Case Report

Vitamin B12 deficiency and cerebral atrophy

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Abstract

Severe vitamin B 12 deficiency produces a cluster of neurological symptoms in infants, including irritability, failure to thrive, apathy, anorexia and developmental regression, which responds remarkably rapidly to vitamin B 12 supplementation. We report 9-month-old male child born to mother who was strict vegetarian and baby was exclusively breast feed, with insidious development regression and generalized cerebral atrophy and ventriculomegaly on CT scan brain which shows marked improvement both clinically and on imaging studies after vitamin B 12 administrations.
Keywords: Vitamin B 12 deficiency, developmental regression, cerebral atrophy.

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INTRODUCTION

Vitamin B12 deficiency is a rare disorder in infants and is generally due to Vitamin B12 (cobalamin) deficiency in mother. In developing countries maternal Vitamin B12 deficiency is usually secondary to pernicious anemia, strict vegetarian diet and malnourishment. Neurological symptoms of Vitamin B12 deficiency include irritability, failure to thrive, hypotonia and developmental regression /delay. We report a 9- month-old infant with insidious developmental regression, hypotonia, macrocytic anemia and generalized cerebral atrophy on CT scan brain which markedly improved after vitamin B12 administration.

CASE REPORT

A 9-month-old male child born of non-consanguineous marriage was admitted to our hospital with high grade fever, cough and dyspnea for period of 4 days. The patient was exclusively breast fed until the age 6 months after that complementary feeding was started. His mother noticed that he developed normally during his first seven months; he learns to support his head at three month age, roll over at five month, sitting without support at six month. From seven month onward he gradually become less active and loss the ability to hold neck, roll over and at nine month of age he was unable to sit without support and develop dysphagia to animal based nutrients such as milk and egg. Upon presentation he was still primarily breast fed. Family history revealed that his mother was vegetarian and had been treated for iron deficiency anemia during the pregnancy. On examination there was pallor, knuckle pigmentation, respiratory distress and hepatomegaly. He did not establish eye contacts, unable to smile, lacked head control and was not able to sit without support. Investigation revealed that hemoglobin 6 gm/dl, white blood cell count 5000 mm^3, platelet count 2.5 lacks mm3, mean corpuscular volume 100fL, red cell distribution width (RDW) 20%. Peripheral smear showed anisocytosis, macrocytosis, poikilocytosis, hyper segmented neutrophils and adequate platelets. Biochemical profile, Thyroid profile, Serum ferritin, Iron level were normal. Serum Vitamin B12 level of baby was 140 ng/L, and of mother was 160 ng/L. During pregnancy mother's hemogram were as follow: hemoglobin 10 gm/dl, white blood cell count 6000 mm^3 platelet counts 2.2 lacks mm^3, hematocrit 30%, mean corpuscular volume 60 fL, mean corpuscular hemoglobin 26 pg/cell, Vitamin B12 level was not done during pregnancy. CT scan brain shows generalized atrophy of brain mainly involving bilateral fronto-parietal lobe and ventriculomegaly (Fig.1A). Child was diagnosed as

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Bronchiolitis with megaloblastic anemia with developmental regression secondary to Vitamin B12 deficiency and started on bronchodilators, antibiotics and Vitamin B12. Initially Vitamin B12 was given intramuscular daily for seven days, and then alternate day for 7 days, followed by weekly for four to five weeks and then started orally. After five days of treatment patient becomes active, began to smile and swallow and shows interest in surrounding. On seventh day of treatment patient developed generalized tremors and myoclonus jerk which subsided by clonazepam therapy for 15 days. His muscle tone improved and achieved head control after ten days of treatment. Child was discharge after fourteen days of hospital stay with proper counseling and advice regular follow up. After three months treatment baby's anemia improved and was able to waves, and walk with support. Repeat CT scan brain done shows marked improvement **(Fig 1B)**.

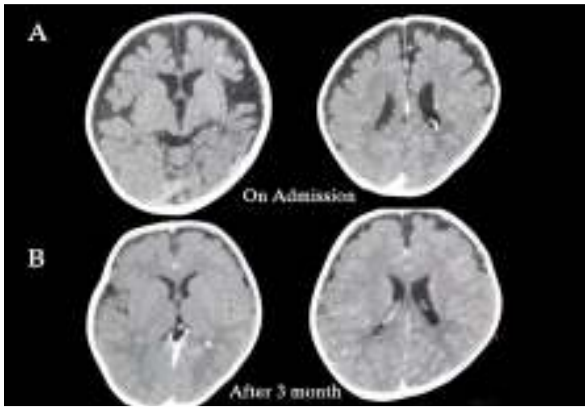

Figure 1: (A) Brain CT scan on admission showed sign of generalized atrophy involving mainly fronto-parietal lobe. (B) Brain CT scan after 3 month shows marked improvement

DISCUSSION

Infantile Vitamin B12 deficiency is a rare but treatable cause of development delay and deterioration affecting exclusively breast fed infants born to Vitamin B12 deficient mother. This deficiency is usually secondary to pernicious anaemia or a strict vegetarian diet. Human do not synthesize Vitamin B12 and their only dietary source are products of animal origin, such as meat, liver, fish, eggs or milk[1]. Vitamin B12 is necessary for the production of methylenetetrahydrofolate which is essential for DNA synthesis. Vitamin B12 deficiency leads to delay DNA synthesis in the rapidly growing hematopoietic cells and this can results in macrocytic anemia, hyper segmentation of neutrophil, leucopenia, thrombocytopenia and pancytopenia. Accompanying neurological abnormalities includes paresthesia, sensory deficits, and loss of deep tendon reflexes, movement disorder, developmental regression, dementia and neuropsychiatric changes. Brain atrophy and delayed myelination can be observed in neuroimaging studies[2,3,4,5]. Vitamin B12 deficiency can be tolerated by adults for many years due to their endogenous reserve; in infants it may produce symptoms 2- 12 months following birth due to inadequate hepatic reserve. Normally a newborn has 25 ug Vitamin content B12 content in the liver, an amount predicted to be sufficient until the end of the first year of life, even with low intake[6]. Patient with Vitamin B12 deficiency present with hematological, neurological (polyneuropathy, combined degeneration of spinal cord) and psychiatric symptoms (like depression) which are more commonly observed in adults. In infants Vitamin B12 deficiency causes fatigue, restlessness, vomiting, difficulty of swallowing solid food and delay or regression of growth and development. Vitamin B12 deficiency can also cause irreversible neurological damage and this effect is more prominent in infants who have been exposed to deficiency during the intrauterine period. Brain atrophy, microcephaly and myoclonic seizure are among the most commonly neurological sequel in Vitamin B12 deficiency[6,7,8,9,10]. Developmental regression, megaloblastic anemia and cerebral atrophy on neuroimaging as seen in our patient is not surprising and have been reported before. Jhadav *et al* first described nutritional Vitamin B12 deficiency in 6 Indian infant aged 6-12 months that presented with megaloblastic anemia, psychomotor regression and hyper pigmentation of the skin[11]. As discussed earlier mother's hematological results during pregnancy were not suggestive of Vitamin B12 deficiency during pregnancy, hence to confirm diagnosis, determination of B12 level was important in our case. Such association has been observe by other investigator before[1]. In our case patient developed generalized tremors and myoclonus jerk after five day of treatment, is not surprising and have been reported before. Ozer *et al* reported 2 Vitamins B12 deficient Turkish infants who developed involuntary movements after vitamin B12 treatment and improved after clonazepam treatment. Ozdemir *et al* also reported involuntary movement after B12 treatment[12,13]. Although Vitamin B12 supplements were reported to result in rapid improvement, concern has been raised regarding long term development. Mongale *et al* reported that two out of six vitamin B12 deficient patient developed long term neurological sequalae even after treatment[2]. Von schenck *et al* reported that early diagnosis done before 10 months age was associated with normal outcome, while those in which diagnosis was delayed made after one year of age had permanent neurological abnormality[10]. The pathogenic mechanism by which Vitamin B12 deficiency cause neurological symptoms is not clear, it is believed that congenital anomalies in homocysteine remethylation

or an abnormality in the methionine synthetase reactions leads to neurological symptoms[14]. In case of patient presenting with hypotonia and development delay physician should obtain antenatal history and dietary history in details instead of thinking extreme diagnosis and doing unnecessary laboratory work up. It is also important to emphasis that vitamin B12 supplementation during pregnancy and lactation should be provided for strict vegetarian and individuals with pernicious anemia to avoid irreversible neurological damage in exclusively breast fed babies. Simple hemogram of both baby and mother should always be performed in such case, in order to avoid delay diagnosis and to improve neurological outcome in babies.

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