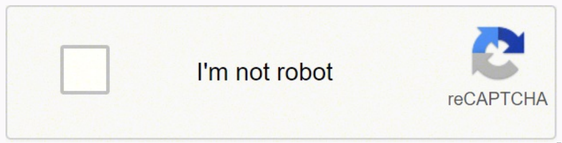

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Neurological, Hematological and Dermatological Manifestations of Vitamin B_{12} Deficiency Secondary to Pernicious Anemia; A Case Report and Literature Review

Abstract

Background: Vitamin B_{12} is a water-soluble essential vitamin. It is essential for the rapid synthesis of deoxyribonucleic acid (DNA) during cell division and thus formation of red blood cells and maintenance of a healthy nervous system as well as the skin. It is found mainly in food of animal origin (e.g. meat, eggs, and dairy products and lacks a reliable plant source. Deficiency occurs due to either poor intake or decreased absorption. Among the most common causes are: pernicious anemia, atrophic gastritis, celiac disease or following gastric surgery. Deficiency of this essential vitamin can lead to potentially irreversible neurological, psychiatric, hematological and/or dermatological symptoms.

Case Summary: We report a case of a 46-year–old omnivorous male patient who presented with gradual onset of weakness and spasticity of both lower limbs and upper limbs, paraesthesia of all limbs with loss of joint position and vibration sensation. These symptoms were associated with memory changes, weight loss and hyperpigmentation of the skin. Magnetic resonance imaging (MRI) showed a long demyelinating lesion in the cervical spinal cord. Extensive laboratory investigations were performed that confirmed vitamin B_{12} deficiency and ruled out other common mimics associated with that condition. He had marked improvement of all his neurological and non-neurological symptoms following vitamin B_{12} supplementation with complete resolution of the cervical demyelinating lesion within 3 months.

Conclusion: Vitamin B_{12} deficiency is a common but under-diagnosed clinical condition that needs to be highlighted. It can present with neurological, psychiatric, hematological and/or dermatological manifestations. It is uncommon to see the whole systems affected together early in the course of the disease. Early diagnosis and treatment may reverse potentially permanent symptoms and signs and can prevent the disability that would otherwise ensue if left untreated. Pernicious anemia is one of the most common causes of vitamin B_{12} deficiency and should be ruled out in all cases even if autoantibodies against intrinsic factor and parietal cells are negative.

Keywords: Vitamin B_{12}; Cobolamin; Methylmalonic Acid; Homocysteine; Megaloblastic Anemia; SCD (subacute combined degeneration); Pernicious Anemia

Case Report

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Introduction

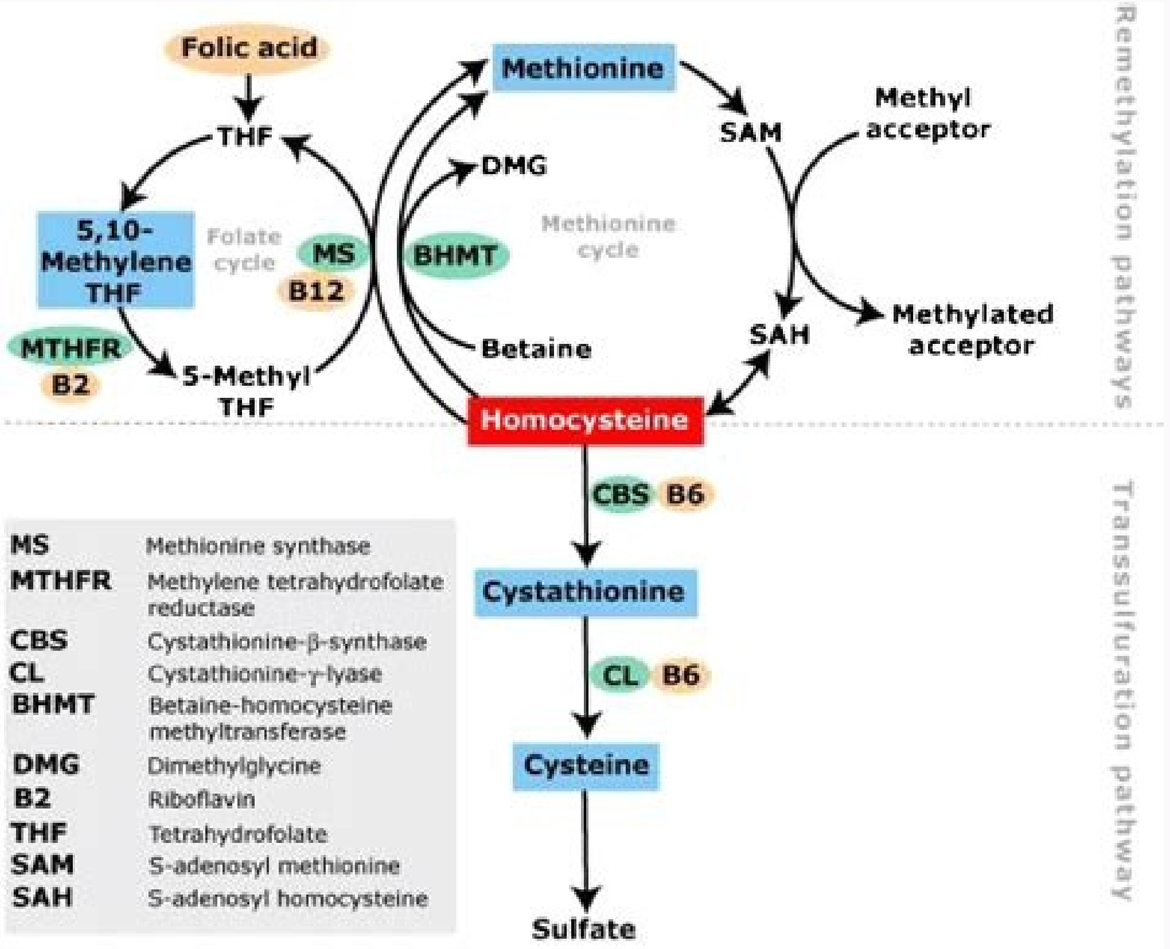
Patients with vitamin B_{12} deficiency can present to different specialties with different types of symptoms. Unless kept in mind in the differential diagnosis, this condition can be easily missed. Deficiency of this vitamin can negatively affect the brain and blood cells as well as the hair and skin. One of the most common causes is Pernicious Anemia (PA) which is a disease that can be fatal if untreated. It has been an area of interest long time ago to the extent that a Nobel Prize was awarded in the past century for the discovery of effective treatment [1].

Case Report

A 46-year-old, Kuwaiti, overweight, omnivorous male, with no family history of autoimmune disease, presented with a subacute progressive course of lower limb numbness, gait abnormality, sense of imbalance, weakness and stiffness of both lower limbs of one month duration prior to admission. Weakness and numbness progressed to involve both upper limbs within 2 weeks of the onset.

He had a history of chronic gastritis for 5 years with recurrent *H. pylori* infection for which he had received recurrent courses of antibiotics in the form of amoxicillin, and clarithromycin with omeprazole. Upper GI endoscopy was performed previously and showed atrophic gastritis and multiple gastric ulcers.

He, also had generalized fatigue, muscle aches, poor food intake with significant weight loss (20kg in 2 years) and heart palpitations. His family also noted a recent decline in his memory with poor attention and concentration. They also noted the darkening of his skin in the past 6 months.



Vitamin B_{12} deficiency

Ralph Green[1], Lindsay H. Allen[2], Anne-Lise Bjørke-Monsen[3], Alex Brito[2], Jean-Louis Guéant[4], Joshua W. Miller[5], Anne M. Molloy[6], Ebba Nexo[7], Sally Stabler[8], Ban-Hock Toh[9], Per Magne Ueland[5,10] and Chittaranjan Yajnik[11]

Abstract | Vitamin B_{12} (B12; also known as cobalamin) is a B vitamin that has an important role in cellular metabolism, especially in DNA synthesis, methylation and mitochondrial metabolism. Clinical B12 deficiency with classic haematological and neurological manifestations is relatively uncommon. However, subclinical deficiency affects between 2.5% and 26% of the general population depending on the definition used, although the clinical relevance is unclear. B12 deficiency can affect individuals at all ages, but most particularly elderly individuals. Infants, children, adolescents and women of reproductive age are also at high risk of deficiency in populations where dietary intake of B12-containing animal-derived foods is restricted. Deficiency is caused by either inadequate intake, inadequate bioavailability or malabsorption. Disruption of B12 transport in the blood, or impaired cellular uptake or metabolism causes an intracellular deficiency. Diagnostic biomarkers for B12 status include decreased levels of circulating total B12 and transcobalamin-bound B12, and abnormally increased levels of homocysteine and methylmalonic acid. However, the exact cut-offs to classify clinical and subclinical deficiency remain debated. Management depends on B12 supplementation, either via high-dose oral routes or via parenteral administration. This Primer describes the current knowledge surrounding B12 deficiency, and highlights improvements in diagnostic methods as well as shifting concepts about the prevalence, causes and manifestations of B12 deficiency.

Vitamin B_{12} (B12; also known as cobalamin) is one of eight B vitamins and its role in cellular metabolism is closely intertwined with that of folate, another B vitamin (FIG. 1). Since the discovery and characterization of B12 more than 60 years ago and the recognition of its central role in preventing the serious disease known as pernicious anaemia, much has become known about B12 deficiency[1,2]. Pernicious anaemia originally acquired its appropriate eponym because of the ultimately fatal haematological and devastating neurological manifestations of the disease and was later shown to be caused by autoimmune destruction of gastric parietal cells and their product, intrinsic factor (also known as gastric intrinsic factor), which is required for B12 absorption. Previously considered to be a nutritional deficiency disease that was largely caused by malabsorption of the vitamin and restricted to older people, particularly those of North European descent, B12 deficiency is now considered to be a problem of global dimensions, frequently caused by dietary inadequacy, particularly among children and in women of reproductive age[2].

The effects of B12 deficiency are mainly seen in the blood and nervous system. The classic manifestations of B12 deficiency were first identified in pernicious anaemia, the cause of which was then unknown[3,4]. Since then, the spectrum has shifted considerably, starting with the renewed recognition that neurological manifestations (such as sensory and motor disturbances (particularly in the lower extremities), ataxia, cognitive decline leading to dementia and psychiatric disorders) often predominate and can frequently occur in the absence of haematological complications[5]. In addition, the identification of subtler degrees of B12 deficiency[2], made possible by the introduction of assays for the metabolites methylmalonic acid (MMA) and homocysteine in clinical practice[6,7] (FIG. 1), has broadened the landscape of what might be attributable to B12 deficiency, but has opened a Pandora's box of controversy regarding what could be considered actual, clinical B12 deficiency as opposed to states of metabolic inadequacy of the vitamin[7,8]. Progression from normalcy to clinical deficiency passes through a stage of inadequacy during which biochemical evidence of B12 insufficiency in the form of increased blood and tissue levels of MMA and homocysteine and declining levels of the portion of B12 bound to transcobalamin (known as holotranscobalamin) precede the appearance of any morbid manifestations of deficiency. This condition has also been referred to as 'subclinical' B12 deficiency and is associated with low or marginal B12 levels[9,10]. Individuals with biomarkers indicating a subclinical deficiency are

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Case Reports

Vitamin B_{12} Deficiency presenting as Pyrexia

RC Negi*, J Kumar, V Kumar**, K Singh**, V Bharti**, D Gupta *, R Kashyap **, S Raina ****

Abstract

Vitamin B_{12} deficiency is an uncommon cause of pyrexia. We report the case of a patient who presented with pyrexia and anaemia, which after exclusion of infective, inflammatory or endocrine causes was attributed to megaloblastic anaemia secondary to vitamin B_{12} deficiency. The patient's fever responded to treatment of vitamin B_{12} deficiency.

Introduction

Megaloblastic anaemia has been reported as a cause of pyrexia and, though rare, is a treatable cause of pyrexia. The potential pathophysiological mechanisms responsible for pyrexia in megaloblastic anaemia are proposed. Megaloblastic anaemia (vitamin B_{12}, folate deficiency) is a reversible cause of pyrexia that should be considered in any patient who presents with pyrexia and pancytopenia.

Case Presentation

A 18 year old male, pure vegetarian since birth, having regular fasts for two months, presented with easy fatigability for one month and high grade pyrexia (upto 104°F) for the last three days. There was no history of cough, headache, rash, arthralgia, urinary or bowel disturbances. There was no history of visit to malaria endemic area and no significant past history. Examination of the patient revealed pulse -118/min, BP -110/60 mm of Hg, temp-103.6° F and marked pallor. There was no icterus, lymphadenopathy, rashes or eschar. There was presence of bald glossy tongue and hyperpigmentation of knuckles. Cardiovascular system examination revealed loud S, and ejection systolic murmur in pulmonary area. Abdominal examination showed mild splenomegaly. Chest and nervous system examination was normal. The profile of complete haemogram at admission is shown in Table 1.Peripheral smear was suggestive of dimorphic anaemia with pancytopenia. Biochemical examination was completely normal. Urine microscopy, gram stain, Z-N stain and KOH mount was normal. Blood and urine cultures were sterile. Weil felix test was negative. Chest X-ray was normal and ultrasonography of abdomen revealed mild splenomegaly only. Based on low neutrophil count on haematological investigation, patient was managed with broad spectrum antibiotics. During third day of hospital stay patient developed severe epistaxis which was managed with two units of platelet concentrate. Patient's CT chest done on fifth day of hospital stay was normal and bone marrow examination revealed severe dimorphic anaemia with pancytopenia without presence of any parasite or granuloma. Patient was still febrile. Vitamin B12 level was 105 pg/ml (normal 140-180 pg/ml) and folate level was 5.05µg/L (normal).Patient's ANA and CRP levels were normal. Patient was started on injection cyanocobalamin 1000 mcg od. Seventy two hours after starting treatment of megaloblastic anaemia, patient was afebrile and remained so thereafter. Patient's antibiotics were stopped and was discharged after next three days. On follow up after two weeks, patients haematological examination revealed correction of anaemia and thrombocytopenia (Table 1). On follow up patient's thyroid function tests were done, which were normal.

Table 1 : Serial hemogram before and after treatment

Parameter	During admission	2 weeks after treatment
Hemoglobin (gm%)	3.8	10.0
MCV (80-100 fl)	105	90
MCH (25-32 pg)	30	32
TLC (cells/cumm)	3200	9200
DLC		
Polymorphs	25	60
Lymphocytes	73	38
Monocytes	1	1
Eosinophils	1	1
Platelets (per cumm)	18000	1,67,000
ESR (mm 1st hr)	12	13

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Discussion

Pyrexia is a feature of megaloblastic anaemia that has been described previously in the literature,[1,2,5] and is thought to be more common in patients with moderate to severe anaemia and thrombocytopenia.[3]

The exact cause of pyrexia in megaloblastic anaemia is not known and previously it has been hypothesised that it may reflect a defect in oxygenation to the temperature regulatory centres in the brain.[3] However, this theory does not explain why the fever seen in patients with megaloblastic anaemia is not a recognised feature of other forms of anaemia. Another proposed mechanism is that megaloblastic anaemia leads to hyperplasia and thus increased activity within the bone marrow leading to systemic pyrexia.[3,5] The mechanism of how pyrexia is induced by an over-productive marrow is, however, unclear.

The level of pyrexia usually correlates with degree of anaemia and resolves one to three days after adequate vitamin supplementation,[4,5] as also illustrated by the case we present and this is felt to be due to immediate improvement in ineffective erythropoiesis.[1]

Patients presenting with fever, anaemia, neutropenia and thrombocytopenia are usually treated on the lines of febrile neutropenia with broad spectrum antibiotics, which if caused by megaloblastic anaemia leads to unnecessary antibiotic use and investigations. Megaloblastic anaemia, though rare, is a treatable

Vitamin b12 anemia ppt. Vitamin b12 anemia deficiency. Vitamin b12 anemia causes. Vitamin b12 anemia treatment. Vitamin b12 anemia symptoms. Vitamin b12 anemia pathophysiology. Vitamin b12 anemia labs. Vitamin b12 anemia diagnosis.

B12 supplements and injections are considered safe and well tolerated, even in large doses (1). However, that does not mean children and younger adults, including those who are pregnant and nursing, may not develop B12 deficiency (5, 6). Unfortunately, B12 deficiency is often overlooked and misdiagnosed. The cells in your body need B12 to function properly. Because a B12 deficiency has a negative impact on the central nervous system, people with LOW or B12 deficiency may feel foggy and have difficulty concentrating and completing tasks (21). Adults coming are particularly at risk for these side effects because the risk of B12 Deficiency increases with age. In fact, many studies have associated low B12 levels with worsening mental function in older adults (22, 23).Fortunately, studies show that mental impairment related to B12 levels can improve with B12 treatment. 2020 Study gave 202 people with mild mental insufficiency and low or normal low B12 levels and homocysteine eleine levels. B12 Replacement therapy for 3 months (21). After treatment, 84% of participants reported significant improvements in symptoms, such as poor attention, decline in memory and forgetfulness (21).Glossitis is a medical term that refers to an inflamed, red and painful tongue. B12 deficiency negatively impacts motor and sensory nerve function, which can cause muscle cramps and weakness (7, 27). Coordination similar. B12 deficiency can cause a variety of symptoms, including fatigue, headache, depression, pale or yellow skin, mental impairment and pain and inflammation of the mouth and tongue. Mill symptoms caused by low B12 levels are not specific to B12 deficiency, which can cause the condition not detected. If you are experiencing any of the above symptoms, it is important to visit a healthcare professional to take appropriate tests and get the right treatment. Written by Jillian Kubala, MS, RD RD Reviewed by Meredith Goodwin, MD, FAAFP - updated December 22, 2021Vitamin B12 is an essential nutrient that your body needs processes, such as DNA synthesis, energy production and the function of the central nervous system (1). Although vitamin is found in many foods, insufficiency and deficiency B12 are relatively common. Men with B12 deficiency can experience erectile dysfunction due to higher levels of homocysteine in the body (28). Visions. Last reviewed Once-reviewed Reviewed The â €

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