Clinical Reports

Spurious hyperkalaemia associated with severe thrombocytosis and leukocytosis

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A patient with marked thrombocytosis and leukocytosis associated with myelofibrosis was found to have spurious hyperkalaemia caused by in vitro cell lysis. Initial failure to recognize the cause of the hyperkalaemia led to an inappropriate and potentially harmful intervention in an effort to optimize the patient's preoperative status.

Une hyperkaliémie factice causée par une lyse cellulaire in vitro a été notée chez un patient avec une trombocytose et une leukocytose marquées associées à une myelofibrose. La cause de l'hyperkaliémie n'a pas été reconnue initialement, entraînant une intervention inappropriée et potentiellement néfaste dans une effort pour améliorer l'état pré-opératoire du patient.

Laboratory analysis, as part of pre-anaesthetic assessment, requires proper specimen collection, identification, processing, and chemical analysis. A failure in the first several steps (the incorrect sample collection or its mislabelling, etc.) usually is a clerical error that will be discovered and corrected when the test is repeated. However, if the test is abnormal due to an artifact which is unique to the laboratory test, then the error will be recognized only if the physician recognizes potential pitfalls associated with a particular test.

The normal range of laboratory tests is developed using "normal" blood samples. In certain situations, especially those associated with malignant haematological disorders, an excess of cells present in the collected blood sample can artifactually alter the results *in vitro*. The resulting information can lead to unnecessary or possibly dangerous intervention. This potential problem, while uncommon, is important to the anaesthetist as patients with haematological disorders may require surgery before their blood disorder is controlled. Unfortunately, there is little information in the anaesthetic literature summarizing these potential problems. In this report, we describe a patient with myelofibrosis who developed thrombocytosis and leukocytosis following surgery. *In vitro* cell lysis resulted in a spuriously high level of potassium that led to inappropriate interventions.

Key words
BLOOD: leukocytes, platelets;
IONS: potassium.

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Case report

A 76-yr-old woman with myelofibrosis was admitted for splenectomy as a treatment for chronic anaemia and abdominal discomfort. The history and physical examination was normal with the exception of the large spleen. The patient was receiving no medications. Admission laboratory investigation demonstrated a mild anaemia, normal platelet and leukocyte counts, and a normal serum potassium concentration (Figure). Following an uneventful splenectomy on day two, the patient developed a wound dehiscence, which required surgical repair. The day before her second operation (scheduled for day 15), the electrolyte determination demonstrated a serum potassium of 6.0 $mEq \cdot L^{-1}$. The specimen was checked for haemolysis, but none was observed. The physician noted that the patient's serum potassium concentration had been increasing steadily following surgery, but the relationship with the parallel increase in the white cell count and platelet count (Figure) was not noticed. No immediate explanation was found for the hyperkalaemia, nor were there any symptoms. The patient was not receiving potassium supplements or cytotoxic therapy. Renal function tests were normal and there was no clinical evidence

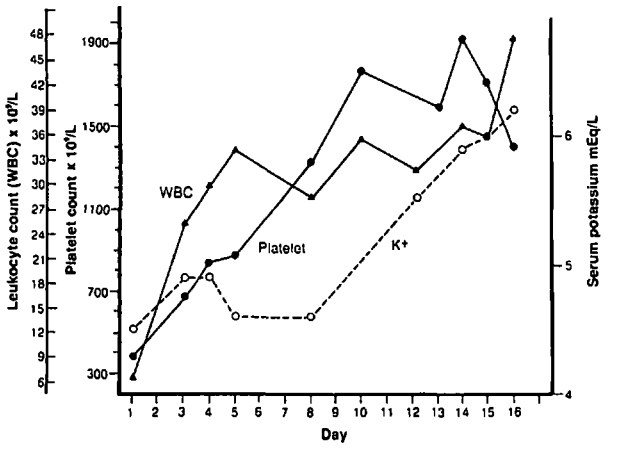

FIGURE The patient's blood platelet and leukocyte counts, and serum potassium concentration.

of adrenal insufficiency and diabetes mellitus. The ECG was normal. To reduce the hyperkalaemia so that the postponement of surgery could be avoided, the physician ordered glucose and insulin, to be followed by a sodium polystyrene sulfate (Kayexalate®) enema. Because spurious hyperkalaemia was suspected, a blood sample was collected into a heparinized tube just prior to glucose and insulin administration. This sample had a potassium concentration of 4.6 mEq·L^{-1}. Fortunately, no adverse effects resulted from the glucose and insulin treatment. The Kayexalate® enema was cancelled.

After the spurious nature of hyperkalaemia was noted, the patient underwent an uneventful abdominal repair under general anaesthesia. The serum potassium concentration was 6.2 mEq·L^{-1} the following day, but the spurious nature of this result was clear and no treatment was given.

All potassium levels were determined with the Kodak Ektachem Potentiometric test, which has a standard deviation of 1–1.2% of the mean in the range of values recorded in this patient.*

Discussion

In blood chemistries, clerical (mislabelling or miscollection of samples) and technical (problems during collection and processing of samples) problems are relatively easy to resolve because a repeat sample is unlikely to produce the same abnormal result. A factitious blood test result represents a true result in the patient, but one that is self-inflicted (for example, surreptitious ingestion of coumadin). A more difficult problem to resolve is a spurious result, which is defined as a technically accurate result that does not reflect the true condition of the patient. Haematological disorders can produce spurious results. For example, *in vitro* cell lysis or metabolism caused by a high cell count can produce spurious abnormalities of the serum potassium, glucose, and blood gases. The patient described in this report represents an example of hyperkalaemia that was initially considered to be true hyperkalaemia, and because of this concern, an unnecessary intervention was initiated.

Spurious hyperkalaemia can result from the *in vitro* release of intracellular potassium from leukocytes and platelets during clotting.[1–4] This has been observed only in patients with very high white cell or platelet counts and using only a serum sample. In previous reports, spurious hyperkalaemia was associated with platelet counts that approached or exceeded 1000 × 10^9 L^{-1}, or leukocyte counts that were significantly above 100 × 10^9 L^{-1}. There were, however, three cases[1,7] of spurious hyperkalaemia linked to leukocytosis of 20–34 × 10^9 L^{-1}. In this case report, the spurious hyperkalaemia was probably secondary to thrombocytosis but a contribution from white cells could not be ruled out. The following points confirmed that this is what occurred in our patient. First, the serum potassium concentration occurred in parallel with the increase in the platelet and leukocyte counts. Second, the patient had no clinical evidence of hyperkalaemia either clinically or as measured on the ECG. Third, other causes of hyperkalaemia were excluded or highly unlikely and the patient was not receiving potassium supplements by any route. Finally, when a blood sample was collected into heparin to prevent clotting, the potassium concentration was found to be normal at 4.6 mEq·L^{-1}.

Most clinicians recognize that hyperkalaemia can result from *in vitro* haemolysis. In fact, chemistry laboratory personnel look for the presence of haemolysis in patients with unexpected hyperkalaemia. Our patient did not have *in vivo* or *in vitro* evidence of haemolysis. Less frequently recognized is the hyperkalaemia associated with thrombocythaemia,[2–8,13] and leukoproliferative disorders including acute and chronic lymphocytic leukaemia,[9,10] acute and chronic myelogenous leukaemia,[11,12,14] and myelofibrosis.[8]

The *in vitro* aspects of pseudohyperkalaemia caused by thrombocythemia and leukocytosis have been studied in some detail.[1–3] The approximate potassium content per litre of cell volume is 70 mEq·L^{-1} for platelets,[2] and 93 mEq·L^{-1} for white cells.[1] The greatest amount of potassium release occurs within minutes of clotting in the test tube,[4] and although the precise mechanism for the release is uncertain, it is known that if clotting is prevented, the potassium concentration will remain within normal limits. This can be accomplished, as in our

*Kodak Ektachem Test Methodologies: Kodak Ektachem Clinical Chemistry Slides (K^+) 1986, Publication MP2-12; 10–86: 3.

patient, by using an anticoagulant such as heparin or ethylenediaminetetraacetic acid (EDTA). However, if heparin is used as the anticoagulant, then potassium based heparin preparations should be avoided.[15] Normally, 0.1–0.2 ml of sodium heparin (1000 $\mu \cdot ml^{-1}$) will more than adequately anticoagulate 5 ml of blood.[16]

We did not perform blood gas analysis or measure glucose levels after the splenectomy. However, it should be noted that both of these important variables are also susceptible to spurious changes caused by cellular proliferation. Spurious hypoxia has been reported in patients with leukocytosis[17–19] and thrombocytosis,[19] which in extreme cases may not be eliminated by keeping the sample in ice.[18] *In vitro* oxygen consumption can be arrested by adding potassium cyanide to the leukaemic blood.[18] Cells metabolize glucose *in vitro* and spurious hypoglycaemia has been described in patients with uncontrolled acute and chronic leukaemia ,[14,20–22] and polycythaemia vera.[23] This hypoglycaemia can be minimized by cooling the blood, or by mixing it with an adequate amount of sodium fluoride. Because platelets consume very small amounts of glucose,[24] spurious hypoglycaemia caused by thrombocytosis is rare.

In conclusion, in the presence of severe thrombocytosis and/or leukocytosis, *in vitro* cell lysis during clotting may result in falsely elevated serum potassium values which can lead to the misdiagnosis of hyperkalaemia or the failure to recognize hypokalaemia. This problem can be overcome by submitting for analysis the blood sample in a heparinized tube.

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