Case report
Reversible cerebral atrophy in vitamin b12 deficient infants after treatment

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A R T I C L E I N F O

A B S T R A C T

Aim and Objective: To study the effects of Vitamin B12 deficiency in infants and to see if there were any changes in the findings on treatment on follow up scans. Materials & Methods: We present three cases, children of age 6, 9 and 12 months of age, whose mothers had vitamin B12 deficiency. Patients underwent MRI brain scans after taking proper consent and were followed up after they were treated for deficiency at 12, 6 and 18 months respectively. Result: On admission, the patients showed delayed milestones and were drowsy, hypotonic and lethargic. Serum vitamin B12 levels were below normal limits. On brain MRI images revealed prominent supratentorial subarachnoid spaces and cerebral atrophy. All the three children were treated for vitamin B12 deficiency and follow up MRI scans were done at 12, 6 and 15 months respectively. The follow up scans showed regression in the supratentorial cerebral atrophy in the patients on treatment for vitamin B12 deficiency resulting in reversible atrophy in the MRI scans, hence concluding that atrophy is not a permanent imaging finding once detected in Vitamin B12 deficient children. Conclusion: Maternal vitamin B12 (cobalamin) deficiency is usually secondary to pernicious anemia or to a strict vegetarian diet and can cause serious neurological abnormalities among exclusively breastfed infants. Brain changes may include diffuse cerebral atrophy, thinning of corpus callosum, cerebellar & spinal cord atrophy and posterolateral cord hyperintensities. When a child presents with atrophy of the brain, it is usually mistaken as a permanent change causing concern among parents of children.

1. Introduction

Vitamin B12 or cobalamin (formerly known as cyanocobalamin) is produced by bacteria in the large bowel of humans and by external bacteria and fungi. However, cobalamin from the former source is not absorbed, and humans need to introduce it solely from the diet. The major sources of cobalamin are animal proteins, mainly meats and eggs. An average non-vegetarian diet in western countries contains 5 to 8 μg of cobalamin per day. The recommended daily allowance is 2.4 μg for men and non-pregnant women, 2.6 for pregnant women, and 2.8 μg for lactating women and 1.5-2 μg for children up to 18 years. Since a vegetarian diet supplies no more than 0.5 μg/day of cobalamin, most vegetarians are at risk of cobalamin deficiency.

The most important cause of vitamin B12 deficiency in infants is maternal dietary deficiency, observed in infants whose mothers are deficient in vitamin B12, invariably affecting breast fed infants.

In country like India, where there is lack of resources of adequate dietary intake of animal protein food, such as meat and dairy products in the majority of the population, citing possible reasons of religious taboos and lack of awareness and resources, the burden of vitamin B12 deficiency is found to be high in India, which could be a contributing factor to various manifestations of B12 deficiency in children. There is also a misconception among many that once diagnosed as cerebral atrophy, there is a concern among the parents and treats this as an irreversible damage to the infant’s brain.

Vitamin B12 is necessary for the methylation of homocysteine, which leads to the formation of S-adenosylmethionine, an important methyl donor in the brain.

In infants with B12 deficiency and people with errors of vitamin B12 metabolism, the deficiency of S-adenosylmethionine is associated with brain atrophy, reversible if treated.
IV.RESULTS

Case 1

A 9 month old male child with vitamin b12 deficiency(122 picograms/ml)

Clinical details:

Born to non-consanguineous married couple.

Baby cried at birth.

He now presents with delayed milestones and tongue tremors

Imaging: MRI brain plain and showed findings of diffuse enlargement of supratentorial subarachnoid spaces and cerebral atrophy, T2 white matter hyperintensities and thinning of the corpus callosum.

Patient underwent treatment for 6 months and a MRI brain follow up was performed, which showed

Marked improvement in the supratentorial regions with near total resolution of the atrophy & thinning of corpus callosum which was seen 6 months back.

1) Pre-treatment:

Fig 1a,b) T2 weighted axial images shows, cerebral atrophy and enlarged subarachnoid spaces (arrows). c) T1 weighted axial image show atrophy .d) FLAIR axial image shows prominent sulci and basal cisterns (arrows)

2) Post Treatment

Fig 2a,b) FLAIR axial images show near total resolution of the cerebral atrophy.

Case 2

A 6 month of female child with vitamin b12 deficiency(118 picograms/ml)

Clinical details:

Born to consanguineous married couple.

Baby cried at birth and has present complaints of delayed milestones (partial head control) and 2-3 episodes / day of posturing with blank stare and lateralisation and symptoms of drowsiness, delayed milestones and dull weak cry.

Imaging: MRI plain screening of the brain and showed findings of diffuse atrophy in the cerebral area, mild ventriculomegaly with focal cystic area adjacent to the left lateral ventricle.

Her follow up scan was done nearly 12 months post treatment and it again showed near total resolution of the cerebral atrophy and improvement of clinical symptoms

1) Pre-treatment
fig 3a,b,c) T2 and FLAIR axial scans show cerebral atrophy and enlarged subarachnoid spaces (arrows)

d) T2 coronal image shows atrophy with areas of periventricular hyperintensities (arrow)
e) T1 axial shows thinned out corpus callosum

2) Post-treatment:

fig 4 a,b,c,d,e) FLAIR axial, coronal and sagittal cuts show regression of the cerebral atrophy and normal corpus callosum (arrow)

Case 3

A 12 month old female child with vitamin B12 deficiency (138 picograms/ml)

Clinical details:

Born to non-consanguineous married couple

Baby cried at birth and has present complaints of delayed milestones (social smile at 5 months) and drowsy and dull since 3 months, shaking since 5 days

Imaging: MRI brain screening showed cerebral atrophy.

Patient underwent treatment and was screened again 16 months later, which showed resolution of the atrophy.

DISCUSSION

Vitamin B12 is a water-soluble vitamin and is necessary for the production of tetrahydrofolate, essential for DNA synthesis. Vitamin B12 deficiency usually presents with manifestations, such as developmental delay, irritability, weakness and failure to thrive.

A strict vegetarian (vegan) diet contains very little cobalamin and increased blood methylmalonic acid (MMA) and homocysteine concentrations.

Vitamin B12 deficiency in infants is usually from mothers with low B12 levels or insufficient diet of cobalamin rich nutrients.

In the nervous system, vitamin B12 acts as a coenzyme in the methyl malonyl-CoA mutase reaction, which is necessary for myelin synthesis. Vitamin B12 deficiency therefore results in defective myelin synthesis, leading to several central and peripheral nervous system dysfunctions.

Regarding the pathophysiological mechanism, lack of adenosylcobalamin (required as a cofactor for the conversion of methylmalonyl-CoA to succinyl-CoA) leads to accumulation of methylmalonyl-CoA, causing a decrease in normal myelin synthesis and incorporation of abnormal fatty acids into neuronal lipids.

The spinal cord manifestation, called subacute combined degeneration (SCD) is clinically characterized by symmetric dysesthesia, disturbance of position sense and spastic paraparesis or tetraparesis. The involvement of the posterior and lateral columns of the cervical and upper dorsal parts of the spinal cord is responsible for the impairment of position sense, paraparesis and tetraparesis. The first abnormality is usually sensory impairment, most often presenting as distal and symmetrical paraesthesias at lower limbs frequently associated with ataxia.
Almost all patients have loss of vibratory sensation, often associated with diminished proprioception and cutaneous sensation and Romberg sign. Corticospinal tract involvement is common in the more advanced cases, with abnormal reflexes, motor impairment and, ultimately, spastic paraparesis.

Peripheral neuropathy can be seen in 25% of patients with vitamin B12 deficiency, and somewhite acute polyneuropathy have nitrous oxide exposure as the preceding event. Pathologic findings reveal axonal degeneration with or without demyelination. The pathogenetic mechanism of cobalamin-deficient neuropathy is a complex network in which also astrocytes and microglia seem to play a role in myelin damage of the type of neuropathy in vitamin B12 deficiency; 76% are axonal, while 24% are demyelinating neuropathy.

Vitamin B12 status has been associated with the severity of white-matter lesions, especially periventricular ones, in some but not all, studies. The partial reversal of white-matter lesion has been documented with cobalamin treatment, emphasizing the importance of early detection and treatment of vitamin B12 deficiency. A correlation of vitamin B12 treatment and decrease in MMA and homocysteinemia has been shown.

Vitamin B12 is necessary for the methylation of homocysteine, which leads to the formation of S-adenosylmethionine, an important methyl donor in the brain.

In infants with B12 deficiency and people with errors of vitamin B12 metabolism, the deficiency of S-adenosylmethionine is associated with brain atrophy, reversible if treated.

CONCLUSION:

Mothers should be screened for vitamin B12 deficiency during pregnancy and proper supplementation must be advised. Children with vitamin B12 deficiency present with various manifestations including brain changes may include diffuse cerebral atrophy, thinning of corpus callosum, cerebellar & spinal cord atrophy and postero-lateral cord hyperintensities. When a child presents with atrophy of the brain, it is usually mistaken as a permanent change causing concern among parents of children. We have shown that with proper treatment these changes can be reversed.

Reference


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