

Pernicious Anemia: Non – Gastroscopic Diagnosis of Autoimmune Atrophic Gastritis with Positive Serological Marker

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Received January 18, 2014; Revised February 16, 2014; Accepted February 21, 2014

Abstract For the last many decades pernicious anemia has been treated as a separate clinical feature. Pernicious anemia is also known as macrocytic anemia which originates due to the lack of vitamin B12 (cobalamin). A protein called intrinsic factor which helps vitamin B12 for its absorption through terminal ileum so, the deficiency of intrinsic factor result in a lack of vitamin B12 absorption, which, in turn, causes pernicious anemia. The gastric parietal cell normally produces chlorhydric acid and intrinsic factor. Atrophic body gastritis (ABG) is a condition which cause the destruction of the oxyntic mucosa and the reduction of the parietal cell hence result in the deficiency of intrinsic factor [1]. Pernicious anemia can present in many different clinical patterns like fatigue (tiredness), headache, dizziness, shortness of breath, pale or yellowish skin, coldness in your hands and feet, and chest pain.

Presentation of Case: We report a case of a 55 year old male who presented with one month history of fatigue ness, dizziness, abdominal pain and short of breath on exertion. On further investigation, it is turnout to be atrophic gastritis which is treated conservatively.

Keywords: pernicious anemia, autoimmune atrophic gastritis, intrinsic factor antibodies, antinuclear antibodies

Cite This Article: Shazia Yasir, Komal Owais, Faisal Moin, Mahmud Z. Jilani, Ejaz Ahmad Vohra, and Abdul Ghani, “Pernicious Anemia: Non – Gastroscopic Diagnosis of Autoimmune Atrophic Gastritis with Positive Serological Marker.” *American Journal of Medical Case Reports*, vol. 2, no. 2 (2014): 32-34. doi: 10.12691/ajmcr-2-2-1.

anemia regarding its pathogenesis, clinical presentation, diagnosis and its management in view of gastroenterology.

1. Introduction

Pernicious anemia (PA) is also known as Biermer’s disease and Addisonian anemia. The first clinical description of pernicious anemia, which is one of the known causes of megaloblastic anemia, has been attributed to Thomas Addison in 1849 [2]. Pernicious anemia is an autoimmune disorder in which gastric autoantibodies act against intrinsic factor and also against parietal cell. Pernicious anemia is often referred as autoimmune gastritis, because pernicious anemia is considered as the last stage of the autoimmune process that leads to rigorous obliteration of oxyntic gastric mucosa [3].

Pernicious anemia can present in many ways like *Helicobacter pylori* (H pylori) infection or bone marrow malignancies but autoimmune atrophic gastritis is a rare presentation and is associated with high morbidity and mortality as it is often diagnosed as gastric adenocarcinoma despite modern methods of detection and treatment. Here we are reporting a rare case of pernicious

2. Case Report

A 55 years old gentleman known smoker with not known comorbids came to emergency department with one month history of fatigueness, dizziness, abdominal pain and short of breath on exertion. The shortness of breath is associated with dizziness and aggravated by climbing stairs or walking few blocks and relieve by taking rest.

The patient had been visiting a number of doctors and received symptomatic treatment, that relieved his abdominal pain and shortness of breath temporarily but the patient was not investigated by any laboratory test or imaging. The patient has epigastric pain associated with nausea, vomiting and fullness after taking meal. Around a decade ago, the patient had a blood transfusion from some non recognized blood centre. The patient had no history of headache, decreased mental concentration, palpitation, chest pain, paresthesia, unsteady gait, clumsiness and

spasticity [4]. Systemic examination including abdomen, cardiovascular, CNS, chest was unremarkable.

During the first 24hrs of admission of the patient in the emergency department, full blood count revealed macrocytic aregenerative anemia, hemoglobin 6.0gm/dl (13.0gm/dl – 17.0gm/dl), mean corpuscular volume (MCV) value of 129fl (80fl – 100fl), absolute reticulocyte was 2.0% (0.8% – 2.5%), white blood cell count 5.1 (4.0X 10E9/L – 10X 10E9/L), platelet count is 120 (150X 10E9/L – 440 X 10E9/L), Neutrophils 42 (40% – 80%), Lymphocytes 37 (20% – 40%), Monocytes 04 (2% – 10%), Eosinophils 15 (1% – 6%). The red blood cells (RBS) morphology shows Macrocytosis. Normochromic. Anisocytosis. Poikilocytosis. Oval macrocytes. The iron profile shows Ferritin 176ng/ml (30ng/ml – 400ng/ml), Iron 227ug/dl (59Ug/dl – 158Ug/dl), TIBC 317ug/dl (259ug/dl – 388ug/dl), % Saturation 61.3% (20% – 40%). In the next 48hrs, the patient bilirubin total 1.86 (< 1.3mg/dl), bilirubin direct 0.39 (< 0.3mg/dl). The patient's Serum B12 <100pg/ml (174pg/ml – 878pg/ml), RBC Folate 45ng/ml (93ng/ml – 641ng/ml). Direct coombs test done, which shows direct antiglobulin antibodies are negative. The patient's Intrinsic factor antibodies are positive and ANA profile shows antinuclear antibodies, Anti-mitochondrial antibodies, anti smooth antibodies are negative, while antigastric parietal cell antibodies (AGPCA) are positive by immunofluorescence. Stool for H-pylori antigen was negative on the 5th day of the admission. Patient was advised to have gastroscopy with gastric biopsy to have tissue diagnosed by gastroenterologist, but they refused and asked to treat empirically. The patient was started on injection vitamin B12 and tablet folic acid 5mg/day and obvious improvement was seen and he was discharged on 7th day of the admission with same treatment and called to consult in medical OPD regularly. The patient is still on follow-up and felt much improvement in his symptoms.

3. Discussion

There is lots of variation in clinical feature of pernicious anemia, ranging from stable to sever illness. Many of the signs & symptoms are due to the anemia itself. Untreated pernicious anemia can be extremely complicated and could cause neurological complications and in its very serious condition it could cause death. However; the identification of serum inhibitor of intrinsic factor (later found to be an autoantibody of intrinsic factor) and autoantibodies to parietal cell laid the foundation for the immunological explanation of the underlying gastritis that cause pernicious anemia.

Atrophic gastritis can be classified into two types. Type A (autoimmune) gastritis involves the fundus & the body of stomach and spares the atrium where as type B (non Autoimmune) gastritis involves the atrium as well as the fundus & bodies. The type A gastritis is linked with pernicious anemia in which autoantibodies against gastric parietal cell and to intrinsic factor, which, in turn, cause achlorhydria and low serum pepsinogen1 concentration and hyperplasia of gastric producing cell cause high serum gastrin concentration. Type B gastritis is usually coupled with helicobacter pylori infection and decreased serum gastrin concentration, because of the obliteration of the

gastric producing cell related with antral gastritis but in this patient stool for H-pylori antigen was negative. Thus, the autoimmune origin of the pernicious anemia depend upon the existence of parietal cell and (/ or) intrinsic factor autoantibodies and could be associated with autoimmune endocrinopathies and antireceptor autoimmunities diseases such as insulin-dependent diabetes mellitus, chronic autoimmune thyroiditis (Hashimoto's thyroiditis), Addison's disease, Graves' disease, primary ovarian failure, vitiligo, primary hyperparathyroidism, myasthenia gravis, and the Lambert–Eaton syndrome.

Stepwise biopsy and Gastroscopy can alleviate any doubt of original misdiagnosis in patient where serologic study shows conflicting result. To perform sampling for histological diagnosis, the patient and their attendant had declined to give their consent. Although, the serum antibodies to gastric parietal cell can be found in about 90% of patients with autoimmune atrophic gastritis, which leads to pernicious anemia. In the similar way about the 70% serum autoantibodies to intrinsic factor are demonstrable in patients with autoimmune atrophic gastritis which lead to pernicious anemia. The remaining 30% patient show either the antibodies is present at cellular level while absent from serum or the final failure of intrinsic factor mediated vitamin B12 absorption occur by the mechanism not dependent intrinsic factor antibodies. The demonstrating of circulating gastric parietal cell antibodies and intrinsic factor antibodies almost diagnostic of autoimmune type A gastritis and pernicious anemia.

This case showed marked improvement in the resolution of symptoms as well as decreased the risk for the development of gastric adenocarcinoma. Therefore, it is recommended that although gastroscopy and stepwise gastric biopsy is gold standard, but the patient with positive serological markers should start regular and recommended vitamin B12 therapy to prevent the severity of pernicious anemia.

4. Conclusion

Pernicious anemia is a condition in which body is unable to absorb vitamin B12 from food so body cannot produce enough healthy red blood cells. Pernicious anemia is very quite condition and under-diagnosed as autoimmune disease. Pernicious anemia has a huge number of causes including autoimmunity, dysfunctional intrinsic factor and absolute intrinsic factor deficiency. Whatever is the actual cause for pernicious anemia, failure to diagnose it, may lead to intense and lifelong medical predicament for the patient.

Acknowledgements

The authors would like to acknowledge the patient who consented to publication: written informed consent was taken from the patient for publication of this case report.

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