



Bleeding Diathesis: When Do We Suspect Vitamin B12 Deficiency?

Authors

**Dr Sushant Mane¹, Dr Sonali Singh², Dr Swapnil Kumar³,
Dr Dattatray Pandurang Shinde⁴**

¹Associate Professor, ^{2,3,4}Junior Residents

Dept of Pediatrics Grant Government Medical College and Sir JJ Group of Hospitals Mumbai

Corresponding Author

Dr Sushant Mane

1205, Horizon Gokhale Road North, Opposite Shushrusha Hospital, Dadar (West), Mumbai – 28

ABSTRACT

Megloblastic anemia is uncommon in pediatric age group. It is most commonly due to vitamin deficiencies or gastrointestinal disorders. Megaloblastic anemia due to Dietary vitamin B-12 deficiency in infants is very rare but may be seen in breastfed infants whose mothers are B-12 deficient. Sometimes absence of carrier protein, transcobalamin, may present with megaloblastic anemia in early infancy. These infants if not treated promptly may develop myelopathy and developmental delay. Other children may sometimes present with bleeding diathesis secondary to qualitative and quantitative defects of platelets and sometimes pancytopenia. We present here a case of 8 year old girl who presented to us solely with ecchymosis and subcutaneous haematomas. Her blood picture showed bicytopenia with high MCV pointing towards the diagnosis of Megaloblastic Anemia. Bone marrow biopsy confirmed the diagnosis. She was given intramuscular methylcobalamine for 2 weeks followed by oral methylcobalamine and folic acid.

Keywords: *Megaloblastic Anemia, Bleeding Diathesis, Bone Marrow Biopsy, Methylcobalamin & Folic acid.*

INTRODUCTION

Megaloblastic anemia is a form of hypo proliferative anemia with delayed DNA maturation, commonly encountered in those with a strict vegetarian diet. In these patients inadequate vitamin B12 or folic acid intake is the commonest cause¹. Vitamin B12 and folic acid are important for DNA synthesis, so their deficiency affects all profile rating cells. In the hematopoietic system all three cell lines get affected with usual sequence being anemia followed by

thrombocytopenia and neutropenia². Commonly, patients present with fever, lethargy, pallor. Thrombocytopenia, though an additional finding is rarely the presenting complaint. Atrophic gastritis and achlorhydria commonly occur in adult patients³. Here we report a girl who presented only with ecchymosis and subcutaneous hematomas, diagnosed as having megaloblastic anemia and subsequent vitamin B12 therapy corrected her symptoms.

CASE REPORT

An 8 year old girl presented with appearance of spontaneous ecchymosis on face and both upper and lower limbs since past 15 days; each lesion lasting for around 5-6 days with self resolution. New lesions kept on appearing even after admission. There was no history of easy fatigability, dizziness, pallor (pale complexion), trauma, fever, history suggestive of repeated infections or of upper respiratory tract infection in last 1 month. There was no history of bleeding from any other site or any prolonged drug intake in recent past. She gave no history of tingling or numbness, change in behaviour, history of bone pains or swellings anywhere. There was no family history of bleeding disorder. She took non-

vegetarian diet once in 1-2 months. On examination she was thin built with significant pallor. Her pulse rate was 98/min, respiratory rate was 20/min, blood pressure was 106/62mm Hg. She had 5 ecchymotic patches (1 on Right forearm, 2 on Right leg and 2 on Left leg); each around 4 × 5 cm in size, non tender, purplish-black in colour.

During her stay in the hospital, she developed hematomas initially on dorsal aspect of left forearm, followed by another on the right leg. She had post-axial polydactyly in left hand. There was no oedema, joint swelling, mucosal bleeds, lymphadenopathy, knuckle hyper pigmentation, bony tenderness, and no organomegaly.



Fig :1 Showing Haematoma on Right Forearm

Her central nervous system examination was normal. Other systems too were unremarkable. Her blood counts were as shown in Table 1.

Table 1 : Serial Blood Counts over a period of 2 weeks.

	14/10/15	15/10/15	17/10/15	20/10/15	26/10/15	31/10/15
HB (gm%)	6.9	8	7.7	7.6	6.9	6.8
WBC (mm ³)	5100	5300	7300	7600	7100	5800
Neutrophils (%)	56	68	63	35.5	29	26
Monocytes (%)	5	3	4	7.8	6	7
Lymphocytes (%)	39	27	31	56	65	67
Platelets (mm ³)	20000	16000	17000	20000	14000	14000
HCT	22	27	27	24.9	23	23.1
RBC	2.29	2.64	2.65	2.53	2.64	2.53
MCV	96.5	103.7	104.7	98.4	104	105.9

MCH	30	30.3	29	30	31.3	31.1
MCHC	31.2	31.2	27.7	30.5	30	29.4

Peripheral smear showed dimorphic erythrocytes with mild hypochromasia, anisocytosis, poikilocytosis, few macrocytes, occasional elliptocytes and schistocytes with 28% hypersegmented neutrophils, 0% band forms, low platelets with few large platelets. Her corrected reticulocyte count was 2.5%, Direct Coomb's test was negative, with a normal coagulation profile, platelet function studies and normal stool examination. Her serum vitamin B12 was 190 pg/ml (200-835pg/ml), folic acid- 7.41ng/ml (5-20), homocysteine-65 µmol/lit (4-17).

Bone marrow examination confirmed the diagnosis of megaloblastic anemia. She was given intramuscular methylcobalamine for 2 weeks followed by oral methylcobalamine and folic acid. Follow up after 2 weeks showed no new lesions, with resolution of previous ones.

DISCUSSION

Liver has a good store of vitamin B12. It takes 2-3 years for deficiency to manifest if vitamin B12 intake is cut off and is commonly seen in vegetarians or those with inadequate diet. In megaloblastic anemia, defective DNA synthesis and impaired cell division results in increased DNA content in megaloblastic cells that have morphologically large volume (Macrocytes) with nuclear dysmaturity. It is a global defect affecting all proliferating cells. In study by Tilak V *et al*⁴, overall incidence of megaloblastic anemia was 68%, with 0.8% - 32.26% of all pancytopenic patients having megaloblastic anemia. Khunger JM *et al* had overall incidence of megaloblastic anemia of 72%⁵.

Besides thrombocytopenia this condition is also associated with qualitative defect in platelets. Platelet response to agonists like adenosine diphosphate (ADP), ristocetin and epinephrine is considerably decreased in vitamin B12 deficiency, which improves with vitamin replacement. There are case reports where vitamin B12 deficiency

was associated with pancytopenia⁶. Thrombocytopenia and bleeding diatheses as presenting features in a case of megaloblastic anemia are rare. In our case bleeding manifestation was the only presenting complaint. Initially Idiopathic Thrombocytopenic Purpura (ITP) seemed to be the likely etiology, however bicytopenia with high MCV pointed towards megaloblastic anemia. Bleeding manifestations in megaloblastic anemia have been reported in up to 25% patients. Sometimes It can also present with hypotension transient delirium⁷. Studies done in children with megaloblastic anemia in north india documented bleeding into skin, subcutaneous tissue, epistaxis⁸. Few of them also presented with significant malena or intracerebral bleed, requiring blood transfusions. Hemostasis is achieved early within 12-24 hours of starting parenteral vitamin B12 injection. Improvement in platelet function precedes the increase in platelet count after B12 therapy. Our patient neither had a platelet function defect nor did she develop new lesions after the first dose of vitamin B12; with resolution of the old lesions over 2-3 days. Though our patient did not develop life threatening bleeds but she had large hematomas, which are otherwise an unlikely finding in cases of thrombocytopenia due to any etiology. There are reports of scurvy in adult patients presenting with bleeding manifestations and anemia. Their peripheral smear and bone marrow picture was suggestive of megaloblastic anemia, though serum vitamin b12 was normal. Our child had no clinical signs of scurvy. With vegan diet becoming a vogue in recent times incidence of megaloblastic anemia is only going to rise. Rare diseases with unknown or unproven management, are unsolved mysteries. However real challenge lies in diagnosing common diseases with uncommon presentations. B12 deficiency is one such disease which affects almost all systems⁹. Thrombocytopenia though a common

haematological finding, rarely produces symptoms. However bleeding in a child with B12 deficiency responds very promptly to B12 therapy¹⁰.

CONCLUSION

Though uncommon, Vit B12 and folic acid deficiency, should be ruled out in pediatric patients presenting with bleeding diathesis. Macrocytic blood picture may point towards such an etiology. Prompt administration of methylcobalamin and folic acid is indicated in such patients.

REFERENCES

1. Hoffman R, Benz EJ, Furie B, Shattil SJ. *Hematology: Basic Principles and Practice*. Philadelphia, Pa: Churchill Livingstone; 2009.
2. Wang YH, Yan F, Zhang WB, et al. An investigation of vitamin B12 deficiency in elderly inpatients in neurology department. *Neurosci Bull*. 2009 Aug; 25(4):209-15.
3. Dali-Youcef N, Andres E. An update on cobalamin deficiency in adults. *QJM*. 2009 Jan; 102(1):17-28.
4. Tilak V, Jain R. Pancytopenia--a clinico-hematologic analysis of 77 cases. *Indian J Pathol Microbiol*. 1999 Oct;42(4):399-404. PubMed PMID: 11127368.
5. Khunger JM, Arcuselvi S, Sharma U, Ranga S, Talib VH. Pancytopenia-A Clinico-hematological study of 200 cases. *Indian J Pathol Microbiol*. 2002;45:375-9.
6. Anitha P, Sasitharan R, Thambarasi T, et al. Vitamin B12 deficiency presenting as pancytopenia and retinopathy in a young boy—*Helicobacter pylori*, a novel causative agent. *The Australasian Medical Journal*. 2014;7(3):143-148. doi:10.4066/AMJ.2014.1872.
7. Zhang Q, Lv X-Y, Yang Y-M. Megaloblastic anemia with hypotension and transient delirium as the primary

symptoms: report of a case. *International Journal of Clinical and Experimental Medicine*. 2015;8(10):18879-18883.

8. Premkumar M, Gupta N, Singh T, Velpandian T. Cobalamin and Folic Acid Status in Relation to the Etiopathogenesis of Pancytopenia in Adults at a Tertiary Care Centre in North India. *Anemia*. 2012;2012:707402. doi:10.1155/2012/707402.
9. Metz, J. (1963). Folates in megaloblastic anaemia. *Bulletin of the World Health Organization*, 28(4), 517-529.
10. CHANARIN I, MOLLIN DL, ANDERSON BB. Folic acid deficiency and the megaloblastic anaemias. *Proc R Soc Med*. 1958 Sep;51(9):757-63. PubMed PMID:13591299; PubMed Central PMCID: PMC1889819.