REVIEW

ISSN (O): 2349-5332
CODEN: IRJPHY

AN OVERVIEW OF PERNICIOUS ANEMIA

Suha Khaiery Ababneh

Department of Biological Sciences, Faculty of Science, The University of Jordan, Amman, Jordan

Submitted on: 28.05.2021; **Revised on:** 02.06.2021; **Accepted on:** 12.06.2021

ABSTRACT:

This is a review study regarding pernicious anemia. The main objective of this study was to introduce an update of pernicious anemia (PA). PAis a megaloblastic anemia caused by a cobalamin (vitamin B12) deficiency caused by a lack of intrinsic factor (IF). This study reviewed PA from different perspectives including etiology, pathology, management, and treatment. We also put a focus on the autoimmunity part of the disease. Taken together, P A is a multifactorial disease, and it should be more studied.

KEYWORDS: pernicious anemia, vitamin B12, intrinsic factor, pathology of PA

Corresponding Author: S. K. Ababneh

E mail: ahed.alkhatib64@yahoo.com

Indian Research Journal of Pharmacy and Science; 29(2021)2532-2536;
Journal Home Page: https://www.irjps.in
DOI: 10.21276/irjps.2021.8.2.3

INTRODUCTION

Pernicious anemia (PA) is a megaloblastic anemia caused by a cobalamin (vitamin B12) deficiency caused by a lack of intrinsic factor (IF). Intrinsic factor is a glycoprotein that attaches to cobalamin, allowing it to pass through the terminal ileum. Due to the discovery of stomach autoantibodies directed against both IF and parietal cells, the condition is frequently referred to as an autoimmune condition. Pernicious anemia is linked to various autoimmune diseases as well as a genetic condition[1].

Pernicious anemia has a wide range of clinical manifestations and a slow start. Fatigue, pallor, paresthesia, incontinence, psychosis, and widespread weakness are all possible symptoms. Due to the limited availability of diagnostic instruments, the diagnosis is difficult. Treatment involves intramuscular injections or oral supplements to replenish therapeutic amounts of vitamin B12. When the disease goes misdiagnosed and untreated for a long time, it can cause neurological issues and even death. The epidemiology, pathophysiology, clinical presentation, evaluation, and management of pernicious anemia are all covered in this exercise [2].

Pernicious anemia has two etiologies, according to research:

Gastric parietal cells are destroyed in autoimmune gastritis, resulting in a deficiency of the glycoprotein intrinsic factor released by these cells. Intrinsic factor antibodies (IFA) and parietal cell antibodies are antibodies linked to autoimmune (PCA). Antibodies to the proton pump ATPase in parietal cells work against it. The alpha and beta proton pump subunits are the principal targets of parietal cell antibodies. Immunoglobulins from the M, G, and A isotypes, which act against both subunits, have been discovered to be parietal cell antibodies[3].

Intrinsic factor antibodies are antibodies of the immunoglobulin G isotype, and they might be type 1 or type 2. Type 1 is antagonistic to the cobalamin binding site. The ileal mucosa receptor is targeted by Type 2[4]. Pernicious anemia, which can be linked to autoimmune diseases like type 1 diabetes (3 percent to 4%), vitiligo (2 percent to 8%), and autoimmune thyroid disease, is another autoimmune condition (3 percent to 32 percent). As a result of this link, researchers have discovered that HLA alleles may be linked to autoimmune gastritis. Autoimmune gastritis is linked to the HLA-DRB1/03 and HLA-DRB1/04 alleles [5].

Epidemiology

According to some research, the prevalence of pernicious anemia is 0.1 percent in the general population, rising to 1.9 percent in individuals over the age of 60 [6]. It affects people of all ages, however it is more commonly associated with those over the age of 60, with a median age of 70 to 80 years. The prevalence in the United States is estimated to be 151 per 100000 people. People of European and African ancestry had a higher prevalence in older adults (4.0 percent and 4.3 percent, respectively) than people of Asian heritage [7].

Pathophysiology

In pernicious anemia, two forms of autoantibodies have been identified: intrinsic factor antibodies (IFA) and parietal cell antibodies (PCA). Antibodies against the parietal cell proton pump ATPase are active in the parietal cell. Autoimmunity begins with the stimulation of gastric dendritic cells, which then

activate CD4+ T cell lymphocytes in the perigastric lymph nodes, resulting in autoimmune disease. CD4+ T cells were activated to look for the proton pump ATPase, which resulted in their immune system being destroyed[8]. The process that causes dendritic cells to become activated is unknown. H. pylori infection has been suggested as a cause in some investigations.The findings suggest that the proton pump ATPase and H. pylori species share molecular mimicry and immunological cross-reactivity [9]. Anti-parietal antibodies are seen in the majority of pernicious anemia patients. Intrinsic factor antibodies are antibodies of the immunoglobulin G isotype, and they might be type 1 or type 2. The cobalamin binding site is targeted by type 1, while the ileal mucosa receptor is targeted by type 2 [4]. B12 and intrinsic factor bind to ileum receptors, allowing for absorption. Once absorbed, vitamin B12 acts as a cofactor for the enzyme methionine synthase, which helps convert homocysteine to methionine. If this process is hampered by pernicious anemia, homocysteine levels rise and pyrimidine bases are unable to synthesize, interfering with DNA synthesis and resulting in megaloblastic anemia. The enzyme methylmalonyl-CoA mutase, which transforms methylmalonyl-CoA to succinyl-CoA, requires vitamin B12. Methylmalonic acid (MMA) levels rise in people with pernicious anemia. Myelin damage is caused by high levels of MMA and homocysteine, which results in neurologic impairments such neuropathy and ataxia [11]. [10] Patients with a cobalamin deficit may experience severe neurological symptoms such as peripheral neuropathy, psychosis, or leukoencephalopathy.

Management / Treatment

During the first week of treatment, patients are given a 1000 mcg B12 intramuscular injection every day or every other day. They will have injections every week for the following month, then monthly injections after that. High-dose oral B12 is an alternative to intramuscular injectable B12. Although it is recommended to utilize the parenteral route in severe neurological symptoms, 1000 to 2000 mcg/day has been shown to be beneficial. There are other B12 sublingual and intranasal preparations that have been approved [11].

If a patient is unable to get IM injections, an oral dose is indicated, although cobalamin levels must be monitored periodically to guarantee absorption. Finally, patients with CNS symptoms should avoid oral treatment [3].

When regular blood tests reveal big red blood cells, vitamin B12 insufficiency is usually suspected. When people exhibit classic symptoms of nerve injury, such as tingling or loss of sensation, doctors may suspect it. The level of vitamin B12 in the blood is examined if a deficit is detected. Doctors usually check the level of folate in the blood to rule out folate deficiency, which can cause big red blood cells. Vitamin B12 supplements should be started promptly after birth for vegan mothers' infants to avoid vitamin B12 insufficiency. Vitamin B12 is frequently given by injection into a muscle to people who have very low levels of the vitamin or who have symptoms related to nerve damage[12].

Hematologic Research

Examination of the peripheral blood reveals macrocytosis with hypersegmented polymorphonuclear leukocytes, anemia, leukopenia, and thrombocytopenia or pancytopenia in patients

with established megaloblastic anemia. Megaloblasts and huge myeloid progenitors ("giant metamyelocytes") are seen in the bone marrow. If the diagnosis is clear, there is no need to examine the marrow. A low serum vitamin B12 concentration and a normal serum folate concentration indicate vitamin B12 deficiency as the cause of megaloblastic anemia [13].

A Schilling test will demonstrate that the vitamin B12 deficit is caused by intrinsic-factor deficit in the intestine. Urinary excretion of orally delivered vitamin B12 is poor in patients with pernicious anemia, but it increases when vitamin B12 is given with intrinsic factor. Serum holotranscobalamin II, the circulating protein that distributes vitamin B12 to cells, is a simpler test. The serum concentrations of holotranscobalamin II decline before those of vitamin B12 in patients with vitamin B12 insufficiency [14].

CONCLUSION:

The ultimate stage of type A chronic atrophic (autoimmune) gastritis is pernicious anemia. The loss of parietal cells in the fundus and body of the stomach is caused by gastritis. Vitamin B12 insufficiency and megaloblastic anemia are caused by the loss of these cells, which is linked to a lack of intrinsic-factor production. The presence of mononuclear-cell infiltration into the gastric mucosa with loss of parietal and zymogenic cells, autoantibodies to parietal cells and intrinsic factor, regeneration of parietal and zymogenic cells after therapy with corticosteroids or immunosuppressive drugs, familial predisposition, and association with autoimmune diseases all support an autoimmune basis for gastritis.

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CONFLICT OF INTEREST REPORTED: NIL; SOURCE OF FUNDING: NONE REPORTED