Case report of unexplained hypocalcaemia in a slightly haemolysed sample

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Abstract

The case presented highlights a common pre-analytical problem identified in the laboratory that was initially missed. It concerns a young, generally healthy adult patient with no significant medical history and no significant family history. They presented with common flu like symptoms to their primary care clinician who considered this was most likely a viral problem that would pass with time. The clinician, however, did some routine bloods to reassure the patient despite a lack of clinical indication. When the sample was analysed the sample was haemolysed with strikingly low calcium. This led to the patient being called into hospital for urgent repeat investigations, all of which turned out to be within normal ranges. On further investigation the original sample was found to be contaminated. This result would normally have been flagged but was missed due to the complication of haemolysis.

Key words: case report; pre-analytical; contamination; K-EDTA

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Introduction

The case presented below highlights the consequences for both patient and hospital when what is a relatively common pre-analytical problem presents in a more complex manner masking the fact that the results may be spurious.

It has been well documented that phlebotomy is a crucial part of the pre-analytical process and that compliance with guidelines is often poor (1-3). This failure to comply with guidelines increases the chance of an error in the phlebotomy process which increases the risk of an error in the patient's blood results and therefore potentially errors in patient care.

One aspect of the phlebotomy process that is often incorrectly performed is the order of draw of the blood samples. The order of draw is a key step in the phlebotomy process and was originally established to minimize the risk of additive carryover from one sample collection tube to the next. Recent evidence around this has been conflicting and has shown that under ideal conditions it is no longer a problem (4,5). However there is good evidence that sample contamination still occurs in the real world (6-12). The situation has been reviewed and the European Federation of Laboratory Medicine's Working Group for Pre-Analytical Phase (EFLM WG-PRE) made the recommendation to continue to recommend and order of draw (13).

The other pre-analytical aspect that this case highlights is that of defensive medicine. This is the practice of ordering more tests than clinically required due to a fear of missing something and facing future litigation (14). The problem with this behaviour, other than cost implications, is that the clinician is increasing the probability of finding an abnormal result which may be of no clinical significance but would result in unnecessary stress for the patient.

From a patient perspective, erroneous results create unnecessary stress and potential inconven-

ience associated with coming to have repeat tests performed to confirm, or disprove the original result. From a hospital perspective there are costs associated with brining a patient in to be re-bled. These costs cover not only the extra consumables required to perform the tests, but also staff time and the fact that while this patient is being assessed unnecessarily another patient is waiting.

Case report

In this case a young, healthy adult patient with no significant medical history and no significant family history presented on a weekday morning with common influence like symptoms to their Primary Care facility. On examination the clinician suspected that this was most likely a viral problem that would pass naturally given time. The clinician, however, did some routine blood science tests to reassure the patient despite a lack of clinical indication. One serum gel sample, one whole blood tube were collected in the GP surgery. The samples were received by the laboratory the same afternoon and sorted for processing with other non-urgent work. All samples were analysed on an Abbott Architect c16000 analyser (Abbott Diagnostics, Abbott Park, USA). When the sample was analysed in the early evening it was found to be haemolysed with strikingly low calcium as shown in Table 1.

Given the critically low calcium result the laboratory contacted the out of hour's clinician with the results in the early evening. The patient was contacted later that evening and asked to come in to the emergency department to have their bloods checked. The patient was brought in by a family member and re-bled. For the repeat test only a serum sample was collected. The results of this follow up are shown in Table 1. When the second sample was analysed all the results which were previously abnormal were normal and, importantly, were much more in keeping with the clinical picture.

What happened?

Given the changes in alkaline phosphatase (ALP) and calcium and the fact that an EDTA sample was also collected with the initial blood draw, potassium-ethylenediaminetetraacetic acid (K-EDTA) contamination is the most likely conclusion. The initial blood results were amended to reflect this.

Discussion

In the case presented here the patient's initial sample clearly gave an erroneous result. This led to the patient being contacted and asked to come into hospital to have the result confirmed. The new results were normal and in keeping with the clinical picture. The patient was discharged. This is clearly a problem on three fronts:

- the patient was put under unnecessary stress and inconvenience due to concerns for their health

Table 1. Laboratory analyses

Parameter	Initial values	Repeated values	Units	Reference values
Haemolysis level	1.2	0.1	g/L	N/A
Sodium	141	143	mmol/L	133–146
Potassium	haemolysed	4.3	mmol/L	3.5–5.3
Creatinine	50	52	umol/L	44–80
Urea	3.1	3.4	mmol/L	2.5–7.8
Calcium	1.65	2.32	mmol/L	2.2–2.6
Albumin	42	41	g/L	35–50
Adjusted calcium	1.64	2.32	mmol/L	2.2–2.6
Alkaline phosphatase	29	65	IU/L	30–130

- the cost of bringing a patient in to be re-bled was unnecessary and a waste of resources
- other patients were made to wait while this patient was seen unnecessarily.

In this sample the cause of the discrepancy was most likely K-EDTA contamination. The indicative factors in this case were the low calcium and low ALP. The calcium was reduced due to chelation by EDTA which is a chelator of divalent cations. Alkaline phosphatase activity is likewise reduced because EDTA chelates magnesium and zinc which are cofactors for ALP.

Routine practice in the laboratory involved is to investigate for K-EDTA contamination based on the potassium result. As the potassium result in this case was haemolysed this did not happen and the contamination was initially missed. Had the potassium been over the 6.0 mmol/L trigger, and the result was not consistent with previous results, calcium would be requested to look for low levels. Scientific and clinical judgment is then used to determine if the sample is contaminated (results hugely abnormal), has a possibility of contamination or is not contaminated. If contamination is confirmed results are removed from the patient record, whereas in suspected contamination a comment is added advising caution. Although calcium was requested in this instance, because there was no potassium the sample did not proceed down the investigative algorithm.

There are other, scientifically better methods to investigate this. For example, the laboratory could have added on a zinc, magnesium and iron depending on availability. Of these zinc is the most sensitive analyte as it has the highest affinity for EDTA (7). If the chosen markers were low this would provide further evidence of EDTA contamination and the result could be phoned or reported with a comment suggesting possible contamination and the clinician, with the clinical knowledge of the patient, can then make a judgment that maybe this is a false result and doesn't need urgent checking. The gold standard for this scenario would be to have a test in place for the measurement of EDTA directly to definitively rule contamination in or out. This has been shown to pick up K-EDTA contamination that would otherwise have been missed via a reliance on the suspicion of laboratory personnel (7-9,15).

It is good practice for the laboratory to have protocols in place to pick up and identify sources of interference (13,16). Once these protocols are in place the laboratory must also have a documented mechanism detailing how any rejected samples are going to be handled and how the requestors are going to be informed (17). In the case presented here results from samples with known contamination are removed and the clinician informed.

The other key point from this case is that if the requesting clinician felt that the patient's symptoms were due to a virus requiring no treatment, then bloods should not have been taken in the first place. Laboratory testing should be used to aid clinical decisions only, not done as a matter of routine or to appear as if something proactive is being done. As can be seen in the case of this patient this then cascaded quite a cost implication and ultimately worried the patient rather than reassured. Tests should not be requested unless there is a valid reason. By definition 5% of blood results will be abnormal due to the method by which reference ranges are calculated and may then trigger follow up investigations. This is a growing problem in a climate of defensive medicine. Clinicians have fear of missing something and facing legal action and patients have access to so much information online attend surgeries demanding blood tests (14). It is important that tests are requested in an evidence based manner.

Key learning points

- Requesting unnecessary tests is a waste of resources and can lead to unnecessary patient stress.
- Statistically, 1 in 20 test results will fall outside a reference range but be perfectly normal for that patient. The laboratory should work with clinicians to reinforce this message.
- K-EDTA contamination is relatively common.

- Contamination (or other interferences) should always be considered if a result does not fit with the clinical picture.
- Laboratories should have algorithms in place to try and identify contaminated samples.
- Clinicians should question results that do not fit with the clinical picture.

Potential conflict of interest

None declared.

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