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Case report

Extremely Elevated Coagulation Parameters in A Patient with End-Stage Renal Disease on Coumadin: A Case Report

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Abstract

A 71-year-old patient was presented to the emergency room with nausea, abdominal pain, vomiting, and diarrhea. The patient had a history of Coumadin anticoagulation therapy, so coagulation tests were ordered. The results of the tests came back critically prolonged for the PT-INR and prolonged for the aPTT as well. The PT was 295.1 seconds, the INR value was 26.1, and the aPTT was 70.6 seconds. Prolongation of coagulation tests can have many causes. Due to the extreme prolongation of the PT and INR and clinicians' skepticism of these results, additional investigative measures were performed. These additional measures confirmed the initial laboratory values and coumadin overdose. The patient was treated with vitamin K and quickly responded with PT/INR returning to therapeutic levels. While there are guidelines that exist for the management of therapeutic doses using the internationalized normalized ratio, it is still common for patients to have Coumadin overdoses, which can lead to fatal hemorrhagic outcomes if not caught promptly.

Keywords: Coumadin; anticoagulation; warfarin

Introduction

We present a case of unintentional Coumadin overdose which resulted in additional investigation by the laboratory. Coumadin is one of the oldest and still most prevalent anticoagulation medicines and has strict monitoring protocols. The patient was following monitoring protocols with regular clinic visits and at-home monitoring. The patient and caregiver were adamant that she did not overdose. The above factors make this case unique as clinicians were skeptical about the extremely elevated coagulation values. The laboratory initiated an investigation to rule out laboratory errors that may have occurred in both the pre-analytical and analytical phases of testing. This resulted in the specimen being recollected multiple times and run on different laboratory analyzers at different clinical locations eventually determining that initial tests were accurate. Thorough investigation revealed a Coumadin

overdose. Treatment with vitamin K quickly returned the patient to therapeutic levels ultimately confirming Coumadin overdose.

Case report

A 71-year-old patient was presented to the emergency room with 6 days of nausea, abdominal pain, vomiting, and diarrhea. The patient had a vast history of health conditions that included hypertension, atrial fibrillation with a mitral mechanical valve, and end-stage renal disease. The patient also had a medication history of Coumadin intake and is currently still taking Coumadin anticoagulant therapy. The patient was not only taking this medication, but she was also being monitored for it. A computed tomography (CT) scan was performed based on her symptoms, and the results revealed periurethral stranding, which led to suspicion of urinary tract infection (UTI). The patient was admitted based on the CT results and was immediately started on antibiotic therapy for the UTI. Routine blood testing was also performed as part of usual medical care and monitoring. Included in these laboratory tests were a coagulation panel that included a PT-INR, an aPTT, and a thrombin time (TT) (Table 1). The coagulation values, particularly the PT-INR results, were critically elevated, warranting immediate clinical attention. The results were as follows:

Table 1: PT, prothrombin time (normal range, 10-13 sec); PT-INR, PT-international normalized ratio (normal range, 1.0-1.1); PTT, partial thromboplastin time (normal range, 25-35 sec); TT, thrombin time (normal range, 12.8-21.7 sec). NP (Not performed).

Variables	Day 1	Day 2	Day 3	Day 4
PT (sec)	295.1	>320	170.2	36.0
PT-INR	26.1	NP	14.6	3.1
PTT (sec)	70.6	NP	66.1	NP
TT (sec)	NP	NP	18.1	NP

a) Prothrombin Time (PT) = 295.1 seconds (normal range, 10-13 seconds),

b) International Normalized Ratio (PT- INR) = 26.1 (normal range, 1.0-1.1), and

c) Partial Thromboplastin Time (PTT) = 70.6 seconds (normal range, 25-35 seconds).

The thrombin time (TT) test could not be reported as the result exceeded the instrument's linearity range, indicating that it was beyond the measurable limits of the analyzer. The PT-INR results were so extremely elevated that the results were questioned by the patient's attending physician. He ordered a recollection and retesting. Recollecting and retesting specimens due to questionable results is a common practice in laboratory medicine. This is done to confirm that there were no preanalytical or analytical errors in the testing process. In this circumstance, the attending questioned the patient about how much Coumadin she took. The patient and her spouse vehemently rejected the idea of an overdose as her coagulation status was monitored regularly at a clinic and she also had an at home INR testing device (that they monitored daily). The specimen was recollected and ran on the same instrument (ACL TOP 350cts Coagulation Analyzer- Manufactured by Instrumentation Laboratory). Results were still extremely elevated.

The following day, the attending physician was still in disbelief of the extremely high results. An additional sample was collected and run on the same instrument and subsequently sent to a sister facility for testing. The sister facility also used the same coagulation instrument. Results continued to be extremely elevated with the PT greater than 320 seconds or outside of instrument linearity. INR could not be calculated. Even with these results there was still the thought that some form of error or interference was occurring. Discussion between the attending physician and medical laboratory director resulted in yet another sample being drawn. This time the specimen was run on the facility's instrument and sent to another sister facility using a different coagulation instrument. The sister facility's instrument was a Stago STA Compact Max K130090. Both instruments showed critically high or prolonged PT-INR results.

The IL ACL TOP 350cts is a highly accurate instrument that measures the PT-INR using light transmittance which automatically adjusts for hemolysis, lipemia and icterus. A coagulation curve is plotted based on turbidity measurement and a coagulation error trigger is generated if the curve is abnormal. Samples with a deficiency of certain clot factors or clotted samples can both lead to an aberrant coagulation curve and, therefore, receive a coagulation error. However, in this case, there were no errors present on the ACL TOPs. The staghorn instrument on the other hand utilizes a mechanical viscosity base detection system. The system is not affected by optical interference. It offers optimum sensitivity for weak clot detection. Due to consistent results over multiple days, multiple instruments, and two different methodologies, the attending physician investigated further the patient's dosage and intake of the Coumadin anticoagulant. Upon further questioning of the patient, it was found that she was not taking the anticoagulant as prescribed and was taking too much of Coumadin, which resulted in an overdose of the medication.

The anticoagulant effect of Coumadin results from the inhibition of the γ carboxylation step in the synthesis of the Vitamin K-dependent clotting factors II, VII, IX, and X. Discussion between the pathologist and attending physician resulted in the patient given vitamin K treatment. Within a day of treatment, the patient's PT was 36 seconds and the INR 3.1 which was therapeutic. The changes in the patient's PT and INR were consistent with reversal of Coumadin overdose by vitamin K therapy.

Discussion

Coumadin or Warfarin is the most used anticoagulant in the world. Coumadin is made up of R- and S- warfarin [1] and is a vitamin K antagonist that inhibits the vitamin K dependent factors II, VII, IX and X [2]. The use of coumadin, although efficacious, can lower the therapeutic range within the patient [3]. Due to its potential adverse effects, dosage must be carefully established for individual patients based on how the patient is responding to treatment. There is a significant correlation between overdose of Coumadin and adverse effects that lead to other life-threatening diseases [4]. Abuse of this anticoagulant drug can predispose the patient to more life-threatening conditions like bleeding (overdosing) and strokes (underdosing) [5]. A thorough investigation is required during history taking to ensure that the patient is adhering to the correct dosage and not accidentally overdosing.

Certain medications like high levels of aspirin or other anticoagulants, such as rivaroxaban and apixaban, increase the levels of PT-INR [6,7]. However, in this case, the only anticoagulant medication that the patient was on was Coumadin. In this case abnormally high coagulation values were being attributed to pre-analytical and analytical causes by the attending physician. This was due to the patient's history of coumadin monitoring by clinics, daily PT and INR monitoring with an at home device and the patient's adamant belief that she did not overdose. After additional investigation/testing was performed pre analytical and analytical errors were excluded. This left only and intrinsic cause for the increased coagulation values. Vitamin K therapy and quick reversal of coagulation values to therapeutic levels confirmed Coumadin overdose.

Conclusion

This case study highlights the importance of different members of the medical team, especially the laboratorians, during patient diagnosis. It also emphasizes the importance of accurate history taking and medication confirmation with the patient. In many instances, patients may assume that they are adhering to their medication dosages, but as clinicians, we should always investigate to rule out an overdose in the context of multiple laboratory values being high. Without the additional investigation and testing to confirm the patient's critically elevated PT and INR levels, the patient may not have received appropriate treatment and could have bled to death.

Conflict of Interest

No potential conflict of interest.

Authors Contributions

AA and JL conceived the presented case studies. AA wrote the first draft of this study. AV and NA helped proofread the study.

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