Case Report
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Vitamin B 12 Deficiency Presenting as Failure to Thrive, Regression of Milestones, and Severe Hemolytic Anemia in an Infant: A Case Report

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Abstract

Vitamin B12 is essential for DNA synthesis and is necessary for the development of the central nervous system. Vitamin B12 deficiency occurs in babies who are exclusively breast-fed by mothers with insufficient stores of vitamin B12. In vitamin B12 deficiency, the clinical features are mainly hematological and neurological. Megaloblastic anemia is the characteristic feature of vitamin B12 insufficiency. Rare haematological manifestations include pancytopenia and hemolytic anemia. The other clinical spectrum of vitamin B12 deficiency comprises vomiting, lethargy, failure to thrive, hypotonia, and retrogression of developmental milestones. We reported a 7-month-old infant with vitamin B12 deficiency who presented with loss of weight and regression of social smile since one month of age. Her weight, length, and head circumference were in the less than 3rd centile range according to the World Health Organisation (WHO) growth chart. She had severe pallor, hyperpigmentation of palms, soles, and knuckles, brownish depigmented brown sparse hair, and hepato-splenomegaly of 4 cm each. The laboratory results revealed Hb of 3.5gm/dl, Mean Corpuscular Volume (MCV) of 99fl, thrombocytopenia, normal ferritin levels, and peripheral smear showed polychromatophils, 19 nucleated Red Blood Cell (RBCs)/100White Blood Cells (WBCs), macrocytes, leucocytes shift to the left with 21% hypersegmented neutrophils, suggestive of hemolytic anemia. Vitamin B12 levels were 146pg/ml [N=200-900 pg/ml]. The baby started smiling 2 days after the vitamin B12 injection, gained 700 g during the follow-up of 3 months, and the pigmentation disappeared from the palms and soles.

Keywords: Failure to thrive, Hemolytic anemia, Vitamin B12 deficiency

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Introduction

Human beings don't synthesize vitamin B12, and animal products are the only dietary source (1, 2). Vitamin B12 deficiency occurs in exclusively breast-fed infants of mothers with insufficient stores of vitamin B12 (1, 2). In infancy, vitamin B12 deficiency is rare (2). The prevalence of Vitamin B12 deficiency is more common in the low- and middle-income countries. In children from developing countries, it is often underreported, with a varying prevalence of 21–45% (3). In vitamin B12 deficiency, the clinical features are predominantly neurological and hematological (2). The clinical spectrum of vitamin B12 deficiency typically occurs between the ages of 2 months to 1 year, which includes vomiting, lethargy, failure to thrive, hypotonia, and regression of developmental milestones (1, 2). Megaloblastic anemia is a characteristic known feature. Hemolytic anemia is an uncommon, important manifestation of vitamin B12 deficiency (4). Timely diagnosis and management of vitamin B12 deficiency is important for long-term prognosis (1, 2). We reported a 7-month-old infant with vitamin B12 deficiency who presented with loss of weight, regression of milestones, along severe hemolytic anemia.

Case Report

We reported a 7-month-old girl brought in with loss of weight and regression of social smile since one month of age. The child was delivered out of a non-consanguineous marriage. She was born at term with a weight of 2.7 kg without any significant natal history. Baby was exclusively breastfed, and the mother started complementary feeds 10 days ago with ragi. Her milestones were achieved at a normal time within one month. Mother is on a pure vegan diet. On examination vitals: -Temp 97.60°F, Respiratory rate (RR) 50/minute, Pulse rate (PR) 160/minute, Blood Pressure (BP) of 90/66 mmHg, Capillary Refill Time (CFT) 2 seconds, and oxygen saturation 98% at room air. Anthropometry:-weight 4.15 kgs, length 63 cms, head circumference 37 cms. All were in less than the 3rd centile range according to the WHO growth chart. She was dull looking, with severe pallor, hyperpigmentation of palms, Soles, and knuckles was present [Fig 1 A and B], hair was sparse with brownish depigmentation brown sparse hair. Abdominal examination revealed hepatosplenomegaly of 4 cm each. Other systems examination was unremarkable. Investigations are shown in Table I. Vitamin B 12 levels of the infant were 146 pg/ml, and the mother's levels were 203pg/ml. [Normal levels of Vitamin B 12 =200-900 pg/ml]. One Packed Cell Volume (PCV) of 10ml/kg given. She was treated with intravenous vitamin B12 1000 µg injections per day for 3 days, followed by oral vitamin B12 500 µg tablets once a day for 6 weeks. The baby started smiling after 48 hours of vitamin B12 injection, gained 700 g in the following month. In another 2 months, the baby gained 1500 g, and pigmentation disappeared from the palms and soles.

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Table I:Hematologic and Biochemical Investigations

Parameters	At Admission	3rd day	4th day
HB (g/dl)	3.5	12.6	12.4
PCV %	11.5	39.5	37.6
RBC COUNT (million/mm^3)	1.16	4.35	4.24
MCV [fl]	99	90	88
MCH [pg]	30.2	29	29
MCHC [gm/dl]	30.4	31	33
RDW%	53.0	15	
Reticulocyte Count %	6.91	8.96	10.05
TLC cells/mm^3	25070	7520	5400
DLC [N,L,E,M,B] %	43,54,0.5,2,0.5	27,65,1,6,1	
Platelet Count [Lakhs/mm^3]	1.17	91000	1.22
ESR mm 1st hour	30	10	
CRP[U/L]	9.6		
Peripheral blood smear	Polychromatophils ++++, Nucleated RBCs=19/100WBCs, spherocytes +, basophilic stippling +Macrocytes ++ Leucocytes shift to the left, 21% Hypersegmented neutrophils		
LDH[U/L][N=230-460u/l]	1789		
Direct Serum Bilirubin [mg/dl]	1.12		
AST [U/L]	16		
ALT [U/L]	51		
Vitamin B 12 [N=200-900 pg/ml] **Mother's vitamin B12 levels**	146 203		
Folic Acid [N= 2.7-17 ng/ml]	7.0		
Iron [N=50-170 microgrm/dl]	45.50		
TIBC [N=270-450 microgram/dl]	204		
Ferritin[N=20-250ng/ml]	245		
Direct Coombs Test	Negative		
Blood urea[mg/dl]	13		
Serum creatinine[mg/dl]	0.13		
Serum albumin[g/dl]	3.3		
Total protiens[g/dl]	5.6		
Vitamin D	37		
Serum calcium[mg/dl]	8.8		
Serum magnesium[mg/dl]	2.1		
Serum phosphorous[mg/dl]	3.4		
Urine bilirubin	Negative		
Electrophoresis by HPCL	HBA 86.8%, HBF 5.7%,HBA_2 2.3%		
Blood and urine culture no growth, Echo normal.			

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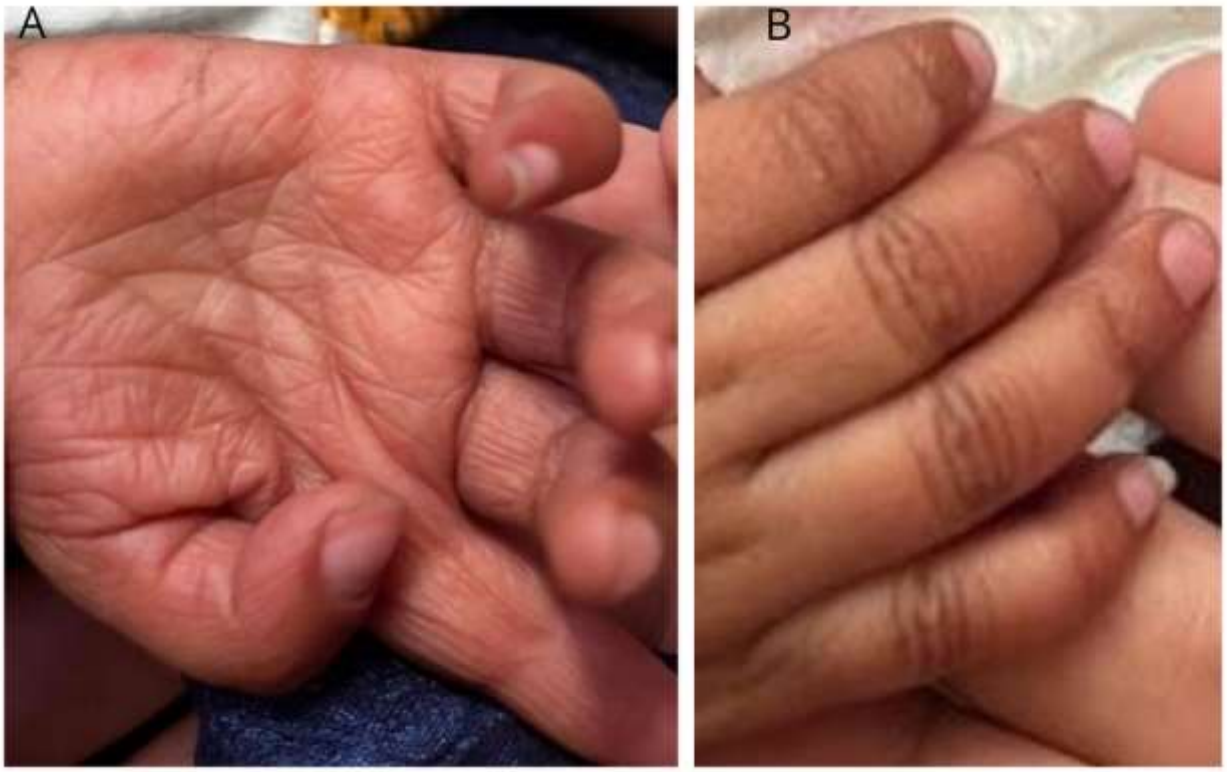

Fig 1 A. Hyperpigmentation of palm
Fig 1 B. Hyperpigmentation of Knuckles

Discussion

For the growth and evolution of the central nervous system, vitamin B12 is essential (1). The pathogenesis of vitamin B12 deficiency includes delayed myelination of nerves, alteration in the S-adenosylmethionine: S-adenosyl homocysteine ratio, and an increase in the lactate levels in the brain (2). Accumulation of methylmalonyl-CoA is known to interfere with lipid biosynthesis, which is needed for myelin sheaths (5). Myelination of the brain is vigorous during the first 6 months of life (1). Vitamin B12 deficiency in infants is an infrequent and treatable cause of failure to thrive and delayed development (1). Out of 121 infants with neurological symptoms, vitamin B12 deficiency was observed in 35 infants, and vitamin B12 levels were normal in 86 infants. Evident life-threatening events and seizures were the most prevalent presentations among B12 deficiency infants relative to infants with normal levels (6). Out of seven nutritionally vitamin B12-deficient breastfed infants, 5 presented with failure to thrive (5). Azad et al reported vitamin B12 deficiency in 22% of 200 infants. They also correlated vitamin B12 levels with the Denver Development Screening Test II (DDST II). In the vitamin B12 deficiency group, 54% had abnormal DDST/DDST-suspect when compared to 15% in the sufficient group ($p < 0.0001$) (7). Our infant presented with a loss of weight of 700 g over two months and loss of social smile. After the vitamin injection, she smiled at his mother within 48 hours. Therapeutic response occurs very rapidly (within a few days) (2, 7). She gained 700 g in one month of therapeutic vitamin B12. Vitamin B12 is essential for the synthesis of DNA. In the bone marrow, during the deficiency of vitamin B12, cell division is inhibited, leading to huge RBC with nuclear or cytoplasmic asynchrony; ineffective erythropoiesis, which is a typical feature of megaloblastic anemia (2). Abdul Hadi et al. reported a one-and-a-half-year-old boy with hemolytic anemia and global developmental delays (4). Microangiopathic hemolytic anemia (MAHA) caused by vitamin B12 deficiency is named as pseudo-thrombotic microangiopathy (pseudo-TMA) (8). Out of 201 vitamin B12 deficiency

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patients, 2.5% presented with pseudo-thrombotic microangiopathy (8). In vitamin B12 deficiency, ineffective erythropoiesis occurs, which may cause severe dysplastic RBC changes. One more cause of the fragmented RBCs is an increase in the serum homocysteine levels. Hyerphomocysteinemia has been shown to cause endothelial damage leading to intravascular hemolysis (8). Overall, hemolysis in vitamin B12 deficiency may result from intramedullary destruction as well as from (intravascular hemolysis) pseudo TMA.

Our infant had severe hemolytic anemia along with thrombocytopenia. Thrombocytopenia and hemolytic anemia occurring together in a vitamin B12 deficiency patient may often be incorrectly diagnosed as thrombotic microangiopathy (TMA), especially thrombotic thrombocytopenic purpura (TTP) (8). In a systematic review by Yadav et al, the authors observed numerous instances of cobalamine deficiency with clinical manifestations of hemolytic anemia and thrombocytopenia incorrectly diagnosed as TTP, resulting in unwarranted expensive plasmapheresis (9). Our infant also had a picture suggestive of hemolytic anemia, like increased Lactate Dehydrogenase (LDH), classical peripheral smear findings, and thrombocytopenia. Her electrophoresis was normal. Kalyan et al. observed vitamin B12 deficiency in 37.6% of seemingly healthy children aged between 6 months to 23 months (10). In the current case, the mother's vitamin B12 level is at the lower limit of the normal [203 pg/ml]. This may be the reason for the deficiency in the baby. Since maternal B12 status forecasts the B12 status in infants, in all probability, it would be preferable to pick out women in early pregnancy or even preconceptionally to avert infant B12 deficiency, instead of newborn screening, which time and again does not reliably identify high-risk children (11). Prevention is better than cure by targeting pregnant and breastfeeding women on vegan diets (1).

Conclusion

The current cases pose a diagnostic challenge at admission. Good nutrition history and clinical examination, like hyperpigmentation of palms, soles, and knuckles, hepatosplenomegaly, gave a clue to the vitamin B12 deficiency. This case also highlights the value of thoughtfulness in considering vitamin B12 deficiency as a diagnosis in children with developmental delays and anemia. Our infant presented loss of social smile, and after a vitamin B12 injection, she smiled at her mother within 48 hours. Therefore, a high index of suspicion, early diagnosis, and treatment are very crucial for preventing long-term neurological consequences associated with vitamin B12 deficiency. Pediatricians should be cognizant of the influence of vitamin B12 deficiency on growth and development in children.

The current case calls attention to the significance of estimating vitamin B12 levels in children with failure to thrive, regression of milestones, and/or hemolytic anemia to avoid misdiagnoses.

Availability of Data

The authors declare that they have the original data of the case report and confidentiality has been maintained at all levels

Ethical Considerations

Informed written consent was obtained from the parents of the patient for publication of this report.

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During the preparation of this work the author(s) did not use AI.

Authors' Contributions

KJK concept and design, VGM data collection and literature search, AR clinical study and manuscript writing, HRN EDITING and writing, KJK guarantor.

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Conflict of Interest

The authors declare that they have no competing interests.

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