can be started before vascular access has been obtained.

Since our patient had severely impaired circulation, considerably reduced absorption could be expected. In conjunction with her critical condition, it was decided to administer her 5 mg nebulised terbutaline, which is 5–10 times the usual dose in hyperkalaemia.

The patient was administered repeated doses of calcium gluconate 10 ml (2.25 mmol calcium), totalling 80 ml. She was also administered fluid resuscitation with 6 litres of fluids in total, with the aim of achieving systolic blood pressure > 100 mmHg. Sodium chloride 0.9 % was administered initially, switching rapidly to 1000 mL glucose 5 % mixed with 20 IU insulin aspart. Her respiratory rate increased to 21 breaths per minute, and her O_2 saturation rose to 89 % on 12 litres of O_2. Follow-up blood gases after 30 minutes found pO_2 increased to 9.8 kPa, potassium decreased to 8.8 mmol/L, but also

glucose increased to 33 mmol/L, lactate increased to 8.2 mmol/L and pH decreased to 7.06. Therefore, the patient was administered an infusion of 1000 mL sodium bicarbonate 167 mmol/L over 30 minutes.
One hour after the patient's arrival in the Emergency Department, her pulse was increasing, pH had increased to 7.21 and lactate levels had fallen to 3.3 mmol/L. Two hours after arrival, she was transferred to the intensive care unit. She was stable, awake and breathing for herself at that time. She had sinus rhythm of 90–100 bpm, adequate blood pressure, potassium of 5.9 mmol/l and pH had almost normalised (7.29).
Twelve hours after arrival, her glucose levels had returned to normal (5.4 mmol/L) and remained within the normal range for the entire hospital admission with no need for insulin administration. Venous blood tests found leukocytes 28.3 × 10^9/L (3.5–11), CRP 3 mg/L (< 5), creatinine 80 µmol/L (45–90), with estimated glomerular filtration rate (GFR) of 79 mL/min/1.73 m^2 (> 70). Phosphate levels were 0.60 mmol/L (0.85–1.50), urea 2.8 mmol/L (2.6–6.4) and HbA_{1c} 38 mmol/mol (27–42).
Repeat echocardiography revealed regression of right heart strain. A chest CT was performed, which confirmed that there was no pulmonary embolism. A dialysis catheter was placed in the patient's right internal jugular vein and continuous haemodialysis took place overnight.
Both glucose/insulin infusion and terbutaline are effective in reducing circulating potassium, but act by redistributing potassium into cells and are therefore relatively short-acting for 2–6 hours. Dialysis ensures actual elimination of potassium.

The woman was transferred to a general ward after 24 hours. At that time, she had normal potassium levels of 4.5 mmol/L. She had no neurological sequelae and no symptoms other than fatigue. Potassium supplementation was resumed at a lower dose, potassium chloride tablets 750 mg four times daily for the first 24 hours, followed by 1.5 g four times daily afterwards. The patient was discharged three days later with stable potassium levels.
The patient was able to report that she had struggled with loose stools for a long time and had therefore started to take loperamide 2 mg capsules on her own initiative. Previously, she had only taken these occasionally and not regularly. These were effective in firming stools. Since loperamide works by prolonging intestinal transit time, the absorption of potassium was improved at the same time. When she eventually noticed muscular weakness, malaise and nausea, she suspected this was caused by hypokalaemia, a condition she had experienced several times before. She later admitted that her symptoms did differ slightly from previous episodes of hypokalaemia, but they were similar enough that she misinterpreted the symptoms. She had never had symptomatic hyperkalaemia before. Therefore, on her own initiative, she had started to increase her potassium intake. As her symptoms increased, she continued to increase the doses. This led to a vicious cycle of rapidly increasing potassium levels.
Following discharge, the patient was followed up by her general practitioner with measurement of potassium levels three times a week. There is an agreement with the hospital laboratory that any abnormal potassium levels will be reported by telephone to the general practitioner or the internal

medicine specialist on duty if the general practitioner is not available. Furthermore, she is free to return to the Emergency Department for potassium measurement if she notices symptoms of potassium imbalance.

Discussion

Circulating potassium is normally effectively regulated by redistribution of potassium into and out of cells, as well as excretion predominantly in urine. If one of these self-regulating systems does not work, potassium imbalances could occur (Figure 3). Hyperkalaemia is typically seen in patients with renal failure or those using medicinal products that affect the renin-angiotensin-aldosterone system (RAAS), such as angiotensin-II receptor blockers, angiotensin-converting enzyme inhibitors (ACE inhibitors) and beta-blockers. Hyperkalaemia is also seen in dehydration, extensive tissue damage caused by trauma or burns, as well as chronic diseases such as type 1 diabetes and Addison's disease (3).

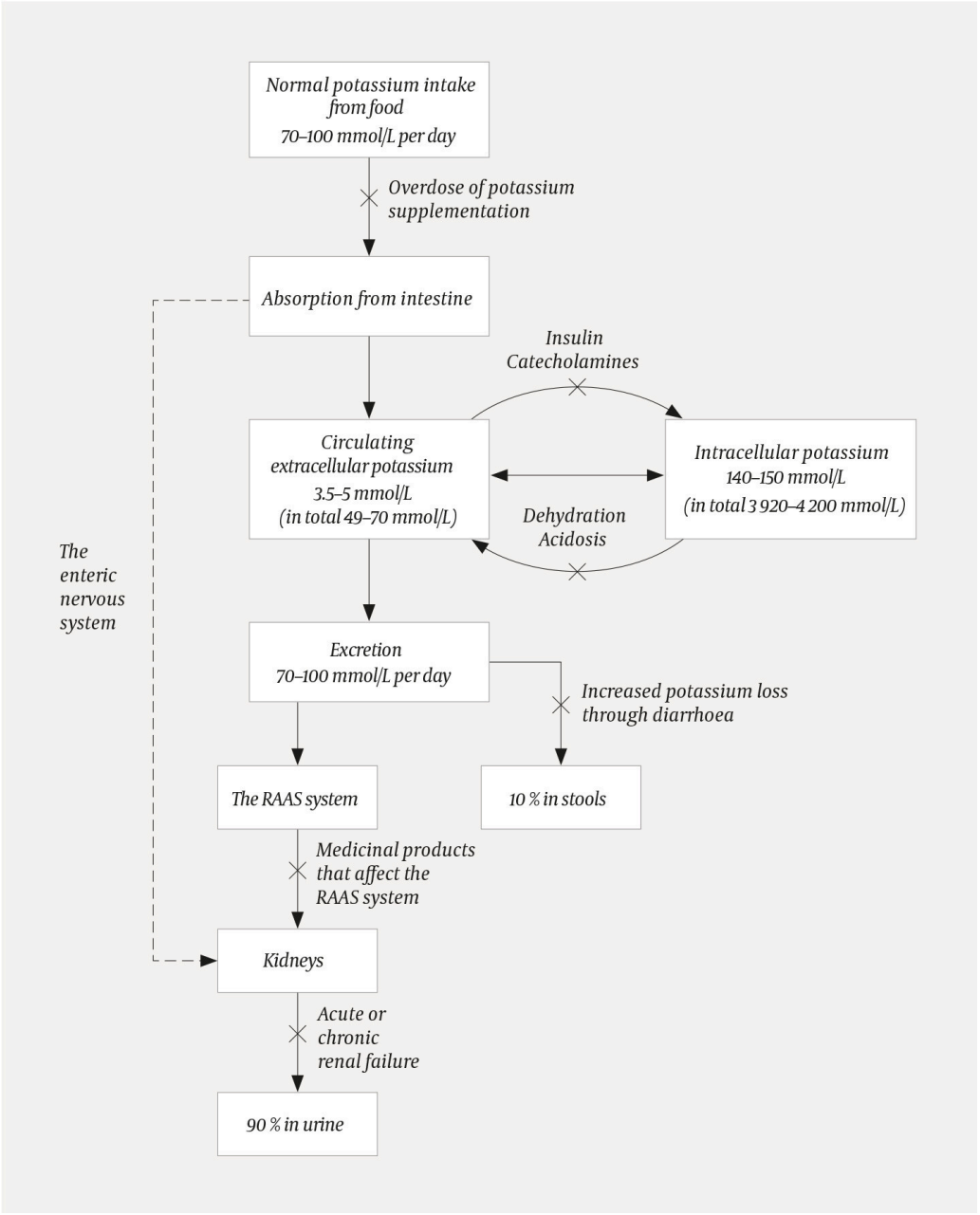

Figure 3 Potassium homeostasis. RAAS = renin-angiotensin-aldosterone system

Our patient did not have impairment of any of these systems, but the very high intake of potassium supplementation exceeded her homeostatic capacity. This is an uncommon cause of hyperkalaemia, but nonetheless it is a cause to be aware of in patients taking high-dose potassium supplementation or when intentional or accidental overdose is suspected. As far as we know, the potassium level of 10.6 mmol/L in this case is the highest potassium level described in the literature where the patient survived without needing cardiopulmonary resuscitation (4).

Another key point in hyperkalaemia is the rate at which the condition developed. If it is secondary to chronic renal failure, the patient will often tolerate considerably higher potassium levels before there is any effect on cardiac electrophysiology. This tolerance is likely due to the fact that the ratio between intracellular and extracellular potassium is more important than absolute values.

Treatment with calcium gluconate should be prioritised in situations with severe hyperkalaemia and ECG changes. It does not lower potassium levels, but antagonises the cardiac effects of potassium and has a membrane-stabilising effect on the myocardium. Calcium gluconate can be repeated if the effect is inadequate. The evidence base for the efficacy and risk of multiple doses is sparse, but British guidelines state that the dose should be repeated until the ECG normalises and that individual patients may require up to 50 ml (5). Our patient required 80 ml. Calcium gluconate has a half-life of 30–60 minutes, and serum calcium levels should be monitored when administering high doses of calcium gluconate. Nevertheless, it is worth noting that hyperkalaemia is significantly more serious than hypercalcaemia.

The patient also had severe hyperchloraemia, probably due to the type of potassium supplement (potassium chloride) and previous diarrhoea. Hyperchloraemia should be avoided as it can contribute to worsening of acidosis, with resulting extracellular shift of potassium.

Acute dialysis is a key alternative treatment in severe hyperkalaemia, as potassium can be removed quickly and effectively by dialysis (6). Although acute dialysis is well established in hyperkalaemia secondary to renal failure, there is limited evidence as to whether acute dialysis improves survival in severe hyperkalaemia secondary to overdose of potassium supplements. Nevertheless, a literature review of published individual case reports concluded by recommending acute dialysis in this patient group (6).

An additional aspect was the fact that our patient had a tendency to hypokalaemia. This meant that oral potassium binders were less suitable because the effect cannot be rapidly reversed, such as in haemodialysis.

Treatment with bicarbonate is debatable in hyperkalaemia and is no longer recommended in uncomplicated cases due to lack of effect and the risk of inducing pulmonary oedema. However, it is indicated in cases with concomitant metabolic acidosis (7).

The changes in our patient's ECG were initially interpreted as a possible ST-elevation myocardial infarction. Bradycardia is not unusual in ST-elevation myocardial infarction and may occur in 15–25 % of cases (8). There are several possible underlying mechanisms, but most cases are transitory, and cardiac rhythm will then normalise within the first 24 hours. If ST-elevation myocardial infarction leads to acute heart failure with significant left ventricular overload, increasing bradycardia may be seen, and eventually asystole.

In our patient, we cannot say that the ST-segment deviation represented myocardial ischemia because it can develop secondary to changes in impulse conduction through the myocardium, referred to as pseudoinfarction. In general, the ST segment must be interpreted with caution if the QRS complex is widened (9). It is worth noting that P-wave absence in a regular ECG, which often occurs in severe hyperkalaemia, would not be expected in coronary artery disease or pulmonary embolism. We also cannot rule out myocardial ischemia based on an ECG like this. Chest pain is not a common presenting symptom in

potassium imbalance, and in our patient this may have developed as a result of coronary hypoperfusion due to insufficient cardiac output resulting from marked bradycardia.

Echocardiography in the Emergency Department revealed flattening of the septum between the right and left ventricles, a sign of increased pressure on the right side of the heart. With acute chest pain, this is often associated with large pulmonary embolism. This finding has not been previously described for hyperkalaemia, but it is conceivable that altered and delayed depolarisation reflected in the extremely widened QRS complex may cause a significant shift in contraction of the left and right ventricles.

It is important to be aware of stress-induced hyperglycaemia in critically ill patients. Adequate and rapid insulin treatment improves survival (10). Our patient arrived with significant hyperglycaemia. This was gradually reduced with insulin/glucose infusion. There were no indications that the patient had undiagnosed or underlying diabetes.

The patient thought that her symptoms were caused by hypokalaemia, when in fact she had hyperkalaemia. Features that the two conditions have in common are muscle weakness and electrophysiological changes in the cardiac conduction system. Both conditions can cause bradycardia, although it is much more common with hyperkalaemia. It will often be possible to distinguish between the conditions with ECG, and obviously by measuring blood levels, but a patient cannot be expected to be able to manage potassium supplementation according to subjective symptom burden. Furthermore, very few people will experience symptoms until potassium levels have fallen below 3.0 mmol/L or risen above 7.0 mmol/L (reference range 3.6–4.7 mmol/L). Awareness of this is particularly important with hyperkalaemia because ECG changes and potentially life-threatening arrhythmias can develop once levels exceed 6.5 mmol/L. Therefore, patients who for various reasons have a tendency to develop hypokalaemia and are receiving high-dose supplementation should be monitored regularly. They should not adjust the supplementation themselves, but should instead have a plan for getting their potassium levels measured rapidly in the event of symptoms.

Summary

This case report shows the importance of a broad and systematic approach to critically ill patients. Based on the case history and pre-hospital findings, the main suspicion was of either coronary artery disease, pulmonary embolism or potassium imbalance. Following ECG, blood gas analysis and focused echocardiography, the first two diagnoses could be ruled out with a high degree of certainty. Elevated potassium levels can occur as a result of haemolysis associated with blood sample collection, so rapid confirmation of the potassium levels should be sought with repeat blood gas analysis. Nevertheless, this should not delay treatment if the diagnosis is highly likely. Treatment with calcium gluconate must be prioritised in the event of hyperkalaemia and ECG changes, followed by medicinal products that shift potassium intracellularly, such as insulin and terbutaline. The next steps must ensure effective and adequate elimination of potassium, and in severe cases haemodialysis is preferable to oral potassium binders.

The patient has given consent for the article to be published.

The article has been peer-reviewed.

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Publisert: 22 March 2022. Tidsskr Nor Legeforen. DOI: 10.4045/tidsskr.21.0664
Received 17.9.2021, first revision submitted 29.11.2021, accepted 20.12.2021.