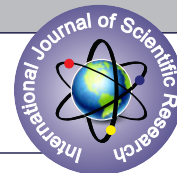


A RARE CASE OF NUTRITIONAL MEGALOBlastic ANEMIA WITH PANCYTOPENIA PRESENTING AS FEVER, WHICH GOT SUBSIDED ON CORRECTING THE VIT B12 DEFICIENCY



General Medicine

Dr. Snigda

Panuganti

Dr Alla Krishnakar

Reddy

Dr. Balu Banoth

Dr. Sindhuja

Chindam

Dr. D. Padmakar

Reddy

KEYWORDS

INTRODUCTION :

Pancytopenia is the presence of anemia, leucopenia, and thrombocytopenia with Hemoglobin (Hb) being less than 13.5g/dl in males or 11.5g/dl in females; the leucocytes count is less than $4 \times 10^3/l$ and the platelets count is less than $150 \times 10^3/l(1)$. The commonest clinical manifestations of Pancytopenia are usually Fever (86.7%), fatigue (76%), dizziness (64%), weight loss (45.3%), anorexia (37.3%), night sweats (28%), pallor (100%), bleeding (38.7%), splenomegaly (48%), hepatomegaly (21.3%), and lymphadenopathy is (14.7%)(2).

The most common causes of Pancytopenia on Bone Marrow examination are Hypoplastic bone marrow (29.05%), Megaloblastic anemia (23.64%), Hematological malignancies i.e. Acute Myeloid Leukemia (21.62%), and Erythroid hyperplasia (19.6%)(3).

Megaloblastic anemia is a rare but known and treatable cause of pyrexia that should be considered in a patient presenting with pyrexia without other infective, inflammatory or endocrine sources. This is of particular importance in patients with pyrexia and pancytopenia picture.

We present a case of Pancytopenia due to nutritional Vit B12 deficiency presenting with a fever of 10 days duration which got subsided after supplementing Vit B12. This case highlights vitamin B12 supplementation as an easily treatable cause of fever in patients with severe Vit B12 deficiency with anemia, before proceeding with more complicated and expensive investigations or starting empiric treatments

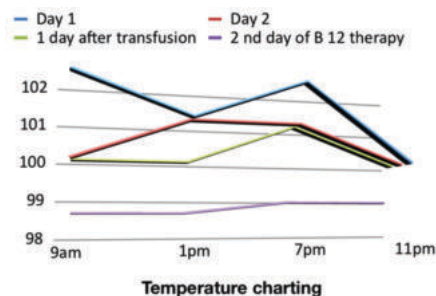
Case Report :

A 40 yr old female, teacher by occupation presented with complaints of fever, SOB, and generalized weakness for 10 days. Fever was high grade continuous not associated with evening rise of temperature, chills, and rigors. Shortness of breath since 10 days initially able to walk more than 100 mts with slight breathlessness which gradually progressed to stage 4 of MMRC that is inability to perform daily activities without breathlessness, not associated with orthopnea, PND. No complaints of cough, cold, diarrhea, headache, burning micturition. No history of Inflammatory bowel disease, TB, asthma, diabetes, or hypertension. She has normal menstruation, there was no history of addictions or any other drug ingestion. Has regular bowel and bladder habits, sleeps adequately. On clinical examination she was febrile with a temperature of 102 F, pulse rate was 130 beats/min, respiratory rate 20/min, and blood pressure of 100/60 mmHg. BMI of 21kg/m². Severe pallor was seen on general examination, no icterus, cyanosis, clubbing, lymphadenopathy, koilonychia, or pedal edema. Abdominal, respiratory, and neurological examination was normal

Investigations:

Hemogram showed pancytopenia with Hemoglobin of 4.1gm/dl, WBC count - 2400 cells/cumm, platelet count of 70000 cells/cumm,

RBC count of 0.9 millions/cumm, Hematocrit -12.2% with peripheral blood picture showing macrocytic Hypochromic RBCs few microcytic Hypochromic RBCs with teardrop cells and pencil forms.



Reticulocyte count of 0.4% with an absolute reticulocyte count of 0.1 and reticulocyte index of 0.05. LFT showed total bilirubin of 2.0mg/dl and normal transaminase levels. S creatinine of 0.6 mg/dl and blood urea of 16mg/dl. Serum Vit B12 level was found to be very low at 75 pg/ml (Normal range 180-914) and serum iron -15mcg/dl and TIBC 222mcg/dl, serum ferritin 222ng/ml. LDH >1200U/L. Urine examination was normal with RBC 0-1/hpf, pus cells 1-2/hpf.

There was no evidence of malarial parasite on blood smear examination, dengue NS1 antigen was negative. HIV, HBsAg, and HCV were all negative. Repeated blood cultures and urine cultures were all negative. Thyroid hormones were in the normal range. Complete stool examination was normal.

Parameters	At presentation	After 1 pint PRBC transfusion	20 days after Vit B12 treatment
Haemoglobin (gm/ dl)	4.1	5.9	10.3
RBC count (millions/ cumm)	0.9	1.7	3.3
WBC count (cells/ cumm)	2,400	3,500	4,300
PCV/HCT (%)	12.2	18%	33.2
MCV (fl)	135.6	105.3	102
MCH (pg)	45.6	34.5	31
MCHC (gm/dl)	33.6	32.8	31
Platelet count(cells/ cumm)	70,000	39,000	2.3 Lakh
Peripheral smear	Macrocytic Hypochromic	Macrocytes with few Normochromic normochromic	Normochromic Normochromic RBCs with occasional Macrocytes

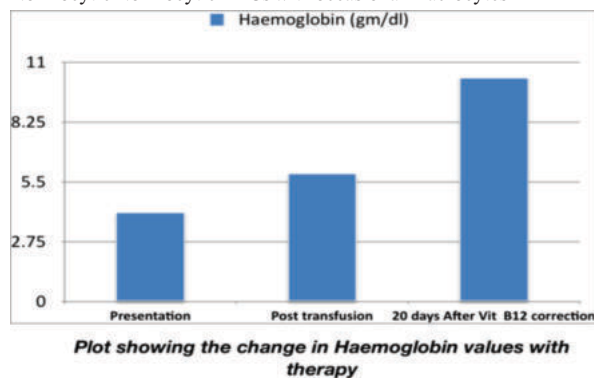
Chest radiograph showed normal lung fields and a normal mediastinum. USG abdomen was normal. 2D echocardiography is normal with EF of 60% with no valve abnormalities.

After common infections, autoimmune, endocrine, and hematological conditions have been excluded, a provisional diagnosis of Vitamin

B12 deficiency induced Pyrexia was postulated and treatment was started with a packed RBC transfusion on day 2 of admission after which HB improved to 5.9 gm/dl.

Parenteral Vit B12 therapy with injection cyanocobalamin 1000mcg OD supplemented. Patient became afebrile 2 days after starting therapy .patient was discharged after giving parenteral Vit B12 therapy.

With advice to take Vit B12 injections every week for 4 weeks .Patient remained afebrile during follow-up after 20 days, showed improvement in Haemoglobin to 10.3 gm/dl, WBC count of 4,300 and Platelet count of 2.3 Lakh cells /cumm and peripheral picture showed Normocytic Normocytic RBCs with occasional Macrocytes



DISCUSSION:

Incidence of low-grade fever in nutritional megaloblastic anemia varies from 28% to 60% (4), but vitamin B12 deficiency rarely presents as the sole cause of fever. Several mechanisms have been put forward in the past to explain the cause of fever in megaloblastic anemia like a defect in the temperature control mechanism of the brain or poor oxygenation of the temperature regulatory area, both of these theories fail to explain why fever is not a feature of other forms of anemia's (5). Another proposed mechanism is that megaloblastic anemia leads to hyperplasia and thus increased activity within the bone marrow leading to systemic pyrexia (6).

The level of pyrexia usually correlates with the degree of anemia and resolves very quickly after starting the treatment. Very few case reports were found where vitamin B12 deficiency was attributed as the sole cause of pyrexia. (7,8,9)

In a study on megaloblastic anemia as a cause of PUO by Bushra Siddiqui et al (7), they found that 4 out of their 15 (26.6%) patients with megaloblastic anemia were associated with fever that had no improvement with antibiotics but experienced marked improvement in fever within 48 h of administration of vitamin B12 and folate.

Patients presenting with fever, anemia, neutropenia, and thrombocytopenia are usually treated as febrile neutropenia with broad-spectrum antibiotics with no improvement. Megaloblastic anemia, though rare, is a treatable cause of pyrexia. Thus patients with pyrexia and features of megaloblastic anemia or pancytopenia should be investigated for vitamin B12 and folate deficiencies after ruling out infectious, inflammatory, and endocrine causes.

Failure of resolution after vitamin supplementation should, however, suggest the probability of an alternative cause for pyrexia. (5)

CONCLUSION

Megaloblastic anemia with pancytopenia presenting with fever and when no other endocrine, infections, the hematological cause is found. Patients have to be treated for vitamin B12 deficiency instead of doing extensive investigations. Thus our case is a good example of how megaloblastic anemia can be the cause of fever as the fever was relieved very quickly after initiating treatment for vitamin B12 deficiency.

REFERENCES:

1. Khunger JM, Arulselvi S, Sharma U, Ranga S, Talib VH. Pancytopenia is a clinicohaematological study of 200 cases. Indian J Pathol Microbiol. 2002;45:375-379. [PubMed] [Google Scholar]
2. Imbert M, Scoazec JY, Mary JY, Jouzult H, Rochant H, Sultan C. Adult patients presenting with pancytopenia: a reappraisal of underlying pathology and diagnostic

- procedures in 213 cases. Hematol Pathol. 1989;3:159-167. [PubMed] [Google Scholar]
3. Jha A, Sayami G, Adhikari RC, Panta AD, Jha R. Bone marrow examination in cases of pancytopenia. JNMA J Nepal Med Assoc. 2008;47:12-17. [PubMed] [Google Scholar]
4. Tahlan A, Bansal C, Palta A, Chauhan S. Spectrum and analysis of bone marrow findings in anemic cases. Indian J Med Sci. 2008;62:336-9. [PubMed] [Google Scholar]
5. McKee LC. Fever in Megaloblastic anaemia. South Med J 1979;72:1423-4.
6. Singanayagam A, Gange N, Singanayagam A, Jones H. Folate deficiency presenting as pyrexia: A case report. Cases J. 2008; 1:275.
7. Bushra Siddiqui, Divya Rabindranath, Shahbaz Habib Faridi, I Azka Anees Khan, Sadaf Haiyat, and Rabindranath Eswaran. Megaloblastic anemia: A common but often neglected cause of pyrexia of unknown origin: J Transl Int Med. 2015 Apr-Jun; 3(2): 64-67.
8. Manuel K, Padhi S, G'boy Varghese RG. Pyrexia in a patient with megaloblastic anemia: A case report and literature review. Iran J Med Sci 2013;38:198-201
9. Negi RC, Kumar J, Kumar V, Singh K, Bharti V, Gupta D, et al. Vitamin B12 deficiency presenting as pyrexia. J Assoc Physicians India 2011; 59:379-80.