

Case Report

Severe Haemolytic Anaemia, a Rare Presentation of Nutritional Vitamin B12 Deficiency: A Case Report

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ABSTRACT

Vitamin B12 deficiency usually presents with megaloblastic anemia, pancytopenia, and neurological symptoms. The cause is usually, nutritional deficiency, increase demand, decrease absorption. This report describes a case with symptoms of apathy and findings suggestive of severe hemolytic anemia, diagnosed with vitamin B12 deficiency. Haemolysis is a rare hematological finding in cases of B12 deficiency, and descriptions of a nutritional vitamin B12 deficiency, without evidence of pernicious anaemia, causing haemolysis, are even scarcer, and this paper was intended to draw physicians' attention to this rare form of presentation.

Key words: Anemia; Cobalamine; Haemolytic; Vitamin B12

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INTRODUCTION

Once encountered with anaemic patient, clinical findings, erythrocytes indexes and peripheral blood smear results are preferred initial parameters, in algorithmic approach towards diagnosing of the cause of anaemia. However, if different aetiologies' are present or with atypical presentations, that mask the clinical scenario, the case becomes complex and difficult to diagnose. Similar was the scenario with the under stated patient, where, though there was a deficiency of vitamin B12, erythrocyte indexes were compatible with microcytic to normocytic anaemia with normal red cell distribution width (RDW) in the background, and an exaggerated rise in LDH, reticulocyte counts & indirect bilirubin was seen, as if haemolytic anaemia.

#CASE REPORT

A 47 year vegetarian male with no reported past medical history presents with complaints of progressive weakness, lethargy, headache and light-headedness over the course of the last 3 months. Additionally, the patient reports that during the course of the last 3 months he had been having an increasingly difficult time performing daily workplace outdoor responsibilities, due to progressive generalized weakness & light-headedness which improved with ample rest. The patient visited his primary care physician for progressive symptoms and was found to be severely anaemic. He affirmed medical evaluation 6 months back, where

he was declared clinically well. He was then referred to the hospital for further evaluation and possible blood transfusion.

In the emergency department, his vital signs were: heart rate of 90 beat/minute, blood pressure of 120/70 mmHg, temperature of 97°F, respiratory rate of 18 breaths/minute, and pulse oximetry of 97% on room air. The physical examination showed mucosal and conjunctival pallor, no scleral icterus, no palpable lymph nodes, non-distended abdomen, normal bowel sound with no organomegaly, and unremarkable cardiac and lung examination. Neurological examination findings were also normal.

Initial laboratory studies revealed white blood cell count (WBC) of 5,600 (4,000-11,000/cumm) with neutrophil accounting 90.5% (40-70%), haemoglobin (Hb) 4.8 gm% (13.5-17.5 gm%), haematocrit 17.2% (40-54%), platelets 160,000 (150,000-450,000/cumm), and a mean corpuscular volume (MCV) 90.5 (80-100 fl), mean corpuscular haemoglobin (MCH) 25.3 (27-32 pg), mean corpuscular haemoglobin concentration (MCHC) 37.9 (31-36%) and reticulocyte count 4 (Ref. 0.2-2%). Erythrocyte sedimentation rate (ESR) was 75 mm/hr. Comprehensive biochemical examinations were as follows: urea 30 (Ref. 10-50 mg/dl), creatinine 1.0 (Ref. 0.6-1.5 mg/dl), Na⁺ 142 (Ref. 135-145 mEq/l), K⁺ 3.6 (Ref. 3.5-5.5 mEq/l), aspartate aminotransferase (AST) 31 (Ref. 17-59 IU/l), alanine aminotransferase (ALT) 21 (Ref. 21-72 IU/l), alkaline phosphatase (ALP) 52 (Ref. 38-126 IU/l), total protein 8.4 (Ref. 6.3-8.2 g/dl), Albumin 4.3 (Ref. 3.5-5.0 g/dl), total bilirubin 2.3 (Ref. 0.2-1.3 mg/dl), direct bilirubin 0.8 (Ref. <0.3 mg/dl), lactate dehydrogenase (LDH) 3473 (Ref. 230-460 IU/L), prothrombin time (PT) 13.1 (Ref. 11-16 sec), international normalised ration (INR) 1.02. Thyroid hormone values were normal. Iron was 42 (Ref. 49-181 µg/dl), ferritin was 131.96 (Ref. 25-350 ng/ml) and TIBC was 238 (Ref. 261-462 µg/dl). Faecal occult blood test was negative. Abdominal ultrasound scan were unremarkable.

Peripheral blood smear results showed mixed normocytic microcytic cells, anisopoikilocytosis with tear drop cell, target cells, fragmented cell, polychromasia, nRBC 7/100 WBC (findings compatible with hemolytic picture). Platelets were adequate in number, with normal morphology. No abnormal WBCs or malignant cells were observed. Also, other tests associated with haemolysis such as glucose-6-phosphate dehydrogenase (G6PD) and haemoglobin electrophoresis were normal, and direct coombs and ANA were negative. Megaloblastic changes were determined in bone marrow aspiration. The patient's serum Folic acid level was 12.03 (Ref. 3.56-20 ng/ml) and vitamin B12 level was 113 (Ref. 239-931 pg/ml). So, other causes of haemolytic anaemias such as G6PDH deficiency, hereditary spherocytosis, autoimmune haemolytic anaemia, and haemolytic uremic syndrome were excluded.

Given the patients' laboratory and clinical features, a diagnosis of haemolytic anaemia secondary to severe vitamin B12 deficiency was made. His nutrition was later assessed after the diagnosis of vitamin B12 deficiency, and revealed that his diet was mostly consistent with vegetables and legumes. Once diagnosed, the patient was started on vitamin B12 supplement, 1000 mcg intramuscular injection initially, which was later switched to oral form. He also received 2 units of packed red cell transfusion during hospital stay. Upper gastrointestinal endoscopy was performed which showed no evidence of upper gastrointestinal source of bleeding or autoimmune erosive gastritis. The patient's

initial symptoms of lethargy, weakness, headache & light-headedness improved significantly, and his haemoglobin was stable at 9.1 gm/dl at the time of discharge. Upon follow-up 3 days after discharge, the patient reported further improvement of his symptoms. His Hb was at 10.6 gm% and haematocrit of 35.3%. Haemolysis was improving with total bilirubin and LDH level normalized. Subsequent visit at 3 months showed resolution of all symptoms with improvement of CBC to Hb 11.1 gm% and normal serum B12 level.

DISCUSSION

Anaemia is usually classified in blood loss, impaired production & increased destruction¹, and their diagnosis is usually guided initially by clinical findings and tests like erythrocytes indexes & peripheral blood smears. This patient presented with severe anaemia, and the associated complains correlated with the clinical scenario. On further evaluation, coexisting hyperbilirubinaemia with elevated indirect bilirubin, high LDH, and multiple fragmented red blood cell noted on peripheral smear indicated erythrocyte destruction or haemolytic anaemia as the cause.

Haemolytic anaemia represents a diverse group of diseases which can be divided in to congenital or acquired. Since the patient did not have history of anaemia in the past, and no history of transfusion, no evidence of hepato-splenomegaly, it is unlikely that this is due to inherited conditions. Other confirmatory tests also eliminated the presence of haemoglobinopathy and G6PD deficiency. Peripheral blood smear examination was not a characteristic of spherocytosis or elliptocytosis.

There are various causes of acquired haemolytic anaemia including but not limited to autoimmune, drug-induced, microangiopathic haemolytic anaemia, infections, chemicals, severe burn, and radiation. Due to multiple aetiologies, numbers of workup were performed for this patient to rule out different causes of acquired haemolytic anaemia. The possibility of haemolytic anaemia secondary to severe burn or radiation exposure was eliminated since the patient denied such history.

Combined autoimmune haemolytic anemia and Vit B-12 deficiency anemia has been reported.^{2,3} However, in this patient, Coombs test was negative, which argue against autoimmune haemolytic anaemia. Drug-induced or chemical-related haemolysis was also less likely since the patient denied taking any medication and he has no history of chemical-related exposure. Microangiopathic haemolytic anaemia, such as thrombotic thrombocytopenic purpura, haemolytic uremic syndrome, and disseminated intravascular coagulation, is also less likely since the patient has normal platelet count, no renal abnormality, and normal coagulation. Another cause for intravascular haemolysis such as valvular heart disease was also excluded since he does not have murmur on physical examination and prior history of cardiac disease. The likely cause of haemolytic anaemia in this case was due to vitamin B12 deficiency, since serum B12 level was low.

Commonly, vitamin B12 deficiency is associated with macrocytic anaemia. However, the patient's mean corpuscular volume (MCV) and RDW were normal which suggested the presence of other pathology like iron deficiency anaemia, hypothyroidism etc, which was ruled out by normal iron profile and thyroid function test results.

In a review of literature, case reports on vitamin B12 deficiency causing haemolytic anaemia are quite rare. Autoimmune and nonimmune haemolytic anemia has been reported in association with Pernicious anemia. However, descriptions of a nutritional vitamin B12 deficiency, without evidence of pernicious anaemia (normal upper gastrointestinal endoscopy), causing haemolysis are even scarcer.⁴⁻⁷ Studies suggest, Vitamin B12 deficiency can present with a haemolytic picture in 1.5% of patients with elevated LDH, low haptoglobin, and elevated indirect bilirubin mostly due to ineffective erythropoietin and intramedullary destruction.⁸⁻¹⁰

In Vit B12 deficiency anemia there is increased level of homocystein and it increases the risk of hemolysis. This mechanism has been demonstrated in vitro.^{11,12} In case of HELLP syndrome, homocystein is the cause for hemolysis.¹³ Pro-oxidant effect of hyocystein is the possible mechanism, in the pattiet with hyperhomocysteinemia. Hemolysis has been resolved after getting normal homocystein level in the blood.¹²

The main source of vitamin B12 is animal product such as meat, milk, egg, fish, and shellfish.¹⁴ Hence, strict vegetarians, like this patient, have a greater risk of developing vitamin B12 deficiency.¹⁴ Managing our patient was challenging as he presented with a severe normocytic anaemia and haemolytic picture, none of which were suggesting vitamin B12 deficiency.

The treatment of cobalamin deficiency required replacement of vitamin B12. Daily high dose oral therapy (1000 to 2000 mcg per day) is as effective as parenteral formula in several randomized studies.¹⁵ Our patient was initially treated with intramuscular injection of vitamin B12 followed by oral supplement which showed significant improvement in symptoms within a week. His Hb and red cell indices continued to improve with complete resolution of haemolysis. Vitamin B12 level have normalized. This case displayed the complexity of vitamin B12 deficiency where clinicians should be familiar. Once the diagnosis is confirmed, further investigation is warranted to explain the aetiology.

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