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A Case of Microcytic Hypochromic Nutritional Anaemia refractory to treatment- Coexistence of Sickle Cell Trait With Celiac Sprue.

Medicine

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ABSTRACT

Introduction: Celiac disease is an immune mediated enteropathy characterised by gluten hypersensitivity. Sickle cell trait is autosomal codominant haemoglobinopathy due to mutation of gene for beta globin chain.

Case report: Here we are reporting a case of middle age female patient of refractory microcytic hypochromic nutritional anaemia with Sickle cell trait and coeliac disease occurring concurrently. Patient was diagnosed as having iron, folate and vitamin B12 deficiency anaemia which was not responding to supplementation of oral or intravenous iron, folate and vitamin B12, and thus on further subjecting to haemoglobin electrophoresis and serum Anti Tissue Tansglutaminase antibody was diagnosed to have Sickle cell trait and celiac disease. And patient responded well to gluten free diet with improvement in Haemoglobin.

Conclusion: Physicians should always be on a look out for commonly prevalent yet less diagnosed malabsorption disorders like celiac disease and haemoglobinopathies like Sickle cell trait in cases of Nutritional anaemias not responding to supplements and thereby improve quality of life of such patients by simple restriction of gluten in diet and simultaneously avoid inadvertent use of haematinics causing toxicity.

KEYWORDS:

Introduction:

Celiac disease also called Non tropical sprue or Gluten sensitive enteropathy is a chronic immune mediated enteropathy, precipitated upon gluten exposure in genetically predisposed individuals[1] and exhibits a wide spectrum of clinical presentations. The classical form called typical celiac disease presents as diarrhoea, steatorrhoea, abdominal bloating, flatulence and nutritional deficiencies[2] and the atypical form presents as anaemia, fatigue, osteoporosis and infertility[3].

It's highest reported prevalence is in west, more so in Finland where prevalence is 2.4%[4]. In India it's prevalent in North India in states of Gujarat, Rajasthan and Punjab[5]. It has slight female preponderance in ratio 1.3:1[6].

Sickle cell disease is a genetic disorder, haemoglobinopathy with autosomal codominant inheritance due to mutation in beta globin gene that changes 6th amino acid from glutamate to valine. It can be homozygous (HbSS, sickle cell disease) or heterozygous (HbAS, sickle cell trait)[7]. Manifests heterogeneously as asymptomatic in people with trait and with symptoms of anaemia, sickle cell crisis, painful digits, ischaemic necrosis of multiple organs, auto splenectomy, acute chest syndrome, aseptic necrosis of heads of femur and humerus and osteomyelitis due to sickling and microvascular occlusions in those with sickle cell disease. Sickle cell disease and trait are highly prevalent in tribal populations of India. In Rajasthan it's highly prevalent amongst Garasia tribe of south Rajasthan (Sirohi district), where prevalence of sickle cell disease is 9.2% out of which 8.4% are cases of sickle cell trait[8] just like in our case patient had sickle cell trait.Here we are reporting an atypical case of a 40yr old female patient who presented with symptoms of generalised weakness and easy fatiguability was initially diagnosed as case of microcytic hypochromic anaemia due to iron, folate and vitamin B12 deficiency but on being refractory to treatment with supplementation of iron, folate and B12 was investigated further for malabsorption syndromes and haemoglobinopathies. Finally was diagnosed as one of its kind case of Sickle cell trait and celiac disease occurring concurrently. Through vast exhausting search of medical literature we report this as probably the only case of sickle cell trait with celiac sprue.

Case report:

We report a case of a 40yr old married, Hindu, multiparous female resident of who presented with chief complaints of generalised weakness and easy fatiguability since two months without any history of fever, joint pains, diarrhoea, blood loss, trauma, pica, weight loss and loss of appetite and has history of intake of balanced diet. She was 2nd child born of non-consanguineous marriage. On examination patient had average built and nourishment with severe pallor, normal vitals and no abnormality on systemic examination. Her complete blood counts revealed Hb- 6.5 mg/dl, MCV- 63 fl, MCH- 15 pg/cell, MCHC- 27 gm/dl, with rest of the counts being within normal limit. Peripheral blood film revealed microcytic hypochromic anaemia. Iron profile revealed serum iron- 27 mcg/dl, serum ferritin- 363 ng/ml, and Total iron binding capacity- 315 mcg/dl. Stool examination for ova, cyst and occult blood was negative, renal function tests, liver function tests and thyroid function were all normal. HIV, HBsAg and HCV were negative. Ultrasound of abdomen and pelvis was also normal.

As per the iron profile patient was started on oral iron and folate replacement therapy with strict follow up to ensure compliance but despite all efforts Hb failed to increase even after one month of therapy, thus vitamin B12 levels were done on follow up and levels were found to be low (180 ng/ml). Hence oral vitamin B12 was also started but still on follow up after a month Hb failed to increase. This refractories to nutritional deficiency correction provoked us to send patient's blood for serum Anti Tissue transglutaminase antibody to rule out malabsorption syndrome, celiac sprue. Serum Anti Tissue transglutaminase antibody levels were > 100 units/ml, highly positive for celiac sprue. Upper GI Endoscopy and duodenal or jejunal biopsy with histopathology, gold standard to confirm celiac sprue could not be done due to unwillingness of the patient herself. She was then put on gluten free diet with nutritional supplements along with iron, folate and vitamin B12 and patient showed improvement within 2 months with Hb reaching level of 11gm/dl but despite this her MCV was 64fl, showing microcytic hypochromic anaemia, thus patient was further subjected to haemoglobin electrophoresis to rule out coexisting haemoglobinopathies. It revealed patient had sickle cell trait with HbS -32% and HbA -57%.

Thus Patient's mother and father too were subjected to Haemoglobin electrophoresis after proper counselling and mother was found to have sickle cell trait and father was found to be normal. Patient's siblings as well as her husband and children could not be screened for, due to lack of resources.Thus the patient was diagnosed as atypical

case of sickle cell trait with celiac disease occurring concurrently in case of microcytic hypochromic nutritional anaemia refractory to treatment with iron, folate and vitamin B12 replacement.

Discussion:

Anaemia more so nutritional anaemia is a major public health problem in India with majority of patients being children and women of child bearing age, belonging to rural India. Reported prevalence as per National Family health survey(2005-06) being 70% in children and 55% in women of child bearing age group[9]. Most common being Iron and folate deficiency anaemia and Vitamin B12 deficiency anaemia. Most of these cases of nutritional anaemia are treated with nutritional replacements given orally or parenterally many do respond and show dramatic rise in haemoglobin levels but there are few cases who repeatedly receive nutritional supplements and yet fail to improve. It's important to recognise these refractory cases and search in them for other causes of anaemia like coeliac disease leading to malabsorption and deficiency of iron, folate, vitaminB12 and pyridoxine, as was done in the case of our patient. Also despite all efforts if haemoglobin still remains low one should subject patient's blood sample for haemoglobin electrophoresis to rule out associated haemoglobinopathies and also test patient for other disorders such as sideroblastic anaemia, hereditary RBC membrane, cytoskeletal or enzyme defects, so as to avoid giving unnecessary nutritional supplements causing toxicity without any improvement in condition of patient and at the same time avoid wastage of resources in a country like India where there is huge scarcity. Thus improve the quality of life in such patients. Also ruling out haemoglobinopathies will help in identifying other members in the family with similar conditions and give them appropriate treatment to improve their quality of life and to have realistic targets in correcting haemoglobin levels.

In this case reported here patient presented to us with history of generalised weakness and fatigue, and laboratory studies revealed iron, folate and vitamin B12 deficiency anaemia. Patient had no history as well as none of the routine investigations revealed loss of iron through gastrointestinal tract, menstrual loss or loss of blood through trauma and despite good compliance to oral iron and folate as well as vitamin B12 supplementation patient had no improvement in Haemoglobin levels. Thus she was further investigated to rule out malabsorption disorders like celiac disease which is prevalent in North India almost equivalent to that in west[10]. Also she was worked up for haemoglobinopathies as prevalence of sickle cell disease and trait is seen in tribal rural population of North India[11].

Celiac disease is a common malabsorption disorder having heterogenous clinical presentation, which is often subclinical and remains undiagnosed. It's an immunological disorder characterised by gluten hypersensitivity in genetically susceptible individuals leading to immune mediated enteropathy characterised histologically as mucosal atrophy, loss of villi and reduced area of absorption, leading to malabsorption of various nutrients[12]. This in turn leads to deficiency of nutrients such as iron, folate, calcium, vitamin B12 etc presenting as generalised weakness and easy fatiguability and nutritional anaemia as was seen in case of our patient who otherwise had no other features of malabsorption like diarrhoea, steatorrhoea, abdominal bloating or flatulence[13]. In the past celiac disease was perceived to be a paediatric disorder but the diagnosis now is beingmade increasingly in adults with mean age at presentation being 45 yrs[14] as was in our case. Also the presentation of celiac disease has changed over past 50 yrs, diarrhoea now is reported less often[15] and presentation is more as nutritional deficiency anaemia as was seen in our case. Thus one should always work up for celiac disease and get levels of Anti Tissue transglutaminase antibody as well as Upper GI Endoscopy for a duodenal biopsy and mucosal histopathology for confirmation.

This case reported here was found to have Sickle cell trait, which often is either asymptomatic or presents with mild anaemia, the implication of this is to have realistic goals while correcting haemoglobin levels in this patient and to screen the family of the patient for this common autosomal codominant haemoglobinopathy. On screening patient's mother and father, mother was found to have sickle cell trait and father was normal. Her other siblings and husband and children could not be screened due to financial constraints.

Celiac disease is often associated with many other autoimmune conditions like insulin dependent diabetes mellitus, primary biliary cirrhosis, Sjögren's syndrome, sclerosing cholangitis and idiopathic haemosiderosis. Also one case of celiac with porphyria and beta thalassemia minor[16] has been reported in literature and few cases of beta thalassemia major with celiac disease have been reported[17]. But through wide search of medical literature(from pubmed and internet) this case that we report here is an atypical case of refractory microcytic hypochromic anemia with sickle cell trait and celiac disease and is probably the first of its kind.

Implication of reporting this case is that cases of refractory nutritional anaemias not responding to nutritional supplements can be distressing for both the patient and physician due to repeated administration of nutritional supplements and sometimes unnecessary blood transfusions when simple work up for commonly prevalent malabsorption disorders like celiac disease, and haemoglobinopathies like sickle cell trait, Hb D Punjab etc can help treat the patient easily by just advising gluten free diet and also make it less distressing for the treating physician by having more realistic targets of anaemia correction respectively. At the same time it improved quality of life of patient in a cost effective way.

Conclusion:

Nutritional anaemias are a major public health problem especially in rural population of India often get misdiagnosed and do not receive appropriate treatment, thus cases of nutritional anaemias not responsive to adequate replacements of iron, folate and Vitamin B12 should be investigated for often prevalent disorders such as celiac disease and sickle cell trait to provide better treatment and improve patient's quality of life as these disorders can often coexist. Also mere restriction of gluten can help the patient live a healthy life.

References:

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