



## Persistently High Plasma Vitamin B12 and the Risks of Malignancies

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### ABSTRACT

A female patient was presented with features suggestive of neuropathy secondary to atrophic gastritis and raised serum gastrin but the surprising findings was the finding of very high Vitamin B12 despite severe gastric atrophy. Her investigations showed multiple small bowel erosions seen by colonoscopy and ileoscopy and confirmed by video capsule.

She has latent Celiac disease with positive Human Leukocyte Antigen HLA DQ2 but poor response to gluten free diet. To our knowledge this is the first case report in our area of very high Vitamin B12 with atrophic gastritis probably attributed to blocking antibodies to the vitamin B12 receptors or associated with hidden hematological or solid cancers.

Her sister developed colon cancer that raises great concerns about possible future development of cancers in this patient. This case study of high vitamin B12 associated with ileal ulceration and chronic auto immune gastritis with latent celiac disease is a new entity that needs further evaluations and awareness is needed to study high level of vitamin B12 and to our knowledge this is the first case of high B12 reported in our area.

Unusually high level of serum vitamin B12 levels is an underestimated entity; it can be paradoxically accompanied by signs of deficiency, reflecting a functional deficiency linked to qualitative abnormalities, which are related to defects in tissue uptake and action of vitamin B12. It can occur with solid neoplasms, hematological malignancies, and liver and kidney diseases. High serum vitamin B12 is defined by a rate above 950 pg/ml (701 pmol/l), which corresponds by biological standards, to the upper limit of biological normality, in the absence of any sign and/or clinical anomaly.

A study of more than 80,000 cancer patients demonstrated that those with elevated plasma vitamin B12 levels prior to diagnosis had higher mortality, indicating more advanced and aggressive cancers. These results could not be explained by cancer type, sex, age, comorbidity or presence of non-localized disease suggesting that these associations reflect underlying alterations in the metabolism caused by the cancer.

**Keywords:** Vitamin B12; Auto immune gastritis; Celiac disease; Metabolism; Cancer

### INTRODUCTION

Unusually high level of serum vitamin B12 levels is an underestimated entity; it can be paradoxically accompanied by signs of deficiency, reflecting a functional deficiency linked to qualitative abnormalities, which are related to defects in tissue uptake and action of vitamin B12.

It can occur with solid neoplasms, hematological malignancies, and liver and kidney diseases [1].

High serum vitamin B12 is defined by a rate above 950 pg/ml (701 pmol/l), which corresponds by biological standards, to the upper limit of biological normality, in the absence of any sign and/or clinical anomaly [2,3].

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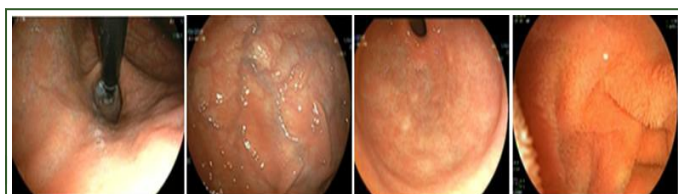
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Our patient is a female patient with multiple autoimmune diseases including auto immune atrophic gastritis, latent celiac disease with ileal ulceration and persistently high vitamin B12 despite the presence of gastric atrophy and high serum gastrin.

## CASE PRESENTATION

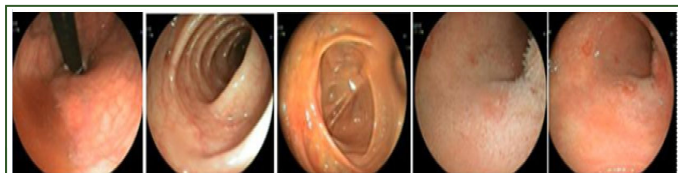
59 years old female from Latin America presented 2013 with abdominal pain, altered bowel habits, muscle spasms, arthralgia with 12 kg weight loss and with history of rectal prolapse surgery (2005) and recurrent vaginal candidiasis.

Family history: Her father died with wasting disease; undiagnosed suspected dissimilated malignancy. She had attacks, dryness of the mouth and with pricking sensation in the extremities and clinical examination unremarkable BMI 20 [4]. Her first endoscopy (2013) showed gastric fundal atrophy with patchy colitis and the biopsies showed chronic gastritis and mild colitis with mild ileitis (Figures 1 and 2).



Gastroscopy thin fundal area, visible vessels, normal duodenum

**Figure 1:** Atrophic stomach: Gastric fundal atrophy with patchy colitis and the biopsies.



Colonoscopy, patchy colonic erythema with multiple ileal small ulcers

**Figure 2:** Ileal ulcers: Chronic gastritis and mild colitis with mild ileitis.

Laboratory investigation showed positive parietal cell antibodies 100 (N10), elevated serum gastrin 295 (N 100), Vitamin B12 was surprisingly very high ranging between 3000-7000 (N 187-883) repeatedly over 7 years in spite of no vitamin supplements. Celiac serology showed one weak positive anti-gliadin antibody, duodenal biopsies were normal but her Human Leukocyte Antigen-HLA DQ2 was positive.

Stool calprotectin fluctuated between 40-800 over 7 years suggestive of inflammatory bowel diseases. The following laboratory tests were normal: Immunoglobulins IgG, IgA, IgM, IgE, normal collagen screen, negative Trypanosoma cruzi antibodies, normal IgG4, ASCA, ANCA, porphyrins except mild elevation of coproporphyrin [5].

The video capsule studied done three times over 3 years showed multiple small bowel erosions suggestive of inflammatory bowel disease or ulcerative jejunitis or auto immune enteropathy (Figure 3).



**Figure 3:** Small bowel multiple ulcers: Video capsules over 6 years multiple small jejunal and ileal ulcers.

Because of the suspicion of hematological malignancies, hematological assessment for the raised vitamin B12 showed heterozygous mutation of A1298C Methylene tetrahydrofolate reductase (MTHFR) gene, grossly elevated B12 over 3000 but normal homocysteine. She responded to 2 months course of prednisolone and was reluctant to continue or to start biologics.

Azathioprine was started but she developed severe reaction including abdominal pains and vomiting and was stopped. The opinion is that inflammatory condition is a possibility, latent celiac disease is a probability, but solid cancers, myeloproliferative diseases and hemopathies need to be followed. She started on gluten free diet in 2016 with little improvement.

Immunofixation was negative for myeloma or immunoglobulin's abnormal bands. She was advised to start biologic agents' infliximab, but she was hesitant to use it. During follow up her sister developed metastatic colon cancer [6].

## RESULTS AND DISCUSSION

This patient was presented with features suggestive of neuropathy secondary to atrophic gastritis, but the surprising thing was the finding of very high Vitamin B12 despite severe gastric atrophy and raised serum gastrin which reflect gastric atrophy.

She has multiple small bowel erosions seen by ileal examination and video capsules suggestive of inflammatory bowel disease and again the surprising finding of high serum vitamin B12 with ileitis and multiple erosions in which we expected low vitamin B12, that added to the ideas that she may have blocking antibodies to the vitamin B12.

She has latent Celiac disease with positive Human Leukocyte Antigen-HLA DQ2 but poor response to gluten free diet. To our knowledge this is the first case report in our area of very high Vitamin B12 with atrophic gastritis probably attributed blocking antibodies to the vitamin B12 receptors or associated with hidden hematological or solid cancers [7].

The occurrence of colon cancer in her sister raises great concerns about possible future development of cancers. A study of more than 80,000 cancer patients demonstrated that those with elevated plasma vitamin B12 levels prior to diagnosis had higher mortality, indicating more advanced and aggressive cancers. These results could not be explained by cancer type, sex, age, comorbidity or presence of non-localised disease suggesting that these associations reflect underlying alterations in the metabolism caused by the cancer [8].

## CONCLUSION

This case study of high vitamin B12 associated with ileal ulceration and chronic auto immune gastritis with latent celiac disease is a new entity that needs further evaluations and awareness is needed to study high level of vitamin B12 and to our knowledge this is the first case of high B12 reported in our area.

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