Teaching Case

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Intelligent Diagnosis, Unexpected Complication in a Munchausen Case of Warfarin Abuse

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ABSTRACT

A 25-year-old man with 10 years history of a migraine headache noticed ecchymotic lesions involving anterior chest wall, both upper and lower limbs that were unrelated to trauma. His laboratory data revealed prothrombin time (PT) 32 seconds, partial thromboplastin time (PTT) 44 seconds, international normalized ratio 6, and normal bleeding time. Mixing study was performed and normalized PT to 13 seconds and PTT to 38 seconds. Factor activity assay revealed a low level of Factors II, VII, IX, and X but normal level of Factor V. Factitious disorders were in high priority in our differential diagnosis. Thus, we evaluated serum warfarin level which was positive. There were no doubts that we encountered Munchausen case that abused warfarin compounds. We decided to use factor eight inhibitor bypassing activity for rapid correction of coagulation disorder. He suddenly complained of chest pain and dyspnea. We encountered to pulmonary embolism.

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Introduction

To set a diagnosis in coagulation disorders the first step after encountering abnormal coagulation test is to perform mixing studies to differentiate between coagulation factor deficiency with factor disability (presence of inhibitors in circulation), as both prothrombin time (PT) and partial thromboplastin time (PTT) corrected with mixing test, factor deficiency is culprit. We present an interesting and challenging case report in this field.

Case Report

A 25-year-old man with 10 years history of a migraine headache, which was controlled

using nonsteroidal antiinflammatory drugs, reported worsening of headache from 4 months earlier. His neurologist started valproic acid for him, but after 1 month he noticed ecchymotic skin lesions that involved anterior chest wall, both upper and lower limbs that were unrelated to trauma. Once more he referred to his neurologist, valproic acid was discontinued and his laboratory data revealed white blood cell count of 6100/µl, hemoglobin level 15.3 g/dl, platelet count 285,000/µl and PT 32 seconds, PTT 44 seconds, international normalized ratio (INR) 6, and normal bleeding time (3 minutes and 30 seconds). His physician prescribed fresh frozen plasma (FFP) and then discharged the patient.

Over preceding 8 months, he experienced multiple episodes of bleeding symptoms including cutaneous ecchymosis, epistaxis, gross hematuria, and melena, each time he received FFP due to abnormal PTT and PT times and after about 1-2 weeks of symptom-free period he re-experienced the same symptoms. A week earlier to this admission, he received FFP and intramuscular injection of Vitamin K and then refers to our center for further workups.

On arrival in the emergency department of our hospital, we encountered a young man that comfortably sat on his bed and had not any sign of distress and anxiety. His blood pressure was 130/70 mmHg, regular pulse rate of 68/minute, oxygen saturation 98% while breathing in ambient air, respiratory rate of 14 breaths/minute and oral temperature was 36.8° C. He weight 101 kg with 181 cm height, and his body mass index was calculated 31.8 kg/m^2. He looked pale and non-icteric. There were no petechial or purpuric lesions in oral cavity, but there were multiple ecchymotic lesions of different sizes all over his trunk and limbs (Figure 1, a and b). Lung and cardiac exam were normal. His abdomen was soft with mild tenderness over epigastrium, and no organomegaly was detected. In the rectal exam, melena was detected and articular ranges of motion were normal.

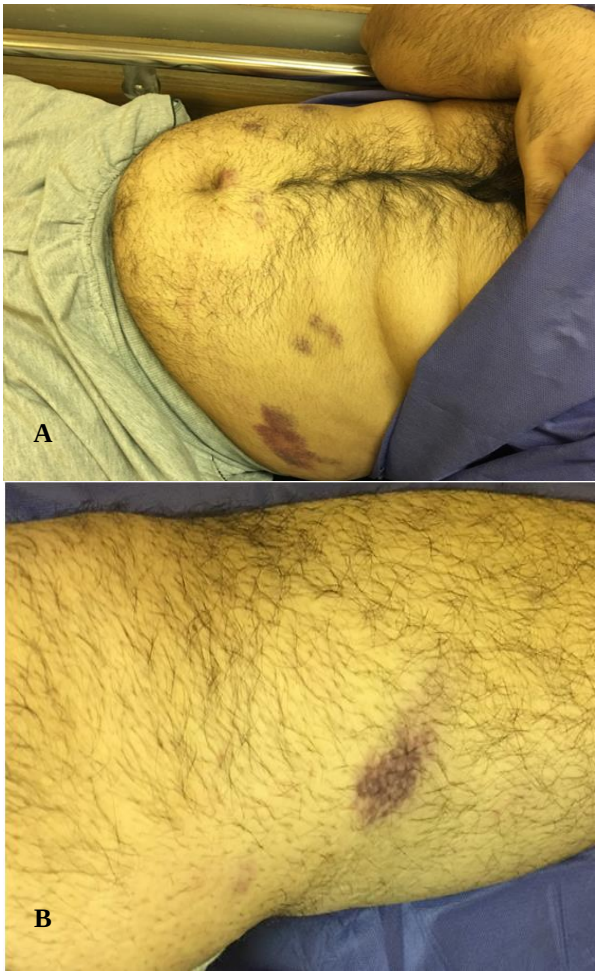

Figure 1. Non-traumatic ecchymotic lesions over trunk (a) and lower limb (b)

Besides a migraine headache, he had no past medical history and consumed ibuprofen as needed and did not use any herbal or other over the counter drugs. He did not smoke, drinking alcohol or using illicit drugs. His grandmother had atrial fibrillation which lives separately, and the rest of his family did not have any illness.

He was a non-married man living with his parents, graduated of electric field and right now he is working with his brother in the small industry of building wooden doors. He did not intended military service.

His initial laboratory exam revealed elevated PT, PTT, INR, and microcytic anemia. His electrolytes, blood chemistries, liver and renal function tests, and urine analysis were normal. Other laboratory tests are shown in table 1.

Table 1. Laboratory data

Variable	Normal range	Value
Sodium (meq/l)	135-145	137
Potassium (meq/l)	3.5-5	4
Calcium (mg/dl)	8.5-10	7.9
Magnesium (mg/dl)	1.8-2.5	2.1
Phosphor (mg/dl)	3.5-5	3.7
Urea (mg/dl)	21-52	36
Creatinine (mg/dl)	0.8-1.3	1.1
Fasting blood sugar (mg/dl)	70-99	91
Aspartate aminotransferase (U/l)	10-45	41
Alanine aminotransferase (U/l)	10-45	66
Alkaline phosphatase (U/l)	50-250	162
Bilirubin (total, direct) mg/dl		0.3, 0.1
Lactate dehydrogenase (U/l)	< 480	1049
Creatine phosphokinase (U/l)	24-195	199
CK-MB (U/l)	< 20% total CK	26
C-reactive protein (quantitative) mg/dl	< 10	2.7
White blood cell count (/µl)	$4\text{-}10 \times 10^3$	7500
Lymphocyte (%)	20-40	30
Neutrophil (%)	40-70	65
Red blood cell count (/µl)	$3.5\text{-}5 \times 10^6$	4.5×10^6
Hemoglobin (g/dl)	13-17	10.3
Mean corpuscular volume (fl)	81-99	79
Platelet count (/µl)	$150\text{-}400 \times 10^3$	260,000
Corrected reticulocyte count	< 2	0.7
PT (seconds)	11-15	70
INR	0.9-1.2	> 7.9
PTT (seconds)	25-40	65
Blood gas		
PH	7.36-7.44	7.37
PCO_2 (mmHg)	35-45	35
HCO_3 (mmHg)	22-26	20
Factor II	50-150	7
Factor V	50-150	55
Factor VII	50-150	7
Factor IX	50-150	4
Factor X	50-150	3
Albumin	3.5-5.5	2.8

PTT: Partial thromboplastin time, PT: Prothrombin time, INR: International normalized ratio

Mixing studies for coagulation test performed and PT normalized to 13 seconds and PTT to 38 seconds. Factor activity assay revealed lower than normal level of Factors II, VII, IX, and X but normal level of Factor V (Table 1). Antithrombin III level was 56% (reference value: 83-128).

Hydration with isotonic saline and intravenous proton-pump inhibitor started for him, concurrently FFP and oral Vitamin K prescribed. Upper endoscopy revealed multiple clean-based ulcers of 2-3 mm in gastric antrum with positive *Helicobacter pylori* rapid test. Abdominal ultrasonography was consistent with normal size liver and spleen without any other abnormalities.

There were some important points in history, the young man appeared completely anxiety free, and there were no signs of distress. Furthermore, he did not attended in military service. In this patient suspicious to factitious attempts was logical. We asked detailed history about consuming herbal drugs or superwarfarin compounds but he denied. Another important point in history was atrial fibrillation in his grandmother who was on

warfarin treatment. He claimed that he did not saw her for more than 3 months and denied using her medication.

As factitious disorder was in high priority in our differential diagnosis, we evaluated serum warfarin level which was positive. There were no doubts that we encountered Munchausen case that abused warfarin compounds.

Anyway, we continued our treatment with oral Vitamin K, but his ecchymotic lesions continued to progress, and he complained of headache and had an episode of hematemesis. Brain computed tomography showed no hemorrhagic lesion. We decided to use factor eight inhibitor bypassing activity for rapid correction of coagulation disorder. His symptoms were started to resolve in 4 days.

He suddenly complained of chest pain and dyspnea with sinus tachycardia and decreased oxygen saturation. The disaster had been happened, computed tomography angiography of chest revealed filling defect in ligula division of the left pulmonary artery in favor of pulmonary embolism.

Discussion

Coagulation test study revealed prolonged prothrombin and PTT. This occurs usually during common pathway coagulation factors deficiency (means Factors II, V, X, and fibrinogen), late stages of Vitamin K deficiency or using direct thrombin inhibitors (such as Dabigatran and Lepirudin) (1). There were no signs in favor of disseminated intravascular coagulation (DIC) or liver disease as both conditions could prolong PT and PTT simultaneously. In DIC the patient usually appears ill and unstable. Furthermore, he had no signs consistent with chronic liver diseases such as spider angioma, palmar erythema, or caput medusa.

To set a clinical pathway, in this case, the first step after encountering abnormal coagulation test is to perform mixing studies to differentiate between coagulation factor deficiency with factor disability (presence of inhibitors in circulation) (1), as both prothrombin and PTT corrected with mixing test, factor deficiency is culprit.

The next step is to determine whether it is a single factor or multiple factors deficiency. To answer this question, we should check individual coagulation factor activity: Factors II, VII, IX, and X deficiency which are all Vitamin K dependent coagulation factors concurrent with normal Factor V level is in favor of Vitamin K deficiency. Vitamin K dependent factors include mentioned coagulation cascade factors and anticoagulant factors including protein C and S and Antithrombin III (2, 3), Antithrombin III level was also decreased in this patient but measuring Antithrombin level is not useful in this setting as it is useful for assessing hypercoagulable state but not in bleeding disorders.

The most probable problem in this patient is coagulopathic disorder that was related to Vitamin K deficiency. The last but most important question in this setting is to answer this question: Why patient had Vitamin K deficiency?

Malnutrition and malabsorption are one of the important causes of Vitamin K deficiency (3). Malnutrition could occur for example in heavy alcohol consumption but our patient did not have any history of alcohol drinking. Bactericidal agents by eliminating gut bacterial flora could disturb Vitamin K production, but again there was not such history. Microcytic anemia (which could cause by iron deficiency) and hypoalbuminemia could be considered as stigmata of malabsorption, but on the other hand, according to the history of frequent bleeding episodes and normal Vitamin D level, malabsorption syndromes are less likely.

Anti-Vitamin K agents such as warfarin and superwarfarin compounds are other important cause of Vitamin K related factor deficiency (4).

Superwarfarin compounds are used in rodenticides that are unfortunately readily available in groceries all over our country causes intractable bleeding until death in victim rodent. Consuming these compounds -

Either accidental or for suicidal attempt- could causes bleeding tendency and coagulation test disturbances for many weeks (2, 5-7). Superwarfarin compounds are considerably more potent than warfarin with higher lipid solubility and affinity to body tissues and have slow elimination rate, leads to recurrent bleeding episodes following initial exposure (2, 8). Detailed history did not show any apparent history of supra warfarin compounds or rodenticides exposure in this patient. But by evaluating the level of serum warfarin, the etiology was revealed.

The effect of valproic acid on coagulation test is controversial, and it could induces thrombocytopenia, Von Willebrand factor dysfunction and alternation in PT and PTT time, but these changes seem not clinically significant (9).

Pulmonary embolism was occurred because of overshoot treatment with prescribing activated factors concentrate in a bed rest patient who had been deprived of warfarin during hospitalization.

This unexpected complication changed the treatment plan from coagulation to anticoagulation protocol. Anticoagulation with heparin and warfarin started and at 16th day of hospitalization, and he discharged from the hospital with warfarin in hand and INR of 2.3.

Hence, the patient who was diagnosed as Munchausen warfarin abuser discharged with warfarin!

Conflict of Interests

Authors have no conflict of interests.

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None.

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