Unexpected outcome (positive or negative) including adverse drug reactions

Does endocarditis require routine coagulation screening?

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Summary

We report a case of probable iatrogenic vitamin K deficiency in the context of antibiotic treatment for endocarditis. The patient was initially admitted with breathlessness and treated for an exacerbation of chronic obstructive pulmonary disease. However, during this period the patient was further diagnosed with endocarditis following repeated temperature spikes. Following initiation of antibiotic treatment for endocarditis the patient was noted to become increasingly anaemic. The patient was noted to have prolonged prothrombin time despite no anticoagulants. Antibiotics have been reported to alter the gut flora causing vitamin K deficiency; thereby, resulting in coagulopathy. We give a brief overview and literature review regarding potential vitamin K deficiency in this clinical context.

BACKGROUND

It is not uncommon to develop anaemia in the context of endocarditis for various reasons. However, iatrogenic vitamin K deficiency secondary to antibiotics is not common and should always be considered in cases on long-term antibiotics.

CASE PRESENTATION

A 78-year-old man presented with increase shortness of breath and productive cough. His past medical history was significant for chronic obstructive pulmonary disease (COPD) on long-term oxygen. He was treated as exacerbation of his COPD according to the local policy.

He was initially found to be anaemic with haemoglobin (Hb) of 9.8 mg/dl with a normochromic normocytic picture. This was noted to be chronic. His iron studies showed saturation of 9% with normal B₁₂, folate and coagulation profile. His gastroscopy, haemolytic and celiac screen were negative. During the work up of his anaemia, he started to develop lower grade fever between 38 and 38.5 °C. Investigations, including chest radiograph and urine culture, came back negative. However, blood cultures grew coagulase negative staphylococcus on three different occasions. Subsequently, transoesophageal ECG demonstrated vegetations in keeping with endocarditis. He was started on vancomycin and rifampicin as per microbiological advice. The inflammatory markers fell with treatment. However, his anaemia was noted to be getting worse and required blood transfusion. He was not well enough to have colonoscopy and his faecal occult blood test was positive on three different samples. There was a noted episode of melaena. Aspirin was stopped and subsequent CT of the abdomen and carcinoembryonic antigen (CEA) levels was normal.

In the context of his endocarditis and anaemia, his haemolytic screen was repeated and was negative. However, his coagulation profile was quite deranged with high prothrombin time, high partial thromboplastin time, normal fibrinogen and international normalised ratio (INR) of 4.8, which was not the case on admission. Unfortunately, he did not have d-dimer as part of the work-up. The blood

picture support a diagnosis of vitamin K deficiency rather than disseminated intravascular coagulation (DIC) as his platelets and fibrinogen level were normal. Liver function tests were normal and liver texture appeared normal on a CT scan. The patient was started on supplement vitamin K and his rifampicin was stopped. Unfortunately, the patient did not have vitamin K measurement as supplement treatment was started immediately.

He made a good recovery and his anaemia stabilised. His repeated INR was 1.1. He was discharged with follow-up regarding his anaemia.

INVESTIGATIONS

Gastroscopy: normal; transoesophageal echo: vegetations on mitral valve; CT abdomen: normal; CEA level: normal.

DIFFERENTIAL DIAGNOSIS

Anaemia of chronic disease, haemolytic anaemia, anaemia secondary to neoplasm and DIC.

TREATMENT

Oral vitamin K supplement and antibiotics.

OUTCOME AND FOLLOW-UP

Anaemia stabilised with no further blood transfusion required. The patient was reviewed in a gastrointestinal outpatient clinic but declined colonoscopy. His repeat coagulation screen, including INR and Hb, were both normal (Hb13.1). The patient had no lower gastrointestinal symptoms or weight loss.

DISCUSSION

Vitamin K is a fat-soluble vitamin that plays a vital role in the production of coagulation factors (II, VII, IX, X, protein C and S). The three main types of vitamin K are K1 dietary phyloquinone, which is absorbed from the small intestine; K2, menaquinone, which is produced by the flora in the ileum and large bowels; and K3, which is a synthetic, water-soluble form used for treatment.

Both phyloquinone and menaquinone are used by the human liver;¹ therefore, any conditions affecting either type can result in vitamin K deficiency. Such conditions include malnutrition, common bile duct obstruction (stones, primary biliary cirrhosis and cholangiocarcinoma), malabsorption syndromes, parenchymal liver disease (cirrhosis) and other conditions such as lupus, multiple myeloma and nephrotic syndrome. It has been hypothesised that antibiotics could cause vitamin K deficiency through two mechanisms: either direct inhibition of hepatic utilisation of vitamin K or antibiotic mediated eradication of vitamin K producing intestinal micro flora resulting in iatrogenic vitamin K deficiency and, possibly, life-threatening coagulopathy.^{2,3}

Our patient had deranged coagulopathy within 2 weeks of being on antibiotics, which could suggest subclinical deficiency prior to the antibiotics usage. Subclinical vitamin K deficiency is difficult to assess through routine blood tests and may require special tests to diagnose (see below). It has been reported in experiments that rifampicin can cause vitamin K deficiency and the effect depends on the dose and duration.⁴

In the critical care settings, there is increased awareness of vitamin K deficiency in this group of patients but it is still a debatable subject. One study showed that vitamin K deficiency is common in the intensive care units setting with up to 25% of admitted patients (using functional coagulation factor II to Echin factor II ratio <0.70 as a method of diagnosis).⁵ However, only 5% of these patients developing coagulopathy required medical attention. On the other hand, long-term antibiotics, like endocarditis, will put patients under increase risk of coagulopathy; hence, this category of patients needs to be monitored especially if they are on rifampicin.

Learning points

- ▶ Coagulation screening is an important test in the work up of anaemia.
- ▶ Patients on long-term antibiotics should have their coagulation screen monitored.
- ▶ Liaison and discussion with the lab regarding vitamin K measurement should be performed prior to supplement initiation especially if an unusual condition is suspected.
- ▶ Antibiotics such as rifampicin may be more likely to cause vitamin K deficiency and should be considered a second option unless necessary and with prompt coagulation monitoring.

Competing interests None.

Patient consent Obtained.

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