An Interesting Case of Anemia

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BACKGROUND

Cobalamin (Vitamin B12) deficiency can result in abnormalities in all cell lines which normalize after cobalamin replacement⁴. Moreover, Andres et al. reported hematological findings in 201 consecutive patients with vitamin B12 deficiency ². Approximately 10% of the patients had life threatening hematological manifestations, including symptomatic pancytopenia (5%), “pseudo”
thrombotic microangiopathy (2.5%), and hemolytic anemia (1.5%). A significant proportion of these patients underwent invasive and comprehensive diagnostic panels to rule out other causes of such abnormalities. At times, these patients were misdiagnosed and treated with aggressive measures such as steroids, polyvalent immunoglobulins, and plasmapheresis².

Concurrent hemolysis in patients with Vitamin B12 deficiency has been attributed to intramedullary destruction of red blood cells (ineffective erythropoiesis)³. Patients demonstrated complete resolution of hemolysis after vitamin B12 treatments⁴. On the other hand, associations with autoimmune cytopenias have been described previously⁵-¹¹, and some features of Pernicious Anemia and these cytopenias can mimic each other. The ineffective erythropoiesis and hemolytic component of cobalamin deficiency can produce increased lactate dehydrogenase activity¹², indirect hyperbilirubinemia¹³,¹⁴, a decreased serum haptoglobin level¹⁵, decreased erythrocyte survival¹⁶,¹⁷, and occasionally even methemalbuminemia¹⁵ and hemosiderinuria¹⁸. Furthermore, a positive direct coomb’s test is a common finding in untreated pernicious anemia¹⁹,²².

**CASE PRESENTATION**

A 45 year old african american female consulted her primary care physician with a two-week history of progressively worsened generalized fatigue, shortness of breath upon exertion and dizziness. Her dizziness was described as lightheadedness especially when standing up from sitting position. She was found to have hemoglobin of 3.9 mg/dL at the office and was immediately referred to our emergency room for further evaluation and treatment. Her past medical history was positive for diffuse osteoarthritis and iron deficiency anemia. Patient denied hematochezia, hemoptysis or hematuria. She had no history of peptic ulcer disease or over the counter non-steroidal anti-inflammatory drugs (NSAIDS) abuse. However, the patient did report unintentional 40 lbs. weight loss over the past year, ice craving and heavy menstrual periods, which came every 28 days and usually lasted 5 days. Her last menstrual period had started seven days prior and was still present on admission with a heavy flow. The patient was taking only over the counter cold medications.

Her initial physical examination revealed a heart rate of 90 beats per minute, pronounced pallor, no jaundice and 1/6 systolic flow murmur over left sternal border. No palpable abdominal organomegaly. The patient was found to have pancytopenia, with a leukocyte count of 2.36 x 10³/µL, a hemoglobin level of 5.8 g/dL, and a platelet count of 97 x 10³/µL. Her coagulation tests showed an activated partial thromboplastin time (aPTT) of 23.9 seconds and an international normalized ratio (INR) of 1.19. Complete blood count revealed normocytic anemia with a mean corpuscular volume (MCV) of 91.1 fl, and an elevated red cell distribution width (RDW) of 31.9%. Further workup for anemia revealed no evidence of Iron Deficiency Anemia, with an iron level of 61 μg/dL, a total iron binding capacity of 290 μg/dL, a ferritin level of 51 ng/mL, and a transferrin level of 207 mg/dL. A pelvic ultrasound revealed a normal size uterus with a small anterior myometrial fibroid; normal endometrial thickness and normal ovaries.

The peripheral blood smear showed marked schistocytosis, anisocytosis, poikilocytosis, moderate macrocytes, slight polycromasia, hypersegmented polymorphonuclear cells, tear-drop red blood cells and ovalocytes. Myeloid precursors were not present neither did blasts. One
percent of nucleated red blood cells were present. Serum vitamin B12 level was 153 pg/mL (normal 150-800 pg/mL), with a folate level of 413 ng/mL, Homocysteine level of 73.3 µmol/L, and Methylmalonic Acid (MMA) 60.93 of µmol/L. Serum chemistry studies were remarkable for elevated lactate dehydrogenase (LDH) levels at 4632 IU/L, which was significantly out of proportion to the degree of elevation of bilirubin at 2.3 mg/dL; and normal Haptoglobin of 26 mg/dL. She also had normal BUN and creatinine with a slight elevation in transaminases (ALT=40 IU/L, AST=90 IU/L). The corrected Reticulocyte count was 0.53%, showing a lack of a significant bone marrow response to the hemolysis. In addition to this, direct coomb’s and fecal occult blood test were negative. Hemoglobin electrophoresis showed normal adult hemoglobin. Further workup revealed normal G6PD (glucose 6 phosphate dehydrogenate) activity, negative Hepatitis B and C serologies, and a positive Hepatitis A IgG indicating prior exposure.

A bone marrow aspiration was performed and cytomorphologic as well as cytogenetic analysis was carried out. Flow Cytometry revealed no detectible evidence for an increased blast population (about 2%). CD56 was aberrantly co-expressed in a subset of the maturing myeloid population. This finding is aberrant and nonspecific, can be associated with myelodysplasia. No evidence for lymphoproliferative disorder was seen. Cytogenetic revealed normal female karyotype without evidence of a chromosomal abnormality. The pathology diagnosis reported was hypercellular marrow with megaloblastic changes. The LDH isoenzymes pattern was non-specific.

During the course of the one-week hospitalization, the patient was transfused with 2 units of packed RBC and started on treatment with intramuscular injections of cobalamin and oral supplementation of folic acid. Further laboratory examinations showed a positive anti-intrinsic factor antibody. An improvement of the pancytopenia, reduction of LDH levels and normalization of bilirubin and transaminases levels were achieved before discharge. Patient was continued vitamin B12 and folate therapy in an outpatient setting.

DISCUSSION

Concurrent hemolysis in patients with vitamin B12 deficiency can result in severe anemia. While its mechanism is not entirely understood, it is believed that the hemolysis results from intramedullary destruction. Our patient presented with irregular menstrual periods and anemia with elevated RDW, but her normal iron indices and normal endometrial thickness, excluded the diagnosis of iron deficiency anemia; and, she had ongoing hemolysis as evidenced by the presence of schistocytes in the peripheral blood smear, high level of LDH and low level of haptoglobin.

The low Reticulocyte count indicated an inadequate bone marrow response to the anemia. However, the hypercellular bone marrow with megaloblastic changes and the peripheral smear with hypersegmented neutrophils indicated folic acid or vitamin B12 Deficiency. The patient’s low normal level of vitamin B12 with high MMA levels and a positive anti-intrinsic factor antibody, demonstrated she had vitamin B12 Deficiency (pernicious anemia), resulting in severe intramedullary hemolysis and ineffective erythropoiesis.
Although vitamin B12 Deficiency normally presents with high MCV, in this case, the normal MCV could be explained by average size of macrocytes and schistocytes. Also the thrombocytopenia occurs often as part of the megaloblastic abnormality in severe cobalamin deficiency. It is not due to immune mechanisms, and the platelet count becomes normal with simple vitamin replacement\textsuperscript{23}, as happened in this case.

Vitamin B12 Deficiency and pernicious anemia can be suspected as they can produce, because of ineffective erythropoiesis, increased LDH activity, indirect hyperbilirubinemia, a decreased serum haptoglobin level, decreased erythrocyte survival, and occasionally even methemalbuminemia and hemosiderinuria. Thus, careful attention should be paid to the possibility of vitamin B12 Deficiency in patients with severe anemia and hemolysis.

FIGURES

![Peripheral smear showing schistocytosis, anisocytosis, and poikilocytosis with hypersegmented neutrophils.](image)

![Bone Marrow Aspiration showing Hypercellularity with megaloblastic changes. Flow cytometry showed no evidence of increase blast cells.](image)
REFERENCES

Hypermucoviscous Klebsiella Pneumoniae Liver Abscess in a Previously Healthy Burmese Male

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Introduction

Discovered over 100 years ago, Klebsiella pneumoniae is a gram-negative pathogen found in the environment and on mammalian mucosal surfaces¹. In the Western world, K. pneumoniae most commonly infects the lungs and urinary tract. The majority of these infections occurs in hospitals and long-term care facilities². However, over the past 20 years, considerable attention has been focused on community-acquired pyogenic liver abscesses (CA-PLA) caused by a hypervirulent variant of K. pneumoniae with a tendency for metastatic spread²,³. Most of these cases have

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