Case Report

Pancytopenia as a presentation of B12 deficiency

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ABSTRACT

We present the case of a 16-year-old boy with hemolytic anemia with investigations showing pancytopenia, which turned out to be due to B12 deficiency. Whenever we see a teenager presenting with pancytopenia, the common causes that we think of are hematologic malignancies, drug-induced cytopenias, hypersplenism, etc. Anemia as a presentation is common in B12 deficiency, yet its occurrence with jaundice is a very uncommon and easily overlooked presentation. The same is the case of B12 presenting as pancytopenia which is a well-described entity, yet omitted initially due to its uncommon nature in this modern developed world.

Key words: B12 deficiency, Hemolytic anemia, Pancytopenia

Cobalamin deficiency is known to cause megaloblastic anemia and a neurologic affliction in the form of peripheral neuropathy, spastic paralysis with ataxia dementia, psychosis, or a combination of many of these features [1]. Minimal cobalamin deficiency, which may manifest as neurologic symptoms without anemia, is seen mainly among the elderly. Vitamin B12 deficiency is a rare cause of hemolytic anemia (approximately 1.5% of cases) [2,3]. Severe hemolytic anemia occurs due to increased folate demand for augmented erythropoiesis and thus may resemble an immune cytopenia. It is also thought to be related to the elevated levels of homocysteine which cannot be converted to methionine. *In vitro* deposition of homocysteine was found to cause hemolysis through lipid peroxidation and cytoskeletal protein derangement [4].

CASE REPORT

A 16-year-old teenager presented to the OPD with complaints of easy fatiguability and dyspnea on exertion which started and progressed over 1 month. There was no history of any palpitations, resting dyspnea, decreased appetite with undue weight gain and constipation, decreased urine output, cough with expectoration, or orthopnea. He had no past history of recurrent abdominal pain (gallstones), any cardiac disorders detected in childhood, or tuberculosis. There was no significant family history of hematologic disorders. He also started noticing gradually progressive yellow discoloration of his eyes over 1 week. There was no history of fever, edema, or drug intake.

Access this article online	
Received - 14 November 2022 Initial Review - 28 November 2022 Accepted - 31 December 2022	Quick Response code
DOI: 10.32677/ijcr.v8i12.3711	

On examination, he was conscious and oriented with stable vitals. The patient was pale with icterus and having hyperpigmented knuckles but there was no cyanosis, clubbing, edema, or any lymph node enlargement. His systemic examination was normal.

Investigations revealed that he had pancytopenia with hemoglobin of 5.5 g/dl, a total white blood cell count of 3800, of which neutrophils were predominant, and a platelet count of 1.3 lakhs. His mean corpuscular volume was 100 and his red cell distribution width (RDW) was 18%. His liver function tests revealed indirect bilirubinemia of 3.3 g/dl with aspartate aminotransferase of 156, alanine transaminase of 48, and a high erythrocyte sedimentation rate of 70. His renal function test was normal. Ultrasound abdomen showed no hepatosplenomegaly. As his laboratory investigation revealed a hemolytic pattern, tests were done in this line which showed an elevated lactate dehydrogenase (LDH) of 13840 (normal <250). The reticulocyte count was 0.8% which makes a reticulocyte production index <2. Direct and indirect coombs tests were negative and antinuclear antibody (ANA-IF) test was negative. Iron studies showed normalcy with serum iron-213, Ferritin-89, and a total iron-binding capacity of 217. A peripheral smear revealed normocytic normochromic red cells with occasional polychromasia and fragmented cells with spherocytes, elliptocytes, and tear-drop cells. White cells had normal count with neutrophil predominance with occasional hypersegmented neutrophils. Platelets were reduced. Hemoglobin electrophoresis showed hemoglobin to be within normal limits. Thyroid-stimulating hormone was 4.3 (normal). In view of the atypicality of presentation and completion, a bone marrow study was done (with consent) which showed erythroid series hyperplasia

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with megaloblastic maturation with a small percentage showing nuclear budding and irregularity along with normal myeloid and megakaryocytic maturation. To rule out any malabsorption, he had undergone an endoscopy which was also normal.

He was managed with 2 pint packed red blood cells transfusion. His hemoglobin improved to 8. In view of a picture suggestive of megaloblastic anemia, he was given a trial of B12 and assessed for reticulocyte response. His repeat reticulocyte count after 3 weeks was 5.6 and hemoglobin was 10 g/dl. Since he has low B12 levels, his vegetarian lifestyle with his food fussiness was thought to be the cause.

DISCUSSION

In this case report, a 16-year-old patient presented with symptoms of increasing fatigue and weakness associated with dyspnea on exertion with very low hemoglobin, confirming the presence of anemia. Concomitant jaundice with elevated direct bilirubin, LDH, and the presence of multiple scattered erythrocytes seen in the peripheral specimen suggest erythrocyte destruction or hemolytic anemia. Hemolytic anemia could be congenital or acquired. Because the patient has no history of anemia, no blood transfusion, and no previous symptoms related to anemia or gallstone disease, it is unlikely that a family history of anemia is also present. Hemoglobin electrophoresis also eliminated the presence of hemoglobinopathy and there was no history that could indicate G6PD deficiency (hematuria, drug use, and fever). His Coombs test, ANA, and antiphospholipid antibodies were negative, ruling out autoimmune hemolytic anemia.

Microangiopathic hemolytic anemia such as thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, and disseminated intravascular coagulation seemed less likely because the patient had normal coagulation parameters and no renal or neurologic abnormalities. Other intravascular hemolysis, such as valvular heart disease, was also ruled out because he had no murmurs on physical examination and a history of heart disease. The probable cause of hemolytic anemia, in this case, was Vitamin B12 deficiency, as the serum B12 level was very low and the diagnosis was confirmed by an elevated homocysteine level. Vitamin B12 deficiency is usually associated with macrocytic anemia without jaundice. The increased RDW was consistent with patterns of poikilocytosis and anisocytosis on peripheral blood examination. A low reticulocyte index (<2) also suggests defective erythropoiesis, which can be explained by severe Vitamin B12 deficiency and iron deficiency anemia. Intramedullary destruction or hemolysis of fragile and abnormal erythrocyte precursors results from ineffective secondary erythropoiesis and cell maturation [1]. The hemolytic picture may resemble microangiopathic hemolytic anemia [1]. If this condition persists, it can deplete iron stores and cause concomitant iron deficiency anemia [5].

Pernicious anemia is the most common cause of cobalamin deficiency worldwide [1]. However, among the elderly, the majority of cases are caused by malabsorption of food and cobalamin due to progressive atrophy of the gastric mucosa and hypochlorhydria [2,3,6]. The syndrome is characterized by an inability to release cobalamin from food for absorption due to decreased gastric acid secretion, but unbound cobalamin can be absorbed normally [2,3]. Folate deficiency can also cause elevated serum homocysteine, but not methylmalonic acid (MMA) [1]. Therefore, concomitant folate deficiency should be sought in patients with suspected Vitamin B12 deficiency. Due to financial constraints, the concentration of MMA and folate could not be controlled. The reason was revealed by further studies.

Our patient never had abdominal pain, reflux symptoms, or antacid use, making it less likely that atrophic gastritis or *Helicobacter pylori* infection was the cause, as shown by esophagogastroduodenoscopy evaluation with pathologic biopsy. Since his diet consists mostly of greens and vegetables, it is doubtful that a folate deficiency was involved. *H. pylori* infection is associated with gastric atrophy that can result first in iron deficiency and later lead to cobalamin malabsorption and perhaps even predispose to pernicious anemia [5-7].

CONCLUSION

Pernicious anemia is the most common cause of cobalamin deficiency worldwide. Anemia as a presentation is common in B12 deficiency, yet its occurrence with jaundice is a very uncommon and easily overlooked presentation. Our patient presented with hemolytic anemia which after investigations showed pancytopenia and finally B12 deficiency which may be due to his vegetarian lifestyle and food fussiness.

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Funding: Nil; Conflicts of interest: Nil.

How to cite this article: Purushothaman P, Rijas K, Ravindran K. Pancytopenia as a presentation of B12 deficiency. Indian J Case Reports. 2022;8(12):395-396.