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Case Report

Paediatrics Section

B12 Deficiency in a Breastfed Infant Due to Maternal B12 Deficiency: A Case Report

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ABSTRACT

We report a case of eight-month-old breastfed male infant presented with developmental delay and knuckle pigmentation. Peripheral smear examination showed microcytic hypochromic anaemia. Knuckle pigmentation has given a clue for vitamin B12 deficiency and got confirmed by detailed biochemical investigations. On examination mother was found to be vitamin B12 deficient who also presented with knuckle pigmentation. Subsequently the infant was administered oral vitamin B12 and responded to the therapy as indicated by weight gain, improvement in development, normalisation of serum B12 and blood haemoglobin level.

Keywords: Developmental delay, Knuckle pigmentation, Red cell indices

CASE REPORT

An eight-month-old male infant visited paediatric outpatient department. He presented with pallor, failure to thrive and developmental delay. He was born at full term with birth weight 2.4 kg and had a good cry at birth. There were no postnatal complications. Developmental milestones were delayed, he did not attained head control, and was not able to sit with support. His height (62 cm) and weight (5.8 kg) was less than 3rd percentile and had normal head circumference (42 cm) at presentation. Physical examination revealed marked pallor, normal tone with brisk elicited Deep Tendon Reflexes (DTR), short systolic murmur heard over the left sternal border, knuckle pigmentation, liver and spleen were not palpable.

His laboratory investigations showed decreased haemoglobin, Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH) and total leucocyte count, increased Red-cell Distribution Width (RDW), normal Mean Corpuscular Haemoglobin Concentration (MCHC) and platelet count [Table/Fig-1]. Peripheral smear examination showed microcytic hypochromic erythrocytes, anisocytosis and poikilocytosis. In view of knuckle pigmentation with microcytic hypochromic anaemia on peripheral smear and red cell indices, biochemical investigations were performed to know the possible cause of anaemia. It showed decreased serum vitamin B12 level. In addition haemoglobin electrophoresis was carried out and iron profile was analysed which included total iron binding capacity, serum iron and ferritin. It was found to be normal and thus it ruled out the possibility of thalassaemia and iron deficiency anaemia [Table/Fig-1]. Urine metabolic screening test showed positive for methylmalonic acid both by the colour reaction and thin layer chromatography which is an indicator of vitamin B12 deficiency.

Vitamin B12 deficiency in an infant is unusual, and it occurs due to maternal deficiency. Maternal history showed that she was strict vegetarian and was not taking vitamins regularly during pregnancy. She had received a blood transfusion at the 8th month of gestation because of low haemoglobin. Clinical examination and lab investigations of the mother also showed knuckle pigmentation, low haemoglobin level (7 gm%), elevated MCV, macrocytic erythrocytes, hypersegmented neutrophils on peripheral smear and low serum B12 level (83.3 pg/mL).

Infant was treated with an oral dose of vitamin B12 (Meconerv 1500 mcg /day) and folic acid (5 mg tab per week) for six months. The child responded well to the therapy which was shown by the reversal of knuckle pigmentation, improvement in milestones, and his ability to sit with support, also gained 1.2 kg weight and 2 cm height in two months. Vitamin B12 (>2000 pg/mL) and serial haematological investigations showed a good response to the therapy [Table/Fig-1].

Test parameters	Pre-treatment	After treatment			Reference range
		15 days	3 months	6 months	
Haematological investigations:					
Total WBC (/µL)	5,400	15,900	11,100	13,800	9,000-16.000
Platelet count (/µL)	2,38,000	12,61,000	6,44,000	4,04,000	1,50,000-4,00,000
Hb (gm/dL)	5.0	8.5	9.9	8.9	11.1 -14.2
MCV (fL)	56.7	61.3	53.3	55.7	72-84
MCH (pg)	18.9	18.8	17.2	17.1	25-29
MCHC (gm/dL)	33.2	30.6	32.2	30.7	32-36
RDW	34.6	34.5	19.8	20.0	11.6-14
Retic %	1.61	5.86	-	-	0.2-2.0
Absolute Reticulocyte (/µL)	0.043x10^6	0.267x10^6	-	-	0.02-0.11 x10^6
Immature reticulocyte fraction	0.13	0.42	-	-	0.163-0.362
Mean reticulocyte volume (fL)	92.1	108.7	-	-	102.7-124.8
Biochemical investigations:					
Iron (µg/dL)	116	-	-	-	50-120
Ferritin (ng/mL)	360	-	-	-	23.9-336
TIBC (µg/dL)	265	-	-	-	200-400
Vitamin B12 (pg/mL)	63.5	>2000	-	-	180-814

[Table/Fig-1]: Haematological and biochemical laboratory investigations of infant, pre treatment and post treatment after 15 days, 3 months, 6 months.

DISCUSSION

Neurological symptoms are the common clinical manifestations of vitamin B12 deficiency, it is having negative consequences on developing brain in infants and rarely may cause cerebral atrophy [1,2]. Infants with vitamin B12 deficiency usually present with

non specific clinical features such as weakness, failure to thrive, developmental delay, irritability, hepatosplenomegaly, pancytopenia, tremor in addition to megaloblastic features [3,4]. Hyperpigmentation of the skin of the elbow, oral mucosa, depigmentation of the hair are the rare signs of vitamin B12 deficiency which are reversible and may give a clue to its diagnosis [5-7]. Clinical examination of the present case of breastfed infant showed pallor, developmental delay, failure to thrive and knuckle pigmentation. These findings gave an indication for further investigations.

Impact of vitamin B12 deficiency varies throughout the life cycle and it is potentially more with elderly people and developing embryo [8]. Risk factors for vitamin B12 deficiency in adults are inadequate dietary intake, decreased consumption of animal foods, use of pharmaceuticals, gastrointestinal problems, advanced age and malabsorption syndrome [9,10]. In infants B12 deficiency is unusual, and it occurs due to a deficiency in the mother [11]. Vitamin B12 is essential for adequate growth of the nervous system, and moderate deficiency may be harmful to CNS [12]. Maternal B12 deficiency also may cause infantile tremor syndrome [13]. Laboratory investigations of a breastfed infant born to the mother who had autoimmune pernicious anaemia showed severe normocytic normochromic anaemia, cobalamin deficit and alpha thalassaemia trait which masked macrocytosis [14]. Studies showed that monitoring maternal intake of vitamin B12 level in women during pregnancy especially in the vegan mother is important. Supplementation should be started preconceptionally or in early pregnancy and continued during lactation period also to prevent neurological sequelae in infants [15,16]. In the present case, detailed maternal history showed that there was decreased haemoglobin in the mother during pregnancy which was treated with blood transfusion. However, the cause of anaemia in the mother could not be detected during the course of pregnancy which probably delayed the diagnosis in the infant. Later we found mother was a strict vegetarian, had knuckle pigmentation, macrocytic anaemia (Hb: 7gm%, MCV: 95 fL, MCH: 30.1 pg, MCHC: 32 gm/dL) decreased serum vitamin B12 level (83.3 pg/mL) and the presence of hypersegmented neutrophils and macrocytic RBCs on peripheral smear. Hence, detecting the cause of anaemia during pregnancy is essential to initiate proper therapy and to prevent neurological damage in the infant.

There is a paucity of publications related to the exact prevalence of vitamin B12 deficiency in infancy as they are rare. Majority of published articles on vitamin B12 deficiency are either retrospective studies or case studies. An eight years retrospective study on a small group of (<30) infants with vitamin B12 deficiency due to maternal deficiency showed that 92% of cases presented with macro-ovalocytes on peripheral smear, a characteristic feature of vitamin B12 deficiency or folate deficiency [3]. Studies also found that anaemia, macrocytosis, and elevated MCV were always not associated with vitamin B12 deficiency, and hence we cannot differentiate the type of anaemia based on haematological parameters [13,17]. In the present case, haematological findings were suggestive of microcytic hypochromic anaemia which was usually seen in iron deficiency anaemia and thalassaemia. Normal iron profile and haemoglobin electrophoretic pattern excluded the possibility of both. Moreover decreased serum vitamin B12 and presence of methylmalonic acid by urine metabolic screening test were suggestive of vitamin B12 deficiency. We could not estimate serum folic acid level in both mother and infant. Infant was treated with vitamin supplementation which included both vitamin B12 and folic acid orally. Normalisation of serum vitamin B12 level and disappearance of knuckle pigmentation were indicative of an improvement in the present case. Serial estimation of haematological parameters related to anaemia such as haemoglobin, red cell indices, and reticulocytes also showed a good response to therapy. Even though B12 deficiency is uncommon in infants, when there is a clinical symptom such as hyperpigmentation, it is crucial to consider detailed laboratory investigations to rule out B12 deficiency both in mother and baby.

CONCLUSION

Clinical suspicion is crucial for proper diagnosis and early intervention of vitamin B12 deficiency, example hyperpigmentation. Screening the mother for vitamin B12 status during pregnancy may prevent neurological damage in infant.

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