

# Megaloblastic Anemia in Early Infancy (A Case Report)

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**Abstract:** Congenital megaloblastic anemia is a rare hematological condition of early infancy and so far few cases have been reported. Infants born to severely B12 deficient mothers develop megaloblastic anemia at 3 to 6 months of age since they are born with low stores of B12 and are then fed breast milk of low cobalamin content. Mothers of such infants are either vegetarians or have unrecognized maternal pernicious anemia. Megaloblastic anemia developing within few weeks of birth is due to congenital transcobalamin II deficiency or abnormality. Transcobalamin II is responsible for the transport of cobalamin from gut to body tissues. Megaloblastic Anemia can also occur due to functional defect in either mitochondrial methyl malonyl COA enzyme or its co-factor ado cobalamin.

Here we report a case of 3months old female child who presented with complaints of bruises, fever, cough and progressive pallor. Her complete blood picture showed bicytopenia (decreased Hemoglobin and platelets) with macro ovalocytes and anisocytosis on peripheral blood smear and low retics count. Bone marrow showed hyper cellularity and megaloblastic erythroid series with no atypical cells. Iron stores were markedly increased and few siderocytes were seen. Hence diagnosis of megaloblastic anemia was made. Since patient was already transfused, her folate and Vitamin B12 levels were not done. However, her maternal Vitamin B12 levels were found out to be markedly low. Unfortunately, before start of specific treatment, patient expired. This case is described due to its rarity and importance of early diagnosis and immediate intervention.

**Keywords:** Congenital megaloblastic anemia, pernicious anemia, Transcobalamin.

## Introduction

Megaloblastic anemia (MA) is a distinct type of anemia characterized by macrocytic RBCs. The RBC precursors are larger than the cells of same stage and exhibit disparity in nuclear-cytoplasmic maturation. Basic underlying pathogenetic mechanism in MA is deficiency of folic acid and/or vitamin B12 at the cellular level with resultant impairment of DNA synthesis.

In developing countries, most cases of MA result from nutritional deficiency of these micronutrients. Nutritional deficiency is far more common in vegetarian than in non-vegetarian families.<sup>1,2</sup> Nutritional MA in adults is known for long. Jadhav et al have been credited to report MA in six South Indian infants for the first time in world literature in 1962.<sup>3,4</sup> So far, very few cases of congenital megaloblastic anemia have been reported. B12 deficiency seen in infants and young children has been particularly related to maternal nutritional deficiency which results in poor body stores at the time of birth.

Vitamin B-12 deficiency is a worldwide problem, however, particularly in the newborn period, due to the combined effects of poor maternal diet and congenital deficiencies of transcobalamin.<sup>7,8</sup> These underprivileged infants who are exclusively/ predominantly breast fed tend to develop B12 deficiency as the breast milk content of B12 in these mothers is far below normal. Cobalamin content of breast milk is lower in vegetarian mothers and is positively correlated with their serum cobalamine levels.<sup>5,6</sup> Prognosis depends on the underlying cause of the megaloblastic anemia and the degree of compliance with therapy. Folic acid deficiency is relatively easy to treat.

## Case Report

A 3months old female child, resident of Rawalpindi, presented to emergency room (ER) of children hospital PIMS with complaints of bruises on whole body for 2 weeks and fever, cough and progressive pallor for 1 week. According to her mother, she was well up to the age of two and a half months when she developed bruises, pallor and fever associated with cough.

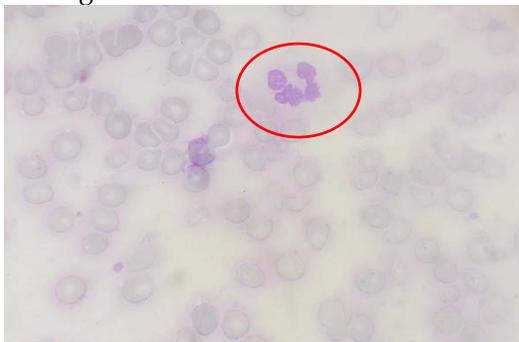
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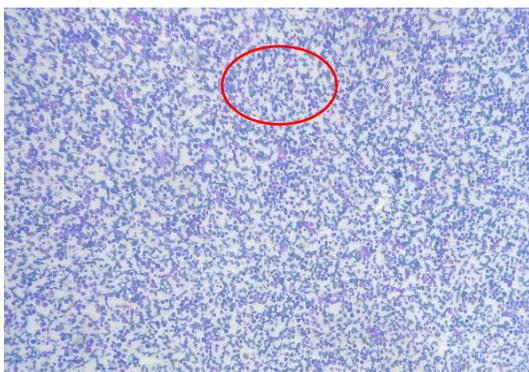
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She was given broad spectrum antibiotics which showed only temporary relief of symptoms but pallor increased.

She was a premature baby, born at 35<sup>th</sup> week of gestation. However, her post-natal history was uneventful. There was history of maternal anemia during pregnancy as the mother was G<sub>5</sub>P<sub>4</sub>. The patient had two previous admissions in hospital due to pneumonia when she was only 2 weeks old. However, she got transfused for the first time at two and a half months of age.



**Figure 1 - Hypersegmented Neutrophil**



**Figure 2 - Hypercellularity**



**Figure 3-Megaloblast and dyserythropoiesis**

On physical examination, she had a temperature of 100°F, pulse rate of 104/min, respiratory rate of

28/min and a severe degree of pallor. Liver was 2cm palpable below the right costal margin, firm in consistency with sharp borders and smooth surface. Rest of the systemic examination was unremarkable.

The investigations showed Hemoglobin 4.7 gm/dl, Platelet count 61 X 10<sup>3</sup>/μl, and TLC 6.6 X 10<sup>3</sup>/μl. The differential counts showed Neutrophils 15 % and Lymphocytes 85 %. Her MCV was 115fl with MCHC of 26g/dL. Peripheral smear showed macrocytosis with anisocytosis and poikilocytosis. Hyper segmented neutrophils were also seen (Figure 1). Reticulocytes were 0.3%. Blood culture showed no growth. Chest X-ray was normal. Ultrasound Abdomen showed hepatomegaly. Bone marrow examination showed a hypercellular aspirate with hyperplastic and megaloblastic Erythroid series (Figure 2&3).

Myeloid series was active and megakaryocytes were adequate. There were no atypical cells. M:E ratio was 4:1. Her iron stores were markedly increased but occasional siderocytes and sideroblasts were seen which ruled out sideroblastic Anemia (Figure4). There was only 4% dysplasia in erythroid series. Hence final diagnosis of congenital megaloblastic anemia was made. Since patient was already transfused, her folate and Vitamin B12 levels were not done. Maternal vitamin B12 level was 150pg/mL, whereas normal B12 level in adults range from 239pg/mL - 931pg/mL. So, mother was found to be B12 deficient. Maternal folate level was 1ng/mL. Unfortunately, before start of specific treatment, the patient expired. This case is described due to its rarity and importance of early diagnosis and immediate intervention.



**Figure 4-Increased Iron**

## Discussion

Congenital megaloblastic anemia is an uncommon disorder which occurs in breast fed infants. Congenital megaloblastic anemia was first time reported in 1962 in Lancet by Jadhav et al<sup>9</sup>. They reported MA in six

South Indian infants for the first time. Another case was reported in June 1971 in Journal of Hematology by Beatrice C. Lampkin et al. They reported a case series of two siblings having congenital megaloblastic anemia with functional enzyme defects. Most recent case was reported by Quentin C et al in European Journal of Pediatrics in 2012<sup>10</sup>. They reported a case of 9-month-old male child who presented with pancytopenia and severe hepatosplenomegaly and his mother was found to be B12 deficient and child was diagnosed as having congenital megaloblastic anemia. Baby showed response to therapy. Findings of this case are similar to our case. In our case, baby B12 and folate levels were not performed due to already being transfused. However, mother was B12 deficient. Presence of less than 15% sideroblasts ruled out sideroblastic anemia. Presence of less than 10% dysplasia in erythroid series rules out congenital dyserythropoietic anemia. So diagnosis of congenital megaloblastic anemia was made. Unfortunately, the child expired before any treatment could be given.

### Conclusion

Here we can conclude that every infant presenting with pancytopenia should be investigated for congenital megaloblastic anemia, especially for children born to multi gravida with evidence of anemia, as early diagnosis and prompt administration of treatment could reduce morbidity and mortality, drastically.

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HISTORY	
Date Received:	20-DEC-2016
Date Sent for Reviewer:	1-JAN-2017
Date Received Reviewers' Comments:	15-JAN-2017
Date Received Revised Manuscript:	25-JAN-2017
Date Accepted:	7-FEB-2017

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