# A Case of Pernicious Anaemia with Psoriasis

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**Abstract**

Pernicious anaemia often poses diagnostic and therapeutic challenges to the clinician. Herein, we representing a 55 years old lady who presented with anaemia along with its classical symptoms and features of peripheral neuropathy due to Pernicious anaemia associated with Psoriasis and Arthropathy without any association of other autoimmune disorder. She had all objective evidences of autoimmune atrophic gastritis in gastric fundic biopsy and positive anti-intrinsic factor antibody. Treatment with injection vitamin $B_{12}$ improved the condition rapidly.

***Key-words:*** Psoriasis, Pernicious anaemia, Autoimmune atrophic gastritis, Anti-parietal cell antibody, Anti- intrinsic factor antibody.

## Introduction

Pernicious means 'fatal'. Pernicious anaemia (PA) can occur due to autoimmune atrophic gastritis that causes a deficiency in vitamin $B_{12}$ (cobalamin) due to its malabsorption[1]. It accounts for 20%–50% of the documented causes of vitamin $B_{12}$ deficiency in adults according to a recent series[2]. In general population[3], the prevalence of PA is 0.1%; in subjects over the age of 60 it reaches 1.9%. Vitamin $B_{12}$ is mostly found in animal products including meat, fish, liver, kidney, heart, poultry eggs, milk and milk products, cheese etc. Vagan diet, small intestinal disorders such as Crohn's disease, Celiac disease, bacterial over growth or intestinal parasites and some immune system disorders like Grave's disease may cause vitamin $B_{12}$ deficiency. The association of PA with autoimmune diseases such as type 1 diabetes, Hashimoto's thyroiditis or vitiligo is common. Other associations have also been frequently described e.g., Sjogren's syndrome, Celiac disease, and Addison's adrenal insufficiency. Cases of multiple autoimmune syndromes including PA have also been documented[4]. Psoriasis is a rare association. The term 'pernicious anaemia' is an anachronism-it dates from the era when treatment had not yet been discovered, and the disease was fatal, but it remains in use for megaloblastic anaemia resulting from vitamin $B_{12}$ deficiency due to lack of intrinsic factor (IF)[5]. Classic pernicious anaemia is caused by the failure of gastric parietal cells to produce sufficient IF to permit the absorption of adequate quantities of dietary vitamin $B_{12}$. It is due to autoimmune atrophic gastritis, predominantly of the gastric fundus. Other disorders that interfere with the absorption and metabolism of vitamin $B_{12}$ can produce cobalamin deficiency, with the development of macrocytic anaemia and neurologic conditions.

Anemia is the most frequently encountered clinical sign in PA, together with accompanying functional manifestations, depending on their severity[6]. The diagnosis of PA is classically established in clinical routine by demonstrating the absence of IF by the study of gastric juice; a rate of secretion of IF, ≤200 U/hour after stimulation with pentagastrin (normal being 2000 U/hour) is specific to PA; or indirectly by performing a Schilling test which highlights abnormal absorption of radioactive cobalamin, which is corrected after administration of IF[7]. But the Schilling test has recently been disappeared and thus, diagnostic criteria have changed in recently published studies. It should nevertheless be kept in mind that the Schilling test and lack of IF secretion remains the gold standard for diagnosis of PA[7].

Pernicious anaemia is characterized by at least the following elements: the destruction of the gastric fundic mucosa, by a process of cell-mediated autoimmunity[8], fundic atrophy accompanied by a reduction in gastric acid secretion, a reduction in intrinsic factor (IF) secretion, and vitamin $B_{12}$ malabsorption, and the presence of various antibodies, including anti-IF antibodies and anti-gastric parietal cell, the latter being specifically directed against the hydrogen potassium adenosine triphosphatase (H+/K+-ATPase) proton pump[9]. The combination of both antibodies for PA yields 73% sensitivity and 100% specificity[10].

Treatment of vitamin $B_{12}$ deficiency related to PA is based on parenteral vitamin $B_{12}$ administered intramuscularly under the form of cyanocobalamin, hydroxocobalamin, or methylcobalamin. Though the recommended dosage and frequency of administration varies in different authority, in the United States and the United Kingdom, the doses range from 100–1000 µg per month for life, in France, cobalamin therapy involves acute treatment at a dose of 1000 µg daily for 1 week, followed by 1000 µg per week for 1 month, then a monthly dose of 1000 µg for life[11].

## Case Report

A 55 years old lady was presented with generalized weakness, increasing tiredness and lethargy and palpitation on exertion for six months. For last 03 months her symptoms worsened and she felt difficulty to perform her daily activities. She also noticed tingling and numbness in both hands and feet for last 06 months. She had history of occasional dizziness and light headedness. She complained of soreness of tongue and burning sensation of mouth also. She developed anorexia, nausea, vomiting and some weight loss. She had been suffering from Psoriasis and cholelithiasis. She had no history of hypertension, diabetes mellitus or other co-morbidity. She is housewife, nonsmoker and non alcoholic. She took iron tablets, multivitamins, and proton pump inhibitors advised by local doctor without significant improvement.

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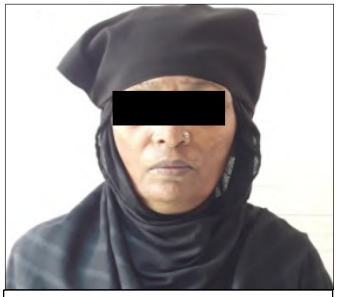

**Figure-1:** Patient, 55 years old lady

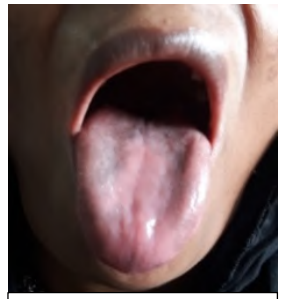

**Figure-2:** Smooth shiny tongue with atrophy of papillae

Clinically patient was moderately anaemic. She had smooth shiny tongue with atrophy of papillae. She had no koilonychia or leuconychia. Her pulse, blood pressure and jugular venous pressure were normal. There were multiple hyperpigmented, thickened, scaly lesions over both palm and sole, popliteal fossa and scalp. There was tenderness in distal inter-phalangeal (DIP) joints of both hands associated with mild restriction of movements. She had impaired pain, touch, and temperature sensation in gloves and stocking pattern with diminished knee and ankle jerks in both lower limbs; vibration and position sense were intact. Peripheral blood film was anisochromic, anisocytic and macrocytic red cells with hypersegmented neutrophils and reduced white cell count; suggestive of bicytopenia (macrocytic anaemia plus leucopenia).

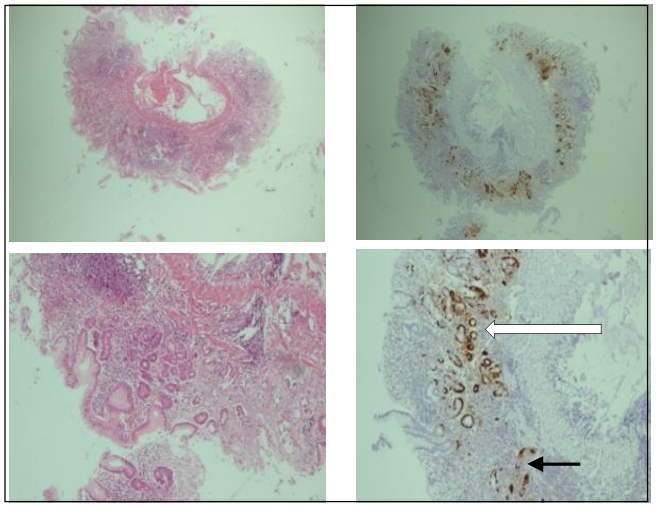

**Figure-3:** Gastric mucosal biopsy, moderate chronic atrophic gastritis, showing moderate loss of mucosal glands associated with moderate chronic inflammatory cells. Chromogranin A immune-histochemical stain shows linear (black arrow) and micronodular (white arrow) neuroendocrine cells hyperplasia.

Serum iron, TIBC and ferritin were normal. Serum Folate >20 ng/ml (Normal: 3-17 ng/ml); serum Vitamin $B_{12}$ < 50 pg/ml (Normal: 174 – 878 pg/ml); bone marrow examination showed hypercellular marrow with reduced M: E ratio; erythropoiesis was hyperactive megaloblastic and shifted to the left; suggestive of megaloblastic erythroid hyperplasia. Upper gastrointestinal endoscopy showed attenuated gastric mucosal folds suggestive of atrophic gastritis; anti-parietal cell antibody was negative (1:20); Anti-intrinsic factor antibody (done from India) was positive (128.79 AU/ml). Abdominal ultrasound showed cholelithiasis. Autoimmune markers including anti-nuclear factor (ANF), anti-ds DNA, Rheumatoid factor (RF), anti CCP antibody, anti TG and anti TPO antibodies were negative. The patient was diagnosed as Pernicious anaemia associated with Psoriasis and arthropathy and cholelithiasis. He was treated with injection Hydroxocobalamin 1000µg intramuscular (I/M) daily for a week, then 1000µg I/M monthly for 03 months, then 1000µg I/M once every 03 months for lifelong along with folic acid 5mg daily for 03 months and lifestyle modification. Anti-Helicobacter pylori treatments along with topical ointments for psoriasis were given. Patient was followed up with full blood count, reticulocyte count initially after 02 weeks and then at 06 monthly interval after normalization of haemoglobin level. On follow up patient was improved symptomatically, and her glossitis and paresthesia were improving. Patient was advised and planned for follow up upper gastrointestinal endoscopy yearly.

## Discussion

Vitamin $B_{12}$ deficiency varies and increases with age. Pernicious anaemia is an autoimmune disease caused by vitamin $B_{12}$ deficiency due to atrophic gastritis or loss of parietal cells or lack of intrinsic factor[12]. A diagnosis of pernicious anaemia is made when patients have a low vitamin $B_{12}$ level and positive intrinsic factor antibody or parietal cell antibody or low serum vitamin $B_{12}$ and presence of atrophic gastric mucosa, establishing the autoimmune nature of the disease and presence of vitamin $B_{12}$ deficiency[13]. In this case we found the patient anaemic, low vitamin $B_{12}$ level as well as anti-intrinsic factor antibody positive and gastric mucosal biopsy shows atrophic features and immunohistochemical stain was suggestive of autoimmune origin. Pernicious anaemia may also occur in a person with spuriously normal value of vitamin $B_{12}$ level in spite of having all clinical or laboratory features of pernicious anaemia[14]. Although PA may be association with a number of autoimmune diseases its association with psoriasis is very rare that we found in this case. However, in recent reviews, Helicobacter pylori had been involved in the development of atrophic gastritis, and it is well established that H. pylori infection can induce gastric autoimmunity. In addition, two – thirds of patients with atrophic gastritis and a large proportion of PA patients have co-existing H. pylori infection[15]. In its classic clinical presentation, vitamin $B_{12}$ deficiency is accompanied by neuropsychiatric changes and bone marrow failure characterized by dyserythropoiesis with cytopenias and blood cell dysplasia[16]. In our case we also found objective evidences of peripheral neuropathy on neurological examinations and blood film showed anisocytosis, anisochromia with macrocytic red cells (MCV 124fL) with hypersegmented neutrophils and bicytopenia (macrocytic anaemia plus leucopenia).

Vitamin $B_{12}$ deficiency can be responsible for neurological impairment, which can occur in the absence of any anemia or macrocytosis in 30% of PA cases[17]. Neurological signs usually generate a clinical picture of sub-acute combined degeneration (SCD) of the spinal cord. Disorders are usually predominant in the lower limbs[18]. Large nerve fiber damage is responsible for ataxia, paresthesia, tendinous areflexia, and deep sensitivity disorders with Romberg's signs. However, neurological signs are inconsistent along with a highly variable clinical spectrum ranging from peripheral neuropathy, optic neuritis, impaired cognitive function to manifestations of depression or reversible dementia. It should also be kept in mind that neurological manifestations may only partially regress despite prolonged and high-dose vitamin $B_{12}$ therapy, leading to – at times – irreversible sequelae[2]. In our case, we observed very

low serum vitamin $B_{12}$ level and paresthesia with reduced lower limb tendon reflexes but no clinical evidence SCD or dementia.

Patients with PA are at a greater risk for the development of gastric neoplasms (both carcinoid and adenocarcinoma). These populations have a prevalence of 1-3% and a risk three times more than the general population for development of gastric carcinoma[19]. Intestinal metaplasia and atrophic gastritis associated with achlorhydria have been postulated as potential pathogenic factor for the development of gastric cancer in patients with PA. Although they have to be considered as a high risk group, guidelines for cancer screening in these patients are still lacking.

## Conclusion

While dealing with anaemic patients, PA should be kept in mind to diagnose and treat it early and hence we can prevent irreversible neurological damage that may be caused by it. Once diagnosed PA, patient should be followed up for life and consequences of atrophic gastritis such as gastric cancer screening should be planned.

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