Case Report

Importance of Vitamin Suppletion During Pregnancy: Pancytopenia in a 3 Month Old Neonate

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Case Report

Importance of Vitamin Suppletion During Pregnancy: Pancytopenia in a 3 Month Old Neonate

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Abstract

Vitamin B12 deficiency in infancy is an uncommon but reversible cause of severe hematologic abnormalities and potential neurologic injury, particularly in exclusively breastfed infants whose vitamin B12 status depends on maternal stores. Because its clinical presentation may mimic bone marrow failure syndromes or hematologic malignancies, diagnosis can be challenging and delayed. We report a case of early infantile pancytopenia ultimately attributed to profound vitamin B12 deficiency secondary to maternal celiac disease. Prompt recognition and treatment with cobalamin supplementation resulted in rapid hematologic recovery and favorable clinical outcome. This case underscores the importance of considering vitamin B12 deficiency in the differential diagnosis of unexplained cytopenias in infants and highlights the critical role of maternal nutritional status in neonatal health. Improved awareness and targeted screening of at-risk mothers during pregnancy and lactation may prevent severe but readily treatable complications in affected infants.

Keywords: vitamin B12 deficiency; pancytopenia; celiac disease

Introduction

Vitamin B12 (cobalamin) deficiency in infancy is a rare but treatable cause of failure to thrive and neurologic developmental delay. Infants are particularly vulnerable due to limited hepatic cobalamin stores at birth and complete dependence on maternal vitamin B12 status, especially when they are exclusively breastfed [1–3]. Maternal conditions associated with reduced vitamin B12 uptake are a strict vegetarian diet, pernicious anemia or other malabsorptive disorders [4–6,15].

The most common hematologic manifestation of vitamin B12 deficiency is macrocytic anemia, however in severe cases, vitamin B12 deficiency can even manifest as pancytopenia or microangiopathic hemolytic anemia (MAHA). When present in infants, pancytopenia poses a significant diagnostic challenge, raising concern for bone marrow failure syndromes, clonal hematologic disease or leukemia, often delaying diagnosis [7–10]. Early recognition of vitamin B12 deficiency during pregnancy and in infancy is essential, as it is associated with adverse maternal and infant health outcomes. Early treatment is crucial since it leads to rapid hematologic recovery and prevents irreversible neurological damage [11–14].

We present a case of a 3-month-old infant with pancytopenia and paleness as the sole symptoms of a severe vitamin B12 deficiency, highlighting the importance of maternal clinical evaluation and nutrition status for early recognition and diagnosis.

Case Description

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A 3-month old male infant was referred to the emergency department for failure to thrive and extreme pallor. Upon physical examination, the infant showed no signs or symptoms of acute distress nor fever. No hepatosplenomegaly or lymphadenopathy was noted and neurodevelopmental assessment was consistent with his postnatal age. However, significant growth restriction was observed, with a body weight of 5.80 kg, corresponding to the 9th percentile for age.

Medical history revealed that he was born at term with a normal birth weight of 3.240 kg. He was exclusively breast fed. Maternal dietary history was reported as normal and she had been taken folic acid regularly during pregnancy. Familial history for thalassemia or other inherited disorders was negative.

Initial laboratory investigations showed pancytopenia with a hemoglobin level of 3.9 g/dL and a normal mean corpuscular volume (MCV) of 96 fL, a platelet count of 18 $x10^9$/L, a leucocyte count of 6.34 $x10^9$/L, and neutrophil count of 1.22 $x10^9$/L. Leucocyte and neutrophil counts further decreased to a level of 3.46 $x10^9$/L and 0.15 $x10^9$/L respectively (see table 1). Peripheral blood smear examination showed pronounced poikilocytosis, in particular tear drop cells and fragmentocytes. Lactate dehydrogenase (LDH) was 1874 U/L, liver function tests showed a total bilirubin of 5,5 mg/dL and indirect bilirubin of 5,1 mg/dL, indicating possible hemolysis. The iron profile of the patient showed no abnormalities. Additional testing included bone marrow biopsy, glucose-6-phosphate dehydrogenase (G6PD), hemoglobin electrophoresis, infectious serology for Parvovirus B19, as well as cytomegalovirus and Ebstein-Barr virus, and PCR for Human Herpesvirus type 6 (HHV6).

The bone marrow biopsy demonstrated a normocellular bone marrow and dysplastic changes involving all three hematopoietic lineages, in particular an extreme dyserythropoiesis with pronounced megaloblastoid changes and nuclear abnormalities (Figures 1-4).

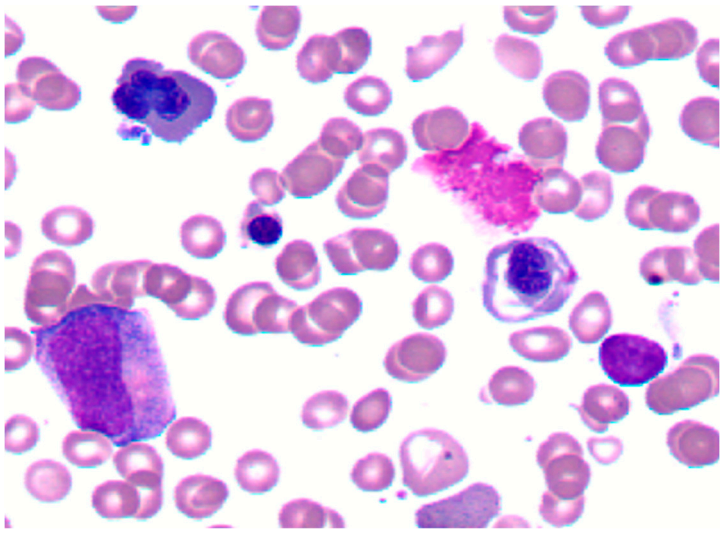

Figure 1. Bone marrow biopsies with morphologic features of dyserythropoiesis demonstrating nuclear budding (abnormal nuclear segmentation) and aberrant chromatin patterns in erythroid precursors.

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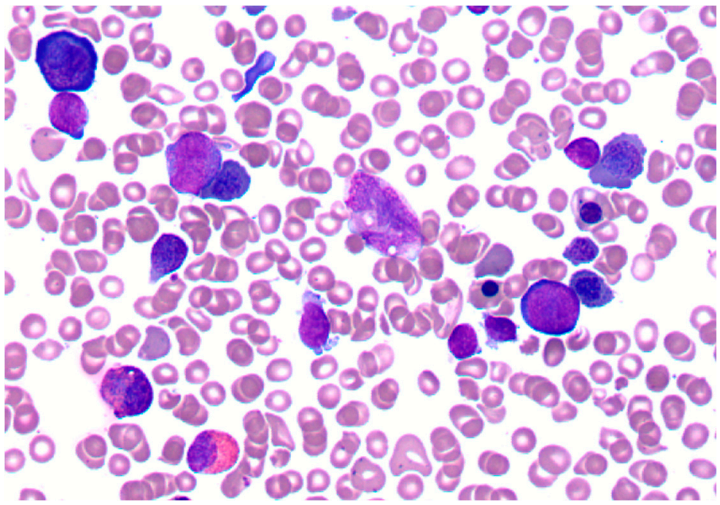

Figure 2. Bone marrow biopsies with morphologic features of dyserythropoiesis demonstrating nuclear budding (abnormal nuclear segmentation) and aberrant chromatin patterns in erythroid precursors.

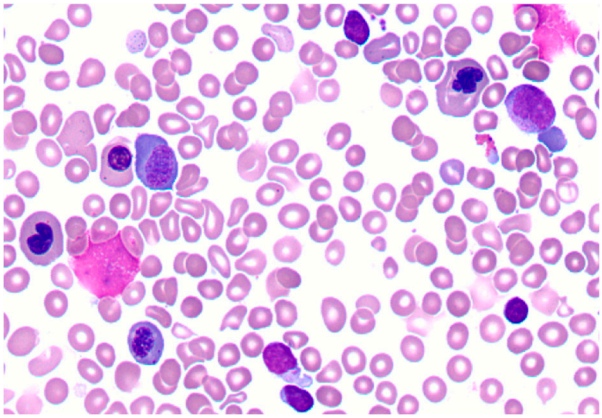

Figure 3. Bone marrow biopsies with morphologic features of dyserythropoiesis demonstrating nuclear budding (abnormal nuclear segmentation) and aberrant chromatin patterns in erythroid precursors.

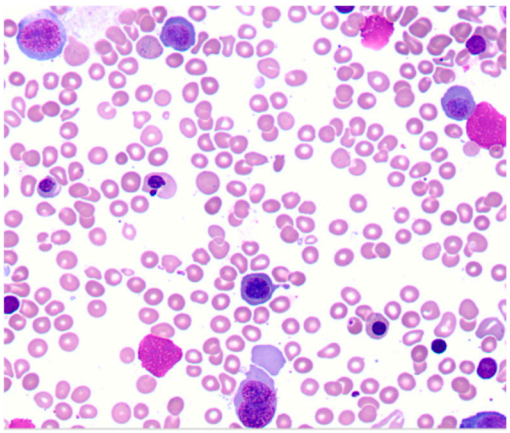

Figure 4. Bone marrow biopsies with morphologic features of dyserythropoiesis demonstrating nuclear budding (abnormal nuclear segmentation) and aberrant chromatin patterns in erythroid precursors.

These findings led to the hypothesis of a possible vitamin B12 or folic acid deficiency with a myelodysplastic neoplasm of childhood or bone marrow failure syndrome in the differential. Acute myeloid leukemia was initially considered, however, flow cytometric analysis demonstrated only a mildly increased blast population, consisting of a combination of myeloblasts and hematogones.

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Vitamin B12 was deficient with a level of 132 ng/L (reference value 211-911 ng/L) and folic acid level was 15.4 µg/L (reference value >3 µg/L). To definitively exclude myelodysplastic neoplasm or an inherited bone marrow failure syndrome, additional diagnostic testing was performed, including - next-generation sequencing (NGS) for myeloid malignancies and whole exome sequencing, as well as diepoxybutane (DEB) testing and telomere length assessment for bone marrow failure.

A complete blood count test in the mother revealed a macrocytic anemia, with high red blood cell MCV of 120 fL and hemoglobin level of 10,7 g/dL. Folic acid was within the range of normal, but vitamin B12 was deficient with a level of 78 pg/mL. Upon further questioning, it was found that the mother suffered from celiac disease.

The patient was treated with an intramuscular injection of 100 mcg cobalamin and received transfusions of packed red blood cells and platelets. After ten days of inpatient management with continuous clinical and laboratory monitoring, the patient was discharged in good clinical condition following an additional intramuscular administration of 100 mcg cyanocobalamin. Further supplementation was not required, as breastfeeding was discontinued and the patient was transitioned to formula feeding.

Catch-up growth was observed, with the patient's weight reaching 10.20 kg at seven months of age (60th percentile). The complete blood count completely recovered within four months after starting treatment (Table 1). Follow-up bone marrow biopsy showed a regenerative bone marrow without megaloblastic changes and nuclear abnormalities in the erythroid lineage. Additional molecular and genetic testing was all within normal range.

Table 1. initial lab results upon admission, lab results four months after admission.

Test	Result	Reference range	Unit	Result	Reference range	Unit
Hemoglobine	3.9	9.5 - 13.5	g/dL	12.2	10.5 - 13.5	g/dL
Erythrocytes	1.24	3.10 - 4.50	$x10^{12}$/L	4.95	3.70 – 5.30	$x10^{12}$/L
RDW	28.8	12.1 – 16.2	%	13.2	11.8 – 14.2	%
Hematocrit	0.119	0.290 – 0.410	L/L	35.5	30 - 42	%
MCV	96.0	74.0 – 108.0	fL	71.7	70.0 – 86.0	fL
MCH	31.5	25.0 – 35.0	pg	24.6	23.0 – 31.0	pg
MCHC	32.8	30.0 – 36.0	g/dL	34.4	32.4 – 35.9	g/dL
Leucocytes	6.34	6.00 – 17.50	$x10^9$/L	11.3	6.0 – 17.0	$x10^9$/L
Neutrophil count	1.22	1.20 – 5.70	$x10^9$/L	5.07	1.50 – 8.00	$x10^9$/L
Lymphocyte count	4.04	4.00 – 13.50	$x10^9$/L	4.38	3.00 – 9.50	$x10^9$/L
Monocyte count	0.80	0.50 – 1.90	$x10^9$/L	0.98	0.10 – 1.20	$x10^9$/L
Eosinophil count	0.04	0.00 – 0.40	$x10^9$/L	0.64	0.02 – 0.25	$x10^9$/L
Platelets	18	307 – 619	$x10^9$/L	389	166 – 396	$x10^9$/L
Reticulocyt count	50.6	37.0 – 104.0	$x10^9$/L	32	24 – 102	$x10^9$/L
Iron	267	16 – 128	µg/dL	54	50 – 120	µg/dL
Transferrin	2.64	1.07 – 3.24	g/L			
ferritin	353	14 – 647	µg/L	51	7 – 140	µg/L
Total bilirubin	5.5	0.1 – 0.7	mg/dL	0.26	0.20 – 1.20	mg/dL
conjugated bilirubin	0.4	0.1 – 0.3	mg/dL	<0.10	<=0.30	mg/dL
Unconjugated bilirubin	5.1		mg/dL	0.22	0.1 – 1.20	mg/dL
ALT (GPT)	28	5 – 33	U/L			
Gamma GT	9		U/L			

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Alkalic phosphatase	272	134 – 518	U/L			
LDH	1874	163 – 452	U/L	293	155 – 286	U/L
CRP	8	<6	mg/L			
Haptoglobin	<0.03	0.00 – 3.00	g/L			
Vitamine B12				723	211 – 911	ng/L
TSH	5.67	0.73 – 8.35	mU/L			

Discussion

This case of severe infantile pancytopenia due to vitamin B12 deficiency highlights the crucial role of maternal micronutrient status in neonatal health and emphasizes the importance of comprehensive prenatal follow-up. Infants are entirely dependent on maternal vitamin B12 stores, particularly during exclusive breastfeeding, as neonatal hepatic cobalamin reserves are limited at birth. Consequently, unrecognized maternal deficiency can rapidly result in significant hematologic abnormalities and, if untreated, irreversible neurologic injury in the infant.

Preventive micronutrient supplementation during pregnancy is an essential public health measure to reduce adverse maternal and fetal outcomes. Among these, folic acid supplementation is universally recommended before conception and throughout early pregnancy due to its important role in the prevention of neural tube defects [1,2]. However, folic acid supplementation alone does not address coexisting vitamin B12 deficiency, which may remain undetected during pregnancy. In such cases, folic acid can normalize or partially correct hematologic findings while masking underlying cobalamin deficiency and allowing neurologic complications to progress [9,15–17].

While folic acid supplementation remains essential and should not be discouraged, exclusive reliance on folate without consideration of maternal vitamin B12 status may be insufficient, particularly in populations at increased risk of deficiency, including women with malabsorptive disorders, restrictive diets, or gastrointestinal disease. This risk is further amplified during pregnancy and lactation, when maternal vitamin B12 requirements are increased and deficiency may directly affect the exclusively breastfed infant [7,8,18].

Despite its essential role in DNA synthesis, erythropoiesis, and neurologic development, vitamin B12 is not routinely screened for or supplemented in many prenatal care programs. Maternal deficiency has been associated with adverse pregnancy outcomes such as low birth weight, intrauterine growth restriction, and preterm birth, and infants born to untreated mothers are at risk for severe hematologic manifestations and neurodevelopmental delays during infancy. In rare cases, vitamin B12 deficiency can present with pancytopenia and bone marrow dysplasia, mimicking acute myeloid leukemia or inherited bone marrow failure syndromes and potentially leading to a diagnostic delay [6–9].

In the present case, maternal vitamin B12 deficiency secondary to celiac disease resulted in severe infantile pancytopenia requiring transfusions and extensive diagnostic evaluation. Earlier recognition through antenatal screening could likely have prevented this presentation. This highlights the need for prenatal care programs to incorporate routine or targeted vitamin B12 assessment alongside folic acid and iron supplementation, particularly in high-risk populations.

In conclusion, this case illustrates that vitamin B12 is as essential as folic acid in prenatal care. Comprehensive prenatal follow-up programs that include early assessment and timely replacement of vitamin B12 can prevent severe and potentially irreversible complications in infants, improve diagnostic accuracy, and enhance both maternal and neonatal outcomes.

Conflicts of Interest: "The authors declare no conflicts of interest.".

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