Unrecognized pseudohyperkalaemia in essential thrombocythaemia

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Patients with raised platelet counts can have pseudohyperkalaemia – this can be differentiated by measuring plasma instead or serum potassium concentration.

Case report

A 99-year-old woman was admitted following a mechanical fall. The patient suffered from frequent falls averaging around six falls per year. On this occasion the patient explained that she had simply lost her balance and denied any further symptoms. The patient's past medical history was significant for essential thrombocythaemia diagnosed 10 years earlier which was initially managed with hydroxycarbamide and followed up via outpatient haematology clinics. In addition to this the patient also had a history of macular degeneration, carpal tunnel syndrome and cognitive impairment. Blood tests on admission showed a platelet count of 1836 with a potassium concentration of 5.9 mmol/L. Repeat blood tests following admission demonstrated platelet count now of 2348 with a subsequent rise in potassium level to 6.9 mmol/L. There were curiously no ECG changes of hyperkalaemia and the rest of the blood results, including renal function and inflammatory markers were normal. Nonetheless the patient was infused with insulin and dextrose which brought the potassium level to 5.6 mmol/L. However the potassium level was difficult to control and continued to consistently rise beyond 6 mmol/L. The patient was subsequently repeatedly treated with insulin and dextrose infusions to lower the potassium level several times. After exhausting the causes of high serum potassium levels a plasma potassium was requested from the laboratory. The result returned as 3.0 mmol/L. The patient was in fact hypokalaemic secondary to repeated insulin dextrose infusions. The diagnosis of pseudohyperkalaemia due to thrombocythaemia was made and only plasma potassium levels were recorded subsequently.

Discussion

Potassium is the most common cation in the body and 98% of it is located intracellularly.[1] Daily intake is about 1.5 mmol/kg and serum levels are usually strictly homeostatically maintained between 3.5 and 5 mmol/L. Its elimination is chiefly by the kidneys, and hence renal disease and acute tubular acidosis is commonly responsible for hyperkalaemia by reduced excretion. Medications (notably NSAIDS and potassium sparring diuretics) and adrenocortical insufficiency are well recorded causes of hyperkalaemia. Innate hormones which affect potassium levels include adrenaline and insulin;[1] both lower its levels with the latter being used in the emergency therapy of hyperkalaemia.

Pseudohyperkalaemia can be defined as a serum potassium concentration 0.4 mmol/L greater than the plasma concentration.[2] The observation of pseudohyperkalaemia in thrombocytosis was published as early as 1955.[1] It was noted that high values of serum potassium were obtained in the absence of other electrolyte abnormalities in patients with high platelet counts. It is due to the degranulation of platelets when clotting *in vitro*, releasing potassium and calcium into the serum.[3–5] Additionally, since platelets have the smallest particle size, they become positioned near the top of the blood tube forming a buffy layer. As a result they are aspirated into the sampling machine preferentially if there is a low quantity of the

specimen. This is a common laboratory erroneous source of hyperkalaemia. A higher platelet count would be expected to proportionally increase recorded potassium levels but this does not occur, probably due to uptake by other cell types (white cells and erythrocytes).[6]

Thrombocytosis will be discussed in this report but it is not the only cause of spurious hyperkalaemia; other cell types such as erythrocytes and leucocytes also give rise to this phenomenon. Hence when assessing leukaemia patients, particular attention should be paid to the time between venepuncture and laboratory plasma separation as any delay will result in a raised serum potassium due to cell degradation.[7,8] Patients with mixed cell type disorders such as polycythaemia vera have more pronounced hyperkalaemia.[9] In addition to this, certain general practical considerations during venepuncture for electrolyte specimens from all patients with or without disease can avoid spurious results. Pearls of wisdom passed down generations of junior doctors such as asking patients to repeatedly clench a hand under tourniquet hand to make veins more visible could raise potassium levels markedly.[10] Leaving a tourniquet on the arm for too long is a well-recognized cause of abnormally high potassium levels as is a tourniquet which is too tight.

Clinically the diagnosis of pseudohyperkalaemia is difficult to make. The absence of any ECG changes in the presence of dangerously high potassium levels is a favourable indicator of the diagnosis.[11] This case report will discuss spurious hyperkalaemia due to thrombocythaemia.

There are many causes of secondary thrombocythaemia ranging from infection (by virtue of platelets being acute phase reactants),[12] cancer, bleeding and even in patients following splenectomy.[13] Essential thrombocythaemia is identified by increased platelet counts (normal $150-450 \times 10^9$/L) from abnormal pluripotent stem cell proliferation resulting in excessive megakaryocyte division. The clinical complications involve the sequelae of abnormal platelet function, namely haemorrhage or thrombosis.

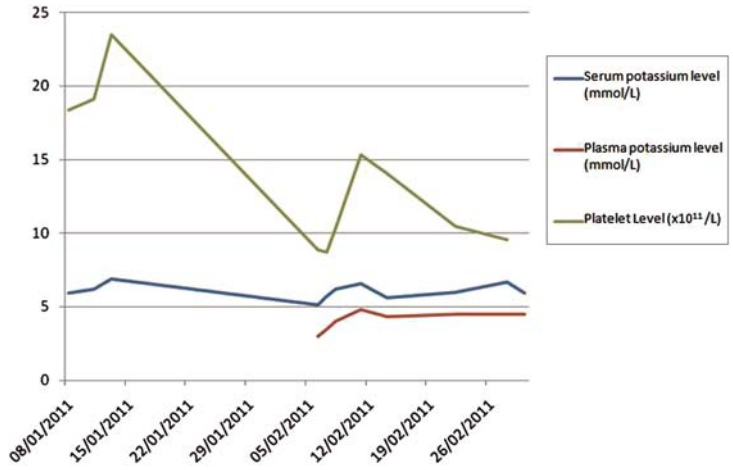
Clinical presentation is often as a result of micro or macro thrombosis as well as bleeding. This can range from myocardial infarction and stroke to headaches and digital occlusion and gangrene. Bleeding, especially from the gastrointestinal tract can occur. On clinical examination, hepatomegaly and splenomegaly may be appreciated. The diagnosis is clinched with full blood count investigations revealing thrombocytosis. Further bone marrow biopsy may show giant megakaryocytes with megakaryocytic hyperplasia.

Electrolytes may show pseudohyperkalaemia as described above. A rise of between 0.07–0.15 mmol/L of potassium can be extrapolated for every $100 \times 10(9)$/L increase in platelet count[14] with as much as 0.7 mmol/L in the serum K+ concentration from large ($1000 \times 10(9)$/L) increases in platelet count[15] depending on the analysing technique used. The mainstay of treatment involves lowering the platelet count in order to prevent the life-threatening complications described above. The management of choice involves hydroxycarbamide and aspirin treatment.[16] The resulting pseudohyperkalaemia requires no further treatment, only acute recognition. Although the hyperkalaemia in this case report was spurious in nature, the patient was treated due to ignorance of this phenomenon. The urgency of treatment was to avoid the well-known complications of true hyperkalaemia which will be briefly discussed below alongside urgent management.

The main complications of untreated hyperkalaemia are its impact on the myocardium. Classic characteristic changes of hyperkalaemia on electrocardiogram include tall 'tented' T-waves, widened QRS complexes, flattened P-waves, prolonged PR interval progressing to life-threatening arrhythmias such as ventricular tachycardia, ventricular fibrillation or asystole. However characteristic ECG findings alone cannot objectively be used to extrapolate potassium levels and often do not lead to early treatment.[17] It was on this basis that the patient in this case was treated despite the absence of ECG changes on sequential ECGs. Hyperkalaemia has few clinical symptoms, thus contributing to its danger. These could include non-specific symptoms such as fatigue, paresthesias, confusion and muscle weakness.[17]

The treatment of hyperkalaemia depends on the level of potassium and its cause. Mild hyperkalaemia can be managed by treating the underlying cause, e.g. renal failure. However, potassium concentrations of above 6, or a lower level with electrocardiogram changes of hyperkalaemia (described above) should be treated immediately. The first priority is to stabilize the myocardium with 10 mL of

Figure 1
Demonstrates a corresponding spurious rise in serum potassium level to increased numbers of platelets. True plasma potassium levels are shown for comparison. This illustrates the importance of plasma potassium levels in these patients



10% calcium gluconate slow IV infusion over 5 min. Then the potassium can be shifted into the intracellular compartment with 10 units of insulin with 50 mL of 50% dextrose. The steady maintenance of potassium levels can be instigated with 15 g of oral polystyrene sulphonate resin (calcium resonium) orally four times a day to remove potassium from the body over the proceeding few days. All potassium-retaining medication should be stopped and potassium concentration should be checked twice daily in these patients.

However, in this case due to the repeated treatment of spurious pseudohyperkalaemia, the patient was iatrogenically made hypokalaemic. Severe hypokalaemia is also a medical emergency. Mild hypokalaemia is often asymptomatic and can be corrected with oral supplementation. However, with more severe cases the patient can present with polyuria or nocturia, abdominal cramps, paresthesias, skeletal muscle weakness, paralysis, palpitations and psychological symptoms. ECG changes can show the presence of U waves, prolonged QT interval, flattened T waves and ST depression. The condition can be life-threatening when the patient develops cardiac arrhythmias and it can lead to ventricular tachycardia or ventricular fibrillation. The treatment is to correct the potassium level immediately. This may require intensive care input and the insertion of a central line to allow rapid replenishment.

The association with essential thrombocythaemia and pseudohyperkalaemia has been documented for many years yet it is still not widely appreciated by many clinicians. Normal electrolytes values are derived from serum levels. In this case the degranulation of platelets was spuriously altering serum potassium levels. It was only when plasma potassium levels were obtained that the true level of potassium was revealed and how the patient had been mistreated prior to this. Figure 1 shows the comparison between the platelet counts in this patient and their respective serum and plasma potassium levels.

Conclusion

Hyperkalaemia is a commonly encountered emergency managed on a daily basis on medical wards. This article has discussed the potential causes of hyperkalaemia and described the significance of excluding haematological conditions such as thrombocythaemia before initiating treatment. Spurious hyperkalaemia due to essential thrombocythaemia is well-documented but poorly recognized among doctors. This case report is not the first time a patient with this essential thrombocythaemia has received unnecessary treatment potentially resulting in iatrogenically life-threatening hypokalaemia. Despite this, the case report importantly highlights the persisting poor awareness of this phenomenon among healthcare professionals.[18] The article has elaborated on this phenomenon and has discussed the aetiology and underlying principles of spurious hyperkalaemia. A plasma potassium levels should be recorded in these patients to provide true potassium levels.

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