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CASE REPORT

Vitamin B12 deficiency: an unusual presentation. Case report

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Abstract

Vitamin B12 or cobalamin is a water-soluble vitamin absorbed in the terminal ileum after binding to intrinsic factor and has important physiologic roles in haematopoiesis, intermediary metabolism, growth, and early brain development. Vitamin B12 deficiency usually causes anaemia, macrocytosis, leukopenia, hyper-segmented neutrophils, and thrombocytopenia. Although most of the vitamin B12-deficient cases have only mild haematological findings, in approximately 10% of patients, life-threatening conditions, such as symptomatic pancytopenia, severe anaemia (haemoglobin level < 6 g/dL), and haemolytic anaemia, have been reported. Since the clinical findings of B12 deficiency are nonspecific, they are often overlooked, leading to a delay in the diagnosis. In this report we describe the case of a 16-year-old boy who presented with severe haemolytic anaemia and pancytopenia secondary to vitamin B12 deficiency, which resolved completely following appropriate replacement therapy.

Keywords: Vitamin B12 deficiency. Haemolytic anaemia. Pancytopenia. Adolescent. Case report.

Défice de vitamina B12: uma apresentação invulgar. Caso clínico

Resumo

A vitamina B12 ou cobalamina, é uma vitamina hidrossolúvel, absorvida no íleon terminal, após ligação ao fator intrínseco, e desempenha um papel fisiológico importante na hematopoiese, metabolismo intermediário, crescimento e desenvolbolmento cerebral. O défice de vitamina B12, geralmente causa anemia macrocítica, leucopenia, neutrófilos hipersegmentados e trombocitopenia. Embora na maioria dos casos o défice de vitamina B12 produza apenas achados hematológicos ligeiros, em aproximadamente 10% dos casos, foram descritos condições ameaçadoras da vida, como pancitopenia sintomática, anemia grave (hemoglobina < 6 g/dL) e anemia hemolítica. Uma vez que os achados de défice de vitamina B12 são inespecíficos, são mutias vezes subvalorizados, levando a um atraso no diagnóstico. Neste artigo, descrevemos o caso de um adolescente de 16 anos, que se apresentou com anemia hemolítica grave e pancitopenia secundárias a défice de vitamina B12, achados que resolveram completamante após terapêutica de reposição apropriada.

Palavras-chave: Défice de vitamina B12. Anemia hemolítica. Pancitopenia. Adolescente. Caso clínico.

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Keypoints

What is known

– Vitamin B12 deficiency is a rare a but treatable cause of pancytopenia.
– The clinical features of cobalamin deficiency are unspecific and may involve both haematological, and neurological systems.
– The clinical presentation of vitamin B12 deficiency can mimic leukaemia, hemophagocytic lymphohistiocytosis, and thrombotic microangiopathy.

What is added

– It is important to include vitamin B12 deficiency in the differential diagnosis of severe anaemia, even in the absence of strict vegetarianism.
– Vitamin B12 deficiency can be the cause of severe anaemia despite the absence of typical haematological findings, as in this patient, where at presentation typical findings of megaloblastic anaemia were not clear in the blood count or peripheral blood smear.
– A correct diagnosis, and timely treatment can prevent long-term damage, even in cases where severe haematological findings are already present.

Introduction

Vitamin B12, or cobalamin, is a water-soluble vitamin which is synthesized by bacteria and archaea. It is absorbed in the terminal ileum after binding to intrinsic factor, which is produced by the parietal cells in the stomach. Vitamin B12 deficiency usually causes anaemia, macrocytosis, leukopenia, hyper-segmented neutrophils, and thrombocytopenia[1].

Although most of the vitamin B12-deficiency cases have only mild haematological findings, in approximately 10% of patients, life-threatening conditions such as symptomatic pancytopenia, severe anaemia (haemoglobin level < 6 g/dL), and haemolytic anaemia have been reported[2].

In this report we describe the case of a 16-year-old boy who presented with severe haemolytic anaemia and pancytopenia secondary to vitamin B12 deficiency, which resolved completely following appropriate replacement therapy.

Case report

A 16-year-old, previously healthy, black male was brought to the emergency department (ED) with fever, and incoherent speech. In the week preceding the admission he had been suffering with abdominal pain, and vomiting. For this reason, he had already accessed primary care and was given probiotics and oral rehydration solution. Additionally, his brother mentioned an unquantified unspecified weight loss during the previous month. He had no history of dietary restrictions, no smoking, alcohol, or drug intake habits. There was no mention of nitrogen protoxide use, but it was not specifically asked.

Physical examination on the ED was remarkable for a Glasgow Coma Scale of 12, with no other neurological signs, muco-cutaneous paleness, icterus of the sclera, and enlarged spleen and liver with no other significant findings.

A preliminary laboratory investigation revealed pancytopenia (haemoglobin 3g/dL [N13-17], Mean Corpuscular Volume [MCV] 93 fL, leucocytes 2,96 x 10 ^ 9/uL [N 4,5-13] with neutrophils 980 x 10 ^ 9/uL [N 1500-8000] and lymphocytes 1550 x 10 ^ 9/uL [N 1000-4800], platelets 75 x 10 ^ 9/uL [N 150-400], reticulocytes 3,1% [N < 2]); high serum levels of indirect bilirubin (2.05 mg/dL N [0-0.8]), lactate dehydrogenase > 5000 U/L (N 135-225), aspartate aminotransferase 100 U/L (N 8-40). Coagulation values were normal (prothrombin time 13.8s [N 11.4-13.8], activated thromboplastin time 22,8s [N 21.4-31.2s] and INR 1.22). Fibrinogen was also within a normal range of 181 mg/dL (N 108-350). Kidney function was preserved with a urea 24 mg/dL and creatinine 0.59 mg/dL.

The peripheral blood smear showed anisocytosis, poikilocytosis with schistocytes, target cells, pencil cells, and erythroblasts (25/100 leucocytes). Uric acid, C reactive protein were normal. Direct Coombs test was negative. The chest X-ray was normal.

Treatment was started immediately with red blood cell transfusion (20ml/kg), and platelet pool transfusion. At this point 4g IV plasma, and IV fibrinogen reposition (1g) were also started, prior to the clotting laboratory results being known, due to concerns as to a possible hidden haemorrhage.

After the red blood cell transfusion, the adolescent showed signs of neurological improvement, with a GCS of 14, and was admitted for further investigation.

A more detailed etiological study showed a low vitamin B12 with 146pg/mL (N 211-911pg/mL). Homocysteine and methylmalonic acid were not obtained before starting treatment. Bone marrow aspiration ruled out leukaemia and the smear was compatible with megaloblastic anaemia. Normal activity levels for ADAMTS 13 excluded thrombocytopenic thrombotic purpura. Hemophagocytic

lymphohistiocytosis was dismissed since ferritin, fibrinogen, CRP, and triglycerides were within normal range, and bone marrow aspiration showed no signs of hemophagocytosis or macrophage infiltrates. Recent infection with Epstein-Barr virus, cytomegalovirus, or parvovirus B19 were ruled out by serology.

The cause of the vitamin B12 deficiency has yet to be determined, even after extensive investigation. The clinical history was revised with the patient and his family, establishing that he did not follow a strict vegan diet. There was no evidence of pernicious anaemia since the search for helicobacter pylori was negative and both the intrinsic factor and parietal cell antibodies were negative. The anti-transglutaminase IgA antibody was negative, which allowed us to exclude celiac sprue as well. Inflammatory bowel disease was ruled out after faecal calprotectin level, and upper GI tract endoscopy and colonoscopy were all normal, with biopsies exhibiting no abnormal findings. Intestinal parasitosis was also excluded as no helminths or protozoa were found in faecal testing.

Oral folic acid supplementation and daily Vitamin B12 IM administration was started and after 14 days the patient showed clinical improvement with complete neurologic recovery and significant weight gain (5.5 kg, about 9% of total body weight).

Upon discharge, he kept regular follow-up in the haematology clinic. There has been no recurrence of symptoms, with sustained values for haemoglobin with monthly cobalamin IM administrations.

Discussion

Clinical and haematological improvement upon supplementation with both vitamin B12 and folate after immediate transfusion with 20ml/kg red blood cells, as well as extensive etiological investigation with no other significant findings other than low levels of cobalamin and a bone marrow smear with aspects compatible with megaloblastic anaemia support vitamin B12 deficiency as the cause for this presentation, even though the cause of this deficiency has yet to become clear.

Although the patient was not strictly vegetarian, the family struggled economically, leading to an imbalanced diet which might have caused this vitamin deficit. Supporting this hypothesis is the nutritional study with low pre-albumin level (13.6 g/dL) and low serum total protein levels (5.9 g/dL), despite an albumin within normal range (4 g/dL).

The cause of the fever at presentation was not determined, but normal CRP levels and negative blood, urine, and stool cultures and a normal chest radiography excluded bacterial infection, with a viral etiology becoming more likely and possibly triggering the clinical presentation of severe chronic anaemia.

Vitamin B12 has important physiological roles in haematopoiesis, intermediary metabolism, growth, and early brain development[3,4]. The human species does not synthesize B12, so exogenous intake is crucial[5], and an inadequate dietary intake or impaired absorption are the most common causes of B12 deficiency[6].

Clinical features of B12 deficiency may include, besides the macrocytic anaemia, neurological, and gastrointestinal symptoms such as lethargy, hypotonia, psychomotor delay or regression; tremor; seizures; encephalopathy; irritability; weakness; diarrhoea; stomatitis; glossitis, and failure to thrive[3-8].

Since these clinical findings of B12 deficiency are nonspecific, they are often overlooked, leading to a delay in the diagnosis. Although supplementation with vitamin B12 quickly reverses the haematological abnormalities, the neurological manifestations may not completely resolve if not treated promptly[3,7].

This case is an example of an uncommon presentation of vitamin B12 deficiency and shows the importance of searching for this vitamin deficiency in such clinical settings and treating it despite not having completely clarified the cause, as a timely recognition and appropriate treatment are fundamental for the complete remission of symptoms and prevention of long-time damage.

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Conflicts of interest

None.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

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