Megaloblastic anaemia with pancytopenia.

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Abstract

Megaloblastic anemia is a form of anemia characterized by very large red blood cells. Most common causes of megaloblastic anemia are deficiency of either cobalamin (vitamin B12) or folate (vitamin B9) due to inadequate food assumption. Pancytopenia is a condition where reduction of red blood cell, white blood cell and Platelets. Widespread of anemia is more is female than male in the age group of 15-35. Most common symptoms are generalized weakness, shortness of breath when undertaking normal tasks, high-grade fever. Hands and feet of patients have no history of par-anesthesia, no history of seizure, no pain in abdomen, no puffiness on face, no splenectomy, no Malena is noted but loss of appetite is seen. On family history examination, no sickle cell anemia or thalassemia is present in the family. On examination Pallor present in conjunctiva and nails, no icterus, hyperpigmentation is seen over the back hands and finger, no lymphadenopathy (lymph node is unaffected) is present. On investigation Sévère macrocyte anemia, leucopénie (decrease in WBC count) and thrombocytopenia (decrease in platelets) were discovered in the laboratory. Peripheral smear showed moderate anisocytosis (RBC of unequal size) with significant macrocytosis (enlarge RBC), Normocytes showing mild to moderate hypochromia. Occasional late normoblasts is seen. Leucopenia with relative lymphocytosis with few rare giant platelets was seen. Most common test which reveals underlining cause of pancytopenia is Bone Marrow test. For treatment Injection vitofol IM should be given for megaloblastic anemia.

Keywords: Megaloblastic anemia, Pancytopenia, pallor, Anisocytosis, Bone marrow test.

Background

The most frequent cause of serious vitamin B12 insufficiency in adolescent as well as in adults globally are inadequate animal food consumption and pernicious anaemia (loss of intrinsic factor due to depletion of parietal cell) [1,2].

Reversible megaloblastic anaemia and Parkinson's disease can both be caused by vitamin B12 deficiency. The intensity of megaloblastic anaemia seen in vitamin B12 inadequate persons shows conversely association to the level of autonomic impairment, for unknown reasons [1].

Although most cases of vitamin B12 deficiency have modest hematological symptoms, lethal illnesses like symptomatic pancytopenia, serious anaemia (in which hemoglobin level of less than 7 g/dL) and anaemia due to inherited blood disorders like sickle cell disease is seen in roughly 10% of patients [3]. We describe a teen who had severe cobalamin insufficiency due to consuming insufficient animal-based foods. When he came, he had severe anaemia, haemolysis, and pancytopenia. The hematological problems fully vanished after receiving sufficient replacement therapy.

Macrocytosis seen without presence of anaemia

Sometimes the presence of large erythrocytes circulating in blood is not usually linked to a pathogenic process or any illness. In fact, red blood cells (RBC) of infants and newly born child (mean MCV- 106ft) are much larger than the normal person red blood cell. Also, in case of pregnancy, large ABC is found even if there is no evident cause. In the absence of any known or present clinical abnormalities, macrocytosis without anaemia may be a normal variety i.e only detected by repeated peripheral RBC indices. In other family members this deviation from normal can be detected if there is presence of any other genetic propensity.

Case description

Patient is 14year old female resident of was brought with Chief complaints of fever since 4 days, generalized weakness, breathlessness on exertion since 15 days.

History of presenting illness

According to the mother's account Patient appeared to be in good health until 15 days ago, when she suffered generalized

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weakness and shortness of breath when undertaking normal tasks. For 4 days, Patient had a high-grade fever that started slowly and wasn't accompanied by chills or rigors. After taking medicine, Patient felt relieved. History of, showed a decrease in food intake and a loss of appetite. Hands and feet have no history of paranesthesia. There has been no history of loss of consciousness. There is no history of inattention or somnolence. No evidence of seizure activity has been seen. H/o PICA is not an option. There is no h/o blood in the stools. There is no h/o constipation. There are no worms in the stools or vomitus. There is no h/o pain in the abdomen. There is no h/o bone discomfort. There is no h/o puffiness on the face.

Patient History

Patient was admitted to the hospital with similar symptoms around a year and a half ago. After a blood transfusion, the patient was released after two days.

Personal history: There were no bowel movement and bladder problems. It was a typical night of sleep. Appetite decreased.

Family history: There have been no other problems in the family. No one in the family has received h/o blood transfusions. There is no sickle cell or thalassemia in the family. There are no thyroid problems in the family. In the family or siblings, there is no h/o bleeding tendencies/ blood transfusions/jaundice/anaemia/gall stones. No one in the family has had an h/o splenectomy.

Environmental history: No h/o any exposure to toxic substances or chemicals.

Socio economic history: Child belongs to moderate socioeconomic class. No open-air defecation was seen.

Dietary history: Vegetarian

1. Breakfast - Poha, Maggie, Upma. No milk or tea.
2. Lunch - Does't prefer to have white rice. Little amount of green leafy vegetables.
3. Dinner - roti, curry.

Menstrual history

1. Age of menarche - 12 years
2. Cycle length - 2 days
3. Number of pads changed - per day 2
4. No passage of clots seen.
5. No lower abdominal pain or back pain. No menorrhagia or dysmenorrhea was reported by the patient.

Development history: No development delay was seen while examing the patient. Achieved milestones as per age. No speech developmental delay. Not so talkative and interactive personality.

Birth history: Full Term Normal Delivery/2.5 kg weight/ Baby cried immediately after birth. No history of Neonatal intensive care unit stay.

No history of: perinatal/antenatal/postnatal complications.

No history of: bleeding from the cord

No history of: any birth injuries.

Antenatal history: A booked case. During pregnency, Iron and Folic acid supplement was receive.

No history of: drug or radiation exposure during pregnancy.

No history of: toxoplasmosis, rubella, cytomegalovirus, herpes simplex and HIV infections during pregnancy.

No history of: antepartum haemorrhage.

On examination

Pallor was present in conjunctiva and nails, no icterus, No hyperpigmentation over the back hands and finger, no lymphadenopathy was seen. A febrile. HR 120/min, RR 28/ min. Pulse well felt. Spo2 98%. BP 108/64 mmhg

Systemic Examination - CVS - s1s2 heard.

Ejection systolic murmur present.

Central Nervous System Examination - conscious alert oriented.

Pulmonary Artery on examination - Soft non tender no organomegaly.

On examination of bone marrow

Enlargement of red blood cell in the presence of a megaloblastic marrow is frequently accompanied with anaemia caused by inefficient erythropoiesis. The bone marrow is hypercellular, with several myeloid cell lines exhibiting aberrant proliferation and maturation. Most abnormalities are seen in erythroid precursors having big megaloblastic erythroblasts appearing in greater quantities throughout the bone marrow. Huge or enormous metamyelocytes and other granulocytic progenitors (additional myeloid elements), show similar morphologic anomalies. Increased lactate dehydrogenase and indirect bilirubin in the serum is resulted from intramedullary hemolysis which was resulted from insufficient erythropoiesis. However, because of the aberrant maturation process, the reticulocyte count is short. Chronic myeloid leukemias show more serious levels of aberrant proliferation and maturation. A bone marrow test is usually not required in patients with macrocytosis who are not anemic and have no other deformity on a peripheral blood smear. In order to comprehend these crucial, subtle hematological anomalies, these must be examined in the bone marrow.

Investigation on macrocytosis

A systematic approach is required when a patient with macrocytosis is evaluated. A detailed history including history of presenting illness, patient history, personal history, environmental history, family history, socio economic history, dietary history, developmental history, birth history, antenatal history and physical examination should be performed first, followed by relevant laboratory tests such as a complete blood count (CBC), a peripheral blood smear and a reticulocyte count. A bone marrow examination may be required in some instances.

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When thalassemia trait, iron insufficiency, or other nutritional deficits occur with a vitamin B12 or folate insufficiency, determining the underlying a etiology of macrocytosis can be extremely difficult. In some cases, mixed variety of macrocytic and microcytic red blood cell may be seen in peripheral blood smear. In alcoholic cases associated with macrocytosis, there is an increase in mean corpuscular volume either due to folate deficiency or due to any other liver disease.

Investigations based on laboratory bases

In the laboratory, value of haemoglobin was 5.2g/dl; Mean corpuscular volume (MCV) was 118fL representing severe macrocytic anaemia, white cell count - 2530/L; neutrophil count - 1220/L representing leucopenia and thrombocytopenia - 106000/mm3. Reticulocyte percentage was found to be 0.7

1. In blood
2. Indirect bilirubin - 565U/L(125-240)
3. Lactate dehydrogenase (LDH) - 140U/L (10-40)
4. Uric acid - 9.2mg/dL (2.5-8.5)
5. Aspartate and Alanin aminotransferase - 50 U/L(10-40)

The screening tests for C reactive protein, direct Coombs, and glucose-6-phosphate dehydrogenase (G6PD) deficiency were all negative. The values of serum vitamin B12, folic acid were 159 pg/mL (210–912), 5.74 ng/mL respectively. The amount of plasma homocysteine was abnormally high (less than 50 mol/L; usual 5–14 mol/l). Previous infection (no recent infection) was indicated by both the virus's cytomegalovirus and Epstein-Barr virus. Previous results supposed to indicate significant vitamin B12 insufficiency.

Peripheral smear showing - moderate anisocytosis with significant macrocytosis. Normocytes showing mild to moderate hypochromia. Occasional late normoblasts seen. Leucopenia with relative lymphocytosis with few rare giant platelets was seen. Liver function test (LFT) and Kidney function test (KFT) are normal. Serum Vit. B12 levels were 159pg/ml which is below normal levels. Post transfusion patients' appetite improved, fatiguability decreased compared to earlier.

Differential Diagnosis

In the differential diagnosis, hemolytic anaemia due to Glucose 6 phosphate dehydrogenase (G6PD) deficiency, sickle cell anaemia, Thalassemia, inherited oval shaped red blood cell, infections due to malaria, Rickettsia, anaemia due to insufficient production of new red blood cell, glycogen storage disease, phosphofructokinase deficiency and Hemophagocytic lymph histiocytosis (caused by pancytopenia and splenomegaly), deficiency of vitamin B12 and folic acid (caused by macrocytic anaemia), and combination of pancytopenia, hemolysis and splenomegaly which causes body to improperly regulate lymphocytes were all evaluated. Leukaemias was ruled out by a bone marrow aspiration test, and laboratory data persistent with serious vitamin B12 insufficiency were assumed to describe all of the unusual diagnostic findings in the patient [4].

Treatment

1. Patient was orally allowed, PRC was transfused @5 ml/kg
2. **Injection:** Vitcofol IM started at 100 mcg/dl per day and folic acid 5mg/day considering B12 and folic acid deficiency.
3. **Discharge Advice**

a) Continue injection: Vitcofol Intramuscular (IM) for 7days at 100 mcg/24hr. Repeat complete blood count (CBC) at 7th day.

b) Then injection. Vitcofol 1000mcg/week for 4 weeks. Repeat S. B12, complete blood count (CBC) and S.folate at 4th week [5,6].

Conclusion

The most prevalent cause of pancytopenia is megaloblastic anaemia. In pancytopenia patients, a single useful investigation that indicates the underlying reason is a bone marrow examination. The severity of pancytopenia and the underlying disease influence the patient's treatment and prognosis. A large portion of pancytopenia is caused by megaloblastic anaemia, which may be treated.

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