

Introduction

Chronic constipation is very commonly observed and it is seen to affect all age groups. It has multiple causes. However, B 12 deficiency presenting as chronic constipation is uncommon. We report a unique of chronic constipation caused by vitamin B 12 deficiency.

Case report

41 yrs old male, nondiabetic and nonhypertensive, had constipation since last 4 -5 yrs. He used to pass hard stools once in 3 days associated with straining. He was dependent on laxatives for passing stool. He presented with pain while passing stool and occasional blood streaked stools since 1 month.

On examination, his blood pressure is 130/80 mm of Hg and pulse of 72/min. General examination, abdominal examination and other systems examination were normal. On per rectal examination, fissure in ano at 6 O'clock position identified, anal tone was lax with mild tenderness. He was treated with laxatives and local anaesthetic ointment. His symptoms pain and stool streaked with blood, improved but constipation persisted. Hence, he was investigated further.

Hb was 10 gm/dl, WBC count was 6700 /cmm, MCH was low 19.2 pg/ml, MCHC was low 29.2 g/dl, MCV was low 65.8 fl. Peripheral smear showed anisocytosis, microcytosis and hypochromasia. Fasting blood sugar was 96 mg/dl and post lunch blood sugar was 118 mg/dl, Thyroid function test were normal, (T3 - 1.24 ng/ml T4 - 6.6 μ g/dl, TSH -1.43 μ IU/ml) Serum Calcium was 9.3 mg/dl. Lipid profile, liver function test, renal function test, urine routine and serum electrolyte were normal. Ultrasonography of abdomen was normal. Serum Iron was low, 31 μ gm/dl, Serum Ferritin was low 12.5 ng/ml. His Serum B12 level was low (118 pg /ml), Serum folic acid level was mildly raised 15.2 ng/ml. He was given oral vitamin B 12 supplements – 1500 microgram per day. After about 2 month Serum B 12 level was checked and it was again low i.e. 83 pg/ml.

In view of persistently low vitamin B 12 deficiency in spite of oral supplement of vitamin B 12, Intrinsic factor antibody and Antinuclear antibody was checked, both were negative. Anti-Parietal cell antibody was checked and it was strongly positive. He was started on injectable vitamin B 12, 1000 microgram per week. His Vitamin B 12 level checked after 1 month was 737 pg/ml. His symptoms of chronic constipation improved after Vitamin B 12 supplement. Now He is not requiring any laxative support for passing stool. He is free of symptoms of constipation.

Discussion

The definition of chronic constipation varies among different people. Decreased frequency of stools or straining while passing stool is interpreted as constipation by many. Few others who describe constipation as a feeling to pass motion, but motion don't happen even after sitting in toilet for long time. The American College of Gastroenterology Chronic Constipation Task Force defined chronic constipation as "unsatisfactory defecation characterized by infrequent stool, difficult stool passage or both at least for previous 3 months". Difficult stool passage includes straining, a sense of difficulty passing stool, incomplete evacuation, hard/lumpy stool, prolonged time to stool or need for manual manoeuvres to pass stool" ¹ Chronic constipation is classified as functional (primary) or secondary. Functional constipation can be divided into normal transit, slow transit, or outlet constipation. Possible causes of secondary chronic constipation include medication use, hypothyroidism, and hyperparathyroidism. Neurological condition such as hemiplegia, paraplegia, Parkinson's disease can also result in constipation. Old age with debilitation can also result in constipation. Sometimes obstructive bowel pathologies such as stricture in colon or growth in colon can also cause constipation.

The evaluation of constipation includes a history and physical examination. One has to specifically look for alarm signs and symptoms. These include evidence of bleeding per rectum, weight loss, iron deficiency anaemia, acute onset constipation in older patients, severe colicky pain in abdomen with distention and vomiting. Those who have these alarm signs and symptoms need to be thoroughly investigated. In chronic constipation, if there is suspicion of metabolic causes, should be investigated with a hemogram, biochemical profile, serum calcium, glucose levels and thyroid function tests. If these give rise to suspicion, serum protein electrophoresis, serum parathyroid hormone and serum cortisol levels can be considered, but this will only rarely be indicated. In those patients whom metabolic work up is normal and they are still symptomatic and those who are having alarm symptoms, colonoscopy can be used to detect the presence of lesions such as rectal ulcers, inflammation or malignancy. In the event if colonoscopy is also normal, physiological tests can be used to assess anorectal disorders, anorectal manometry²the balloon expulsion test ³ and colon transit studies4. These test would help in further diagnosis of dyssynergic defecation and colonic motility disorder.

Causes of vitamin B12 deficiency can be due to decreased intake, malabsorption, pernicious anemia, gastrointestinal surgeries and weight reduction surgery⁵. Antiparietal cell antibodies is an advantageous tool for screening for autoimmune atrophic gastritis and pernicious anemia. Antiparietal cell antibodies are present in 7.8 to 19.5% of general healthy population⁶. Pernicious anemia is a disease of autoimmune origin with atrophy of gastric mucosa involving body and fundus of stomach, reduction in number of parietal cells that produce the intrinsic factor necessary for absorption of vitamin B 12 which in turn is indispensable for erythropoiesis and myelin synthesis. The autoimmune nature of the process that brings on gastric atrophy and pernicious anemia is documented by the presence of autoantibodies against intrinsic factor and gastric parietal cells. The prevalence of

35

pernicious anemia was 0.1% in the general population and 1.9% in subjects over 65 years⁷.

Vitamin B12 deficiency though commonly associated with haematological manifestations like macrocytic anaemia, it could rarely present with neurological manifestations in the absence of anaemia or macrocytosis⁸. Demyelination is the initial finding, which progresses to axonal degeneration and neuronal death if left untreated. The initial symptoms include peripheral numbness and paraesthesia, with subsequent development of weakness and ataxia.

In our case the B 12 deficiency resulted in autonomic dysfunction affecting parasympathetic nervous system which resulted in chronic constipation. Our patient had chronic constipation since many years and was chronically using laxative resulting in fissure in ano. However he did not have alarm symptoms of weight loss, hematochezia or melena, hence no upper or lower GI scopies were carried out. His metabolic work up revealed severe B 12 deficiency. Macrocytosis was masked and he presented with microcytosis on peripheral smear secondary to iron deficiency. He was given oral iron and vitamin B12 supplementation but B 12 deficiency persisted. His anti-parietal cell antibody was strongly positive so it was concluded that he is having defect in absorption of vitamin B 12 and given injectable vitamin B 12 which resulted in normalisation of serum B 12 level with remarkable improvement in chronic constipation. Now he does not require any laxative.

Abdul Hafeez et.al. reported a rare case of Juvenile cobalamine deficiency in a 17 yr old patient causing autonomic dysfunction leading to adynamic ileus, normocytic anemia, acute post renal failure. In this case also expected macrocytosis was masked by underlying alpha thalassemia trait. He showed excellent response to parenteral cobalamine treatment⁹.

The term pernicious anaemia is commonly used to describe B 12 deficiency caused by atrophic gastritis, parietal cell loss or absence of intrinsic factor¹⁰. Autoantibodies to parietal cell causing B 12 deficiency is observed in pernicious anemia. To our knowledge, there is no case report of association of Vitamin B 12 deficiency presenting as chronic constipation in adult.

Conclusion

Severe chronic constipation need to be investigated thoroughly to look for underlying etiology including vitamin B 12 deficiency resulting from autoimmune disorder. If treated in time it can be reversed completely. It would be prudent to label this case as 'Pernicious Constipation' which marks its resemblance with similar autoimmune related condition of 'Pernicious Anemia'.

References

- Brandt LJ, Schoenfeld P, Prather CM, et al (2005). An evidence-based approach to the management of chronic constipation in North America. Am J Gastroenterol.; 100(Supp 1):S5–22. DOI: 10.1111/j.1572-0241.2005.50613_2.x
- Jones MP, Post J. Crowell MD, et al (2007 Apr) High-resolution manometry in the evaluation of anorectal disorders: a simultaneous comparison with water-perfused manometry. Am J Gastroenterol; 102(4):850-5. DOI: 10.1111/j.1572-0241.2007. 01069.x.
- Rao SS, Hatfield R, Soffer E, Rao S, Beaty J, Conklin JL, (1999 Mar). Manometric tests of anorectal function in healthy adults. Am J Gastroenterol; 94(3):773-83. DOI: 10.1111/j.1572-0241.1999.00950.x
- Nam YS, Pikarsky AJ, Wexner SD, Singh JJ, Weiss EG, Nogueras JJ, Choi JS, Hwang YH (2001 Jan). Reproducibility of colonic transit study in patients with chronic constipation. Dis Colon Rectum; 44(1):86-92. Retrieved from www.ncbi.nlm.nib.org/nubmed/1180556
- Staff, Nathan P., and Anthony J. Windebank. (12 Jan. 2018.) "Peripheral Neuropathy Due to Vitamin Deficiency, Toxins, and Medications." Continuum : Lifelong Learning in Neurology 20.5 Peripheral Nervous System Disorders (2014): 1293–1306. PMC. Web. DOI: 10.1212/01.CON.0000455880.06675.5a
- Rusak E, Chobot A, et al (2016 Sep) Anti-parietal cell antibodies diagnostic significance Adv Med Sci;61(2):175-179. DOI: 10.1016/j.advms.2015.12.004. (Epub 2016 Jan 13.)
- Andres E, and Serraj K, (2012): Optimal management of pernicious anemia. J Blood Med; 3: pp. 97-103. DOI: 10.2147/JBM.S25620
- Dissanayake Mudiyanselage Priyantha Udaya Kumara Ralapanawa, Kushalee Poornima Jayawickreme, et al (2015) B12 deficiency with neurological manifestations in the absence of anaemia. BMC Res Notes: 8: 458. DOI: 10.1186/s13104-015-1437-9
- in the absence of anaemia, BMC Res Notes.; 8: 458. DOI: 10.1186/s13104-015-1437-9
 Siddiqui, Abdul Hafeez; Ansari, Aamir MD et al (March 2012), Juvenile Cobalamin Deficiency in a 17-Year-Old Child with Autonomic Dysfunction and Skin Changes, Journal of Pediatric Hematology/Oncology. 34(2):140-142 DOI: 10.1097/MPH. 0b013e31822817bb
- Stabler S.P and Allen R.H.(2004): Vitamin B12 deficiency as a worldwide problem. Annu Rev Nutr; 24: pp. 299-326 DOI: 10.1146/annurev.nutr.24.012003.132440