International Journal of Current Research in Medical Sciences
ISSN: 2454-5716
(A Peer Reviewed, Indexed and Open Access Journal)
www.ijcrims.com

Review Article

Volume 7, Issue 5 -2021

DOI: http://dx.doi.org/10.22192/ijcrms.2021.07.05.003

Megaloblastic Anaemia - A Review

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Abstract

Megaloblastic anemia is type anemia, which is caused by inhibition of DNA synthesis during erythropoiesis. The most common cause of defects in red blood cell DNA synthesis is vitamin deficiency, especially vitamin B12 deficiency or folic acid deficiency. Micronutrient loss can also be a cause. Moderate deficiency can include swollen tongue and neurological problems, including abnormal sensations such as a tingling sensation, while severe deficiency can include decreased heart function and more serious neurological problems.

Keywords: megaloblastic anemia, vitamin B 12 deficiency, folic acid deficiency

Introduction

Megaloblastic anemia is an anemia , the reason is that DNA synthesis is inhibited in the red blood cell production process (eMedicine, Year 2009). When DNA synthesis is impaired, the cell cycle cannot progress from the G2 growth phase to the mitotic (M) phase. This causes cells to continue growing without dividing, which manifests as megacytosis. Megaloblastic anemia has a slower onset, especially compared to other anemias. The most common cause of defects in red blood cell DNA synthesis is vitamin deficiency, especially vitamin B12 deficiency or folic acid deficiency. The loss of micronutrients can also be a cause. It has been found that excessive amounts of zinc caused by excessive oral consumption of zinc-containing denture fixation creams lead to copper deficiency (Berkowitz, 2012). Megaloblastic anemia caused by non-vitamin deficiency can be caused by antimetabolites that directly poison DNA production, such as certain chemotherapeutic drugs or antibacterial drugs (such as azathioprine or trimethoprim).

The disease state of megaloblastosis is characterized by the presence of many large, immature, and dysfunctional red blood cells (megaloblasts) in the bone marrow, as well as excessive division of neutrophils (defined as the presence of six or more Leaf neutrophils may have more than 3% neutrophils with at least five leaves) (Bain, 2016). These highly segmented neutrophils can be detected in peripheral blood.

Reason

1. Vitamin B12 deficiency:

Vitamin B12 deficiency, also known as cobalamin deficiency, is a disease with low levels of vitamin B12 in the blood (Herrmann, 2011). In a mild deficiency, a person may feel tired and the number of red blood cells decreases (Hunt, 2017).

A moderate deficiency can cause inflammation of the tongue and the onset of neurological problems, including abnormal sensations such as a tingling sensation, while a severe deficiency can include decreased heart function and more serious neurological problems. Nervous system problems can include reflex changes, poor muscle function, memory problems, decreased taste, and in extreme cases, psychosis. Sometimes temporary infertility can occur. Symptoms in young children include poor growth, delayed growth, and difficulty moving. Without early treatment, some changes can be permanent (Lachner, 2012).
Common causes include gastric or intestinal malabsorption, reduced intake, and increased demand. Reduced absorption can be due to pernicious anemia, gastrectomy, chronic inflammation of the pancreas, intestinal parasites, certain medications, and certain genetic diseases (Hunt, 2017). Vegetarians or malnourished people can reduce their intake. People with HIV/AIDS and people with rapid red blood cell degradation are in greater demand (Hunt, 2017). The diagnosis is usually based on blood levels of vitamin B12. Elevated levels of methylmalonic acid may also indicate deficiency. There is usually an anemia called megaloblastic anemia, but this is not always the case.

Treatment includes oral or injection of vitamin B12; high doses are initially taken daily, and then the dose is reduced as the condition improves (Wang, 2018) If a reversible cause is found, the cause should be addressed as much as possible (Hankey, 2008).

If a reversible cause is not found or cannot be eliminated, supplementing with vitamin B12 for life is generally recommended. Vitamin B12 deficiency can be prevented with vitamin supplements: it is recommended for pregnant vegetarians and vegans, and it is harmless for others. The risk of toxicity caused by vitamin B12 is very low (Health Professional Fact Sheet, 2016)
The incidence of vitamin B12 deficiency in people under 60 years of age in the United States and the United Kingdom is estimated to be around 6 %, and the incidence in people over 60 years of age is approximately 20%. 60 years old. In Latin America, this proportion is estimated to be 40% and may reach 80% in parts of Africa and Asia (Hunt, 2017).

Signs and symptoms

Vitamin B12 deficiency can cause anemia and neurological diseases. A mild deficiency may not cause any obvious symptoms, but as the deficiency becomes more severe, symptoms of anemia may appear, such as weakness, fatigue, dizziness, rapid heartbeat, shortness of breath, and pale skin. It can also cause easy bruising or bleeding, including bleeding gums, gastrointestinal side effects, including sore tongue, stomach upset, weight loss, diarrhea or constipation. If the defect is not corrected, it may cause nerve cell damage. If this happens, vitamin B12 deficiency can cause tingling or numbness in fingers and toes, difficulty walking, mood swings, depression, memory loss, disorientation, and in severe cases, dementia.

The main type of vitamin B 12 deficiency anemia is pernicious anemia. It is characterized by the triad:
1. Anaemia with pre-myelomegalocytosis (megaloblastic anemia). This is due to the inhibition of DNA synthesis (especially purine and thymidine).

2. Gastrointestinal symptoms: changes in bowel movements, such as mild diarrhea or constipation, and loss of bladder or bowel control. They are thought to be due to erroneous DNA synthesis that inhibits replication at sites with high cell turnover. **This** may also be due to the autoimmune attack of gastric parietal cells by pernicious anemia. It is related to GAVE

syndrome (often called watermelon stomach) and pernicious anemia.

3. Nervous system symptoms: sensory or motor deficits (loss of reflexes, weakened vibration or soft touch), subacute combined degeneration of the spinal cord, seizures, and even dementia or other psychiatric symptoms may occur. Symptoms of deficiency in children include developmental delay, degeneration, irritability, involuntary movements and hypotonia (Kliegman, 2016)

The presence of peripheral sensorimotor symptoms or subacute combined degeneration of the spinal cord clearly indicates a B12 deficiency rather than a folate deficiency. If B12 is not handled correctly, methylmalonic acid will remain in the myelin sheath, causing brittleness. Dementia and depression are also linked to this deficiency, possibly due to the inability to convert homocysteine to this product, leading to insufficient production of methionine. Methionine is an essential cofactor for the production of a variety of neurotransmitters.

Each of these symptoms may appear alone or in conjunction with other symptoms. The nervous system complex, defined as cord myelopathy, consists of the following symptoms:

1. Impaired deep touch, perception of pressure and vibration, loss of touch, very bothersome and persistent paresthesia
2. Spinal ataxia dorsal
3. Deep tendon reflex weakening or loss
4. Pathological reflex-Babinski, Rosolimo, etc., and severe paresis

Vitamin B12 deficiency can cause serious and irreversible damage, especially to the brain and nervous system. After correcting the hematological abnormalities, these neuronal damage symptoms may not be reversed, and as neurological symptoms appear, the chance of complete reversal decreases. The elderly are at higher risk of such damage (Stabler, 1997). In infants, due to the mother's malnutrition or pernicious anemia, many neurological symptoms may appear. These include slow growth, apathy, lack of food cravings, and developmental regression. Although most symptoms can be resolved with supplements, some cognitive and developmental problems may persist (Black, 2008)

Tinnitus may be related to vitamin B12 deficiency.

Cause

Insufficient dietary intake of vitamin B12. Vitamin B12 is found in animal products (eggs, meat, milk) and some edible algae (Croft, 2005). B12 isolated from bacterial cultures is also added to many fortified foods and can be used as a dietary supplement. If not supplemented, vegans and minor vegetarians may also be at risk for vitamin B12 deficiency due to insufficient dietary intake of vitamin B12. Due to insufficient dietary intake, children are at increased risk of vitamin B12 deficiency because they have less vitamin storage and relatively large vitamin needs from caloric intake from food.

Due to the lack of internal factors, the selective absorption of vitamin B12 is impaired. This may be due to loss of gastric parietal cells in chronic atrophic gastritis (in this case, the resulting megaloblastic anemia is called "pernicious anemia"), or it may be due to extensive gastric resection (for any reason), or due to Rare genetic causes, the synthesis of intrinsic factors is altered. B12 deficiency is more common in the elderly, because atrophic gastritis leads to a lack of gastric factors necessary for the absorption of vitamins.

In the case of a more extensive malabsorption syndrome or dyspepsia, the absorption of vitamin B12 is impaired. This includes any form due to structural damage or extensive surgical removal of the terminal ileum (the main site for vitamin B12 absorption).

Achlorhydria (including those artificially induced by drugs such as proton pump inhibitors and histamine 2 receptor antagonists) can cause malabsorption of B12 in food because acid is required to separate B12 from dietary proteins and saliva-binding proteins . This process is

considered to be the most common cause of low vitamin B12 levels in the elderly, who usually have some degree of achlorhydria without formal low intrinsic factor. This process does not affect the absorption of small amounts of B12 in supplements such as multivitamins, because it does not bind to protein, just like B12 in food.

Surgery to remove the small intestine (for example, in Crohn's disease), leaving the patient with short bowel syndrome and unable to absorb vitamin B12. This can be treated with regular injections of vitamin B12.

Long-term use of ranitidine hydrochloride can cause vitamin B12 deficiency.

Untreated celiac disease can also cause poor absorption of this vitamin, which may be due to damage to the lining of the small intestine. In some people, despite treatment with a gluten-free diet and the need for supplementation, vitamin B12 deficiency may persist.

Some bariatric surgeries, especially those that involve the removal of part of the stomach, such as RouxenY gastric bypass surgery. (Programs like the adjustable gastric band type do not appear to significantly affect B12 metabolism.)

Bacteria overgrowth in parts of the small intestine, such as can occur in blind loop syndrome (a condition caused by loop formation in the intestine), can cause these bacteria to increase intestinal vitamin B12 intake.

• The diabetes drug metformin may interfere with the dietary absorption of B12.
• Inherited diseases, transcobalamin II deficiency may be a cause.
• Alcoholism, if the “diet” of excessive drinking is replaced by an adequate diet containing B12 sources.
• Exposure to nitrous oxide and recreational uses.
• Tapeworm infection Diphyllobothrium latum
• Long-term exposure to toxin-producing molds and mycotoxins in water-damaged buildings.
• Increased body needs due to AIDS or hemolysis (breakdown of red blood cells).

1. Folic acid deficiency:

Folic acid deficiency is the low content of folic acid and its derivatives in the body. The signs of folate deficiency are usually subtle. Anemia is the late discovery of folic acid deficiency, and folic acid deficiency anemia is the term for this disease (Huether, 2004). It is characterized by the appearance of large abnormal red blood cells (megaloblasts), which are formed when folate storage in the body is insufficient (Tamparo, 2011)

Signs and symptoms

Loss of appetite and weight loss may occur. Other symptoms include weakness, tongue pain, headache, palpitations, irritability, and behavioral disturbances (Haslam, 1998). In adults, anemia (megaloblastic giant cell anemia) can be a sign of advanced folate deficiency.

Pregnant women with folic acid deficiency are more likely to deliver low birth weight premature babies and babies with neural tube defects. In infants and children, folic acid deficiency can lead to delayed or slower growth, diarrhea, mouth ulcers, megaloblastic anemia, and neurological impairment. Microcephaly, irritability, developmental delay, epilepsy, blindness, and cerebellar ataxia may also occur

Cause

When the body's need for folic acid increases, dietary intake or absorption of folic acid is insufficient, or the body excretes (or loses) more than usual Too much folic acid. Medications that interfere with the body's ability to use folic acid can also increase the demand for this vitamin. Some studies have shown that exposure to ultraviolet light, including the use of tanning beds, can cause folic acid deficiency. This deficiency is most common in pregnant women, infants, children, and adolescents. This may also be caused by poor eating habits or alcoholism.

Furthermore, the homocysteine methyltransferase defect or lack of B12 can lead to the so-called "methyl trap" of tetrahydrofolate (THF), in which

THF is converted to a store of methyltetrahydrofuran, which cannot be used later. Metabolism and as a sink for THF leading to subsequent folate deficiency. Therefore, B12 deficiency will produce a large amount of methyltetrahydrofuran, these methyltetrahydrofurans cannot react and will mimic folate deficiency.

Folic acid (pteroylmonoglutamate) is absorbed throughout the small intestine, although it is found primarily in the jejunum and binds to specific receptor proteins. Diffuse inflammation or degenerative diseases of the small intestine, such as Crohn's disease, celiac disease, chronic enteritis or intestinal fistula, can reduce the activity of pteroyl polyglutaminase (PPGH), necessary for the absorption of folic acid Hydrolase specific, leading to a deficiency of folate.

Situation

Some conditions that increase the need for folic acid include:
• Bleeding
• Kidney dialysis
• Liver disease
• Malabsorption, including celiac disease and fructose malabsorption
• Smoking during pregnancy and lactation (lactation)

Drink

2. Comprehensive deficiency: Vitamin B12 and folic acid.
3. Hereditary disorders of pyrimidine synthesis: orotic aciduria

Orotic aciduria (also known as hereditary orotic aciduria) is a disease in which the ability to synthesize pyrimidines is reduced by an enzyme deficiency. It is the only known enzyme deficiency in the de novo pyrimidine synthesis pathway.

Orotic aciduria is characterized by the inability to convert orotic acid to UMP, resulting in excessive secretion of orotic acid in the urine (Tao, 2017). It can cause megaloblastic anemia and may be related to physical and mental retardation.

4. Genetic diseases of DNA synthesis
5. Toxins and drugs:
o Folic acid antagonist (methotrexate)
o Purine synthesis antagonist (6-mercaptopurine)
o Pyrimidine antagonist (cytarabine)
Ni 4 4 4 4 4 Nickel Oxide Acute Leukemia

Erythroleukemia is a rare acute myeloid leukemia (less than 5% of AML cases) in which myeloproliferation is a precursor of erythroblasts. It is defined as "M6" based on FAB signs and symptoms. The most common symptoms of AEL are related to pancytopenia (shortage of blood cells of all kinds), including fatigue, infection, and bleeding in the skin and mucous membranes. Almost half of patients with AEL have weight loss, fever, and night sweats at the time of diagnosis. Almost all people with AEL are anemic, and 77% have hemoglobin levels below 10.0 g / dl. Signs of thrombocytopenia are found in approximately half of patients with AEL.

Cause

The cause of AEL is unknown. Prior to reclassification by the World Health Organization in 2008, cases evolving from myelodysplastic syndromes, myelodysplastic tumors, other cancer chemotherapy, or toxin exposure were defined as secondary AEL. These cases are now likely to be classified as acute myeloid leukemia with myelodysplasia-related changes or treatment-related AML.

1. Congenital mutation of the gene for methionine synthase
2. Di Guglielmo syndrome
3. Congenital erythropoiesis anemia

Diagnosis

The gold standard for diagnosing vitamin B12 deficiency is low levels of vitamin B12 in the blood. Low levels of vitamin B12 in the blood are

a finding and can and should usually be treated with injections, supplements or diet or lifestyle recommendations, but this is not a diagnosis. Vitamin B12 deficiency can be caused by a variety of mechanisms, including the mechanisms listed above. In order to determine the cause, further medical history, testing and empirical treatment may be required clinically.

Methylmalonic acid (methylmalonic acid) measurement can provide an indirect method to partially distinguish between vitamin B12 and folate deficiency. The methylmalonic acid level does not increase during folic acid deficiency. Direct measurement of cobalamin in blood remains the gold standard because the elevated methylmalonic acid test is not specific enough. Vitamin B12 is one of the prosthetic groups required for methylmalonyl-CoA mutase. Vitamin B12 deficiency is just one of the conditions that cause the accumulation of this enzyme dysfunction and its substrate, methylmalonic acid, and elevated levels of methylmalonic acid can be detected in urine and blood.

Due to the lack of available radioactive vitamin B12, the Schilling test is now largely a historical product. The Schilling test has been conducted in the past to help determine the nature of vitamin B12 deficiency. One advantage of the Schilling test is that it usually includes vitamin B12 with intrinsic factors.

Blood test results

A blood smear may indicate a vitamin deficiency:

• Red blood cell count (RBC) and hemoglobin level decreased
• Mean red blood cell volume (MCV,> 100 fl) and mean red blood cell hemoglobin (MCH) increased
• Average red blood cell hemoglobin level Normal concentration (MCHC, 32-36 g/dL)
• The count of reticulocytes decreases due to the destruction of abnormal and fragile megaloblast precursors.

The platelet count may decrease.

• Neutrophils can have multiple nuclei ("senile neutrophils"). This is believed to be due to the reduced production of circulating neutrophils and the compensatory extension of life span, which increases the number of nuclear segments with age. [Citation needed]

• Heterocytosis (increased changes in the size of red blood cells) and Heterocytosis (abnormal shape of red blood cells).

• There are giant cells (red blood cells that are larger than normal).

• There are oval cells (elliptical red blood cells).

• HowellJolly bodies (chromosome remnants) are also present.

Blood chemistry will also show:

• Increased levels of lactate dehydrogenase (LDH). The isoenzyme is LDH2, which is a typical serum and hematopoietic cell.

• Homocysteine and methylmalonic acid increase in vitamin B12 deficiency

• Homocysteine increases in folic acid deficiency
Normal levels of methylmalonic acid and total homocysteine can almost certainly be ruled out Clinically significant cobalamin deficiency.

The bone marrow (usually uncontrolled in patients with suspected megaloblastic anemia) shows megaloblastic hyperplasia.

Conclusion

Megaloblastic anemia is an anemia in caused by the inhibition of DNA synthesis during erythropoiesis. The most common cause of defects in red blood cell DNA synthesis is vitamin deficiency, especially vitamin B12 or folic acid deficiency. In moderate deficiency, tongue inflammation and neurological problems may begin.

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How to cite this article:
Emmanuel Ifeanyi Obeagu', Quratulain Babar and Getrude Uzoma Obeagu. (2021). Megaloblastic Anaemia - A Review. Int. J. Curr. Res. Med. Sci. 7(5): 17-24.
DOI: http://dx.doi.org/10.22192/ijcrms.2021.07.05.003