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Vitamin B12 deficiency as the sole cause of hemolytic anemia: A case report

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Abstract

Vitamin B12 is an essential vitamin that is required for an effective hematopoeisis and normal development and maintenance of the function of the central nervous system. Its deficiency can cause megaloblastic anemia, psychiatric disorders, as well subacute combined degeneration of the spinal cord. Hemolytic anemia due to intramedullary hemolysis is a quite rare presentation related to vitamin B12 deficiency. We report a case of a 28-year-old woman who presented for generalized fatigue and dyspnea; her investigations revealed nonautoimmune hemolytic anemia and profound thrombocytopenia associated to severe vitamin B12 deficiency. She has remarkably improved after adequate supplementation. This report highlights the case of a patient who presented with one of the rare complications related to vitamin B12 deficiency.

Keywords

Vitamin B12; Hemolytic anemia; Thrombocytopenia; Pernicious anemia.

Introduction

Vitamin B12 deficiency is a relatively common condition. Several etiologies exist such as inadequate uptake, pernicious anemia (loss of intrinsic factor secondary to atrophic gastritis), and decreased iliac absorption. Dietary vitamin B12 deficiency and pernicious anemia are considered the most common causes of severe vitamin B12 deficiency in children and adults, respectively [1]. Symptoms of vitamin B12 deficiency can range from mild fatigue to severe neurological impairment. Hematological manifestations include megaloblastic anemia, pancytopenia, and hyper-segmented neutrophils [2,3]. However, vitamin B12 deficiency can also present as hemolytic anemia; which is a rare presentation, making the diagnosis more challenging. Therefore, high clinical suspicion is needed to ensure early diagnosis and to provide adequate treatment of this condition.

Case Presentation

A 28-year-old woman with no past medical or surgical history, presented with a two week history of worsening fatigue, malaise and dyspnea on exertion.

On presentation to the emergency department, she was conscious, cooperative and oriented. She was afebrile, her blood pressure was 100/60 mmHg, her heart rate was 95 beats per minute, her respiratory rate was 18 breaths per minute, and she had capillary oxygen saturation of 98% on room air. She denies any history of fever, no cough or sputum production, no chest pain, no headache or other neurologic symptoms. Physical examination revealed icteric sclera, poorly injected conjunctiva and glossitis. No palpable lymphadenopathies were detected. Lung auscultation was clear. Heart auscultation revealed regular rhythm with no added murmurs. On abdominal palpation, no hepatomegaly or splenomegaly were present. The neurologic and musculoskeletal examinations were normal.

Initial laboratory studies (Table 1) showed severe normocytic anemia and thrombocytopenia. Further investigations were indicative of hemolysis: elevated indirect bilirubin (3.84 mg/dL), elevated LDH (5559 IU/L) and low haptoglobin (<0.08 g/L). Peripheral smear showed hyper-segmented neutrophils, with no evidence of schistocytes. She has a normal ferritin level, a negative direct and indirect Coombs test, and a reticulocyte production index of 0.52; which indicates an inappropriate bone marrow response. Vitamin B12 and folate levels were barely detectable (<83 pg/mL and <2 ng/mL respectively). TSH level was within normal range.

Serology testing was negative for cytomegalovirus, Epstein–Barr virus, parvovirus B19, human immunodeficiency virus, as well as hepatitis B and C viruses. Bone marrow aspirate was performed; and findings were consistent with normal cellularity and different cell types at various stages of maturation with no detected dysplastic alterations. A thoracic and abdominal CT scan was done and showed no evidence of hepatomegaly, splenomegaly or lymphadenopathy.

Gastroscopy was performed and was consistent with atrophic gastritis suggestive of pernicious anemia. Anti-intrinsic factor and anti-parietal cells antibodies were requested; however they were not done due to financial problems.

After inquiry, she was found to follow a vegan diet. She was never hospitalized before, and she has never received transfusions.

She was started on intravenous hydration and received packed red blood cells transfusions, as well as daily intramuscular injections of 1000 mcg vitamin B12, and oral folic acid supplementation. The thrombocytopenia worsened during the first four days, then improved significantly with normal level (209,000/microL) attained at day eight of starting vitamin B12 supplementation.

Table 1: Laboratory findings.

Parameters	Reference values	Results upon admission
Hemoglobin	12.0-14.5 g/dL	3
Hematocrit	31-45 %	9
Mean Corpuscular Volume	75-89 fL	90
Platelet	150-450 x 10^9/L	60
White Blood Cell	4-12 x 10^9/L	3.5
Creatinine	0.74 to 1.35 mg/dL	0.8
Alanine Transaminase	4 to 36 U/L	24
Aspartate Transaminase	8 to 33 U/L	25
Gamma Glutamyl Transferase	0 to 30 IU/L	21
Alkaline Phosphatase	44 to 147 IU/L	60
International normalized ratio	0.8-1.1	1
Activated partial thromboplastin time	30-40 seconds	35 seconds
Reticulocyte	0.5-1.5%	2.22
Fibrinogen	1.5-4.1 pm/L	1.5
LDH	125-220 U/L	5990
Ferritin	11 to 307 mg/L	120
Indirect Bilirubin	0.2-0.8 mg/dL	3.84
Haptoglobin	0.5-2.2 g/L g/L	<0.08
Direct Coombs	NA	Negative
Indirect Combs	NA	Negative
Schistocytes	Less than 0.2%	Absent
Thyroid stimulating hormone	0.4 to 4.0 mIU/L	2
Vitamin B12	138-652 pmol/L	83
Folate	2.7 to 17.0 ng/mL	2

NA: Not available.

Discussion

The patient presented with symptoms of fatigue and dyspnea. Her initial workup revealed severe nonautoimmune hemolytic anemia and thrombocytopenia. The most important concern was to rule out Thrombotic Thrombocytopenic Purpura (TTP) as a differential diagnosis, since it is an emergency and requires prompt recognition and management [4]. However, the absence of fever or altered mental status on presentation, as well as the absence of schistocytes on peripheral smear, in the setting of normal creatinine level have make the diagnosis of TTP unlikely in this case.

Hemolytic anemia can also be triggered by viral infections. In fact, coombs-negative cytomegalovirus induced severe hemolysis has been described in the literature [5] and acute hemolytic anemia can occur in 1 to 3% of patients with infectious mononucleosis [6]. Hemolytic anemia may also occur in the course of parvovirus infection [7], Influenza A, herpes simplex virus, and rarely hepatitis B virus infection [8]. Viral serologies were negative in this case excluding the possibility of an underlying viral infection.

After an extensive anemia workup, very low vitamin B12 and folate levels were detected along with hyper segmented neutrophils. Vitamin B12 deficiency was considered as the culprit of the hemolytic anemia and thrombocytopenia. In addition, the initiation of cyanocobalamin supplementation has resulted in significant clinical as well as hematological improvement.

Although there are numerous causes of non-autoimmune hemolytic anemia; few cases described in the literature were related to Vitamin B12 deficiency [9,10].

Vitamin B12 is naturally found in meat, milk, egg, fish, and shellfish [11]. Deficiency of vitamin B12 is usually caused by decreased absorption, mainly in conditions such as history of lineal resections and pernicious anemia [12]. The latter is an autoimmune condition characterized by the presence of anti-intrinsic factor antibodies; leading to impaired absorption of Vitamin b12 at the level of terminal ileum and subsequent Vitamin B12 deficiency [13].Vitamin B12 deficiency can also be secondary to decreased intake. Strict vegetarians are predisposed to a greater risk of developing vitamin B12 deficiency [14]. Large stores of vitamin B12 are present in the adult liver; but a strict vegan diet for approximately three years can be sufficient to cause B12 deficiency [12]. Patient with vitamin B12 deficiency are at risk of developing hematological complications, neurological complications such as peripheral neuropathy, subacute combined degeneration of the cord, as well as neuropsychiatric complications such as delirium and psychosis [15].

The ineffective erythropoiesis in the setting of Vitamin B12 deficiency can lead to intramedullary hemolysis and it can cause release of lactate dehydrogenase, characteristics that are also present in case of microangiopathic hemolytic anemia [1]. Although the mechanism is not well clear, 1.5% of patients with vitamin B12 deficiency present with findings of a hemolytic anemia. In fact, Elevated homocysteine levels and the pro-oxidative qualities of homocysteine can lead to intramedullary hemolysis [16].

This patient in this case has characteristic findings on gastroscopy that are very suggestive of pernicious anemia; and she was also a strict vegetarian. Both conditions may have contribute to the severity of her presentation.

Severe vitamin B12 deficiency can present with potential serious neuro-psychiatric and hematological complications [17]. Previous cases showed significant improvement in hematological parameters after initiation treatment with cobalamin [18].This patient also was able to be discharged soon after initiation of cobalamin supplementation.

Conclusion

Hemolytic anemia secondary to vitamin B12 deficiency is a rare and serious condition which is sometimes unrecognized. High clinical suspicion is warranted especially in patients following vegan diet presenting with severe anemia; in order to make early diagnosis and initiate treatment. Improvement of hematological findings was noted in this case once the patient was started on cobalamin supplementation.

Declarations

Declaration of patient consent: Informed consent was obtained from the patient described in this report.

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Conflicts of interest: The authors have no conflicts of interest to declare.

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