Introduction

Vitamin B12 is part of numerous methylation processes involving proteins, phospholipids, DNA, and neurotransmitters. As animal proteins like meat, liver, and eggs are the best sources of vitamin B12, populations who are mostly vegetarian are at a greater risk of developing cobalamin deficiency.[1] Various studies show that 47% to 66% of the Indian population may be deficient in vitamin B12.[2] Vitamin B12 deficiency has a wide array of clinical manifestations, most of which could be classified as hematological, gastrointestinal, psychiatric, and neurological disorders. Myelopathy, neuropathy, dementia, subacute combined degeneration (SCD) and less often, optic nerve atrophy are neurological manifestations.[3] Neuropsychiatric manifestations may precede hematologic signs.[1] Here, we are presenting a case of vitamin B12 deficiency, which on initial presentation looked like meningitis and was diagnosed based on typical hematological and MRI findings. This is of great importance to the primary care physician to know the varied presentation of vitamin B12 deficiency for their timely diagnosis and treatment.

Case Report

A 14-year-old male, born to a nonconsanguineous couple, presented with fever on and off for the past 2 months and abnormal body movements for 1 month. Abnormal movements were acute onset, generalized tonic posturing of the body lasting nearly 2–3 min, associated with up rolling of eyes without bladder or bowel incontinence. There was no history of vomiting, blurring of vision, rash, or trauma. There was no history of similar illness in the family or history of any tubercular contact.

On examination, the patient was afebrile with a pulse rate of 92/min, respiratory rate of 22/min, and blood pressure of 96/60 mm of Hg. General physical examination revealed pallor and icterus. Fundoscopy revealed bilateral papilledema.
and splinter hemorrhages in the retina. On central nervous system (CNS) examination, the patient had a Glasgow Coma Scale score of 15/15. Bilateral pupils were equal and reactive to light. Cranial nerves, motor-sensory, and cerebellar findings were within normal limits. Meningeal signs were positive.

The patient was hospitalized, supportive management (IV fluids, antiepileptics, and IV antibiotics) was started after performing a guarded lumbar puncture for CSF studies.

Hematological evaluation revealed pancytopenia (Hb- 2.7 g/dL, TLC- 2950 cells, platelets- 25000) with a mean corpuscular volume (MCV) 127.9 fl. Hyper-segmented neutrophils, anisopoikilocytosis, and teardrop cells were seen on peripheral smear. Aspartate aminotransferase (AST) (322 U/L) and alanine aminotransferase (ALT) (219 U/L) were elevated, with mild hyperbilirubinemia (total bilirubin- 2.22 mg/dL. Serum lactate dehydrogenase (LDH) was high as well (3902 U/L). CSF examination was done which showed eight cells (80% lymphocytes and 20% polymorphonuclear cells) and a glucose level of 61.8 mg/dL (corresponding RBS- 98 mg/dL). Serum vitamin B12 and folate levels were 172 pg/mL and 4.4 ng/mL, respectively.

Contrast-enhanced magnetic resonance imaging (CE-MRI) head and spine were done which showed multiple discrete areas of contrast enhancement and altered signal intensity involving deep white matter in the right frontal lobe, corpus callosum, and left gangliocapsular region [Figures 1 and 2].

After 5 days, antibiotics were stopped. Vitamin B12 supplementation was continued in therapeutic doses. As the patient was responding to vitamin B12 supplementation (disappearance of meningeal signs), he was discharged after 8 days of hospital stay.

Discussion

One-fifth of the children in India who are vitamin B12 deficient have neurological symptoms.[2] Mostly it presents as peripheral neuropathy, myeloneuropathy, ataxia, optic atrophy, delirium, dementia, psychosis, or mood disorders.[3] Vitamin B12 deficiency has been also associated with decreased attention, cognitive decline, memory impairment, and electroencephalography changes.[1,4] Instances of encephalopathy ascribed to vitamin B12 deficiency are also reported.[5] Recent studies have also shown vitamin B12 to be protective against pneumococcal meningitis in mice models.[6] However, in our search, we could not find any report of vitamin B12 deficiency presenting with fever and meningeal signs.

Meningitis is a major disease in Indian children with studies attributing up to 22% of under five deaths to meningitis and pneumonia.[7] The classical triad of altered consciousness, fever, and meningeal irritation is seen in only 46% of cases.[8] Given the high morbidity and mortality, the presence of these signs warrants further investigation and treatment in line with meningitis or CNS infection unless proven otherwise. Papilledema also serves as an indicator of raised intracranial pressure in cases of CNS infection. However, other causes of papilledema, including anemia and vitamin B12 deficient disc edema[9] have been reported.

Typical CSF findings in case of CNS infection includes increased CSF total leukocyte count with reduced sugars and elevated proteins. Lack of typical CSF findings in our case, coupled with characteristics hematological manifestations of B12 deficiency prompted a neuroimaging. Neuroimaging too was not suggestive of meningeal inflammation but showed the findings mentioned above.

MRI findings seen in vitamin B12 deficiency, include reduced brain parenchymal volume, white matter changes, vascular infarcts, and microstructural alterations.[10] The most well-known association between vitamin B12 deficiency and CNS involvement is subacute combined degeneration. On MRI, it is seen as a symmetrically increased T2 signal intensity, localizing

Figure 1: Discrete, patchy, contrast-enhancing altered signal intensity area in deep white matter in the right frontal lobe likely subacute infarct

Figure 2: Patchy, enhancing, diffusion-restricting area involving the posterior part of body and splenium of the corpus callosum with multiple microhemorrhages
to posterior and lateral columns in the cervical and thoracic spinal cord. Fluid-attenuated inversion recovery (FLAIR) and T2-weighted images showing areas of a high-intensity signal in the periventricular white matter, frontal cortex and focal signal change on T2 and DWI in the splenium of the corpus callosum have also been described in vitamin B12 deficient individuals.[1] These findings are similar to those described in our patient.

Hence, with suggestive MRI findings and documented deficient levels of vitamin B12 and folate in our patient, along with a response to treatment, the diagnosis was established, despite atypical presentation.

**Conclusion**

Meningitis is an important cause of morbidity and mortality in the pediatric population, and the slightest suspicion warrants a full investigation. However, in developing countries like India, where the population is predominantly vegetarian and deficiency diseases and malnutrition rates are very high, primary care physicians should be aware of atypical presentations of vitamin B12 deficiency. Accurate diagnosis in this case not only cured the patient but also prevented unnecessary prolonged antibiotic course and hospital stay.

**Key points**

- Vitamin B12 deficiency may present with clinical features suggestive of meningitis and bilateral disc edema and splinter hemorrhages in the retina.
- Early diagnosis and timely treatment have a better prognosis of neurological manifestations and disc edema related to vitamin B12 deficiency.

**Declaration of patient consent**

Written and informed consent was taken from the patient and his family members for using his individual and clinical data for publication and research purposes.

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**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Briani C, Dalla Torre C, Citton V, Manara R, Pompanin S, Binotto G, et al. Cobalamin deficiency: Clinical picture and radiological findings. Nutrients 2013;5:4521-39.
2. Umasanker S, Bhakat R, Mehta S, Rathaur V, Verma P, Bhat N, et al. Vitamin B12 deficiency in children from Northern India: Time to reconsider nutritional handicaps. J Fam Med Prim Care 2020;9:4985-91.
3. Lachner C, Steinele NI, Regenold WT. The neuropsychiatry of vitamin B12 deficiency in elderly patients. J Neuropsychiatry Clin Neurosci 2012;24:5-15.
4. Almoallim H, Mehdawi FS, Cheikh MM, Al-dhaheri F, Aqeel AM. Reversible vitamin B12 deficiency presenting with acute dementia, paraparesis, and normal hemoglobin. Case Rep Neurol Med 2016;2016:4301769.
5. Hughes G, Moran E, Dedicoat MJ. Encephalitis secondary to nitrous oxide and vitamin B12 deficiency. BMJ Case Rep 2019;12:e229380.
6. de Queiroz KB, Cavalcante-Silva V, Lopes FL, Rocha GA, D’Almeida V, Coimbra RS. Vitamin B12 is neuroprotective in experimental pneumococcal meningitis through modulation of hippocampal DNA methylation. J Neuroinflammation 2020;17:96.
7. Jayaraman Y, Veeraraghavan B, Chethrapilly Purushothaman GK, Sukumar B, Kangusamy B, Nair Kapoor A, et al. Burden of bacterial meningitis in India: Preliminary data from a hospital based sentinel surveillance network. PLoS One 2018;13:e0197198.
8. Akaishi T, Kobayashi J, Abe M, Ishizawa K, Nakashima I, Aoki M, et al. Sensitivity and specificity of meningeval signs in patients with meningitis. J Gen Fam Med 2019;20:193-8.
9. Sethi HS, Naik M, Gandhi A. Megaloblastic anemia and bilateral disc edema: An enigma... Have we figured it out yet? Taiwan J Ophthalmol 2020;10:71-5.
10. Tu M-C, Hsu Y-H, Lo C-P, Huang C-F. Vitamin B12 deficiency and impact on MRI morphometrics: Association between cognitive impairment and neuroimaging findings. In: Preedy V, Patel VB, editors. Handbook of Famine, Starvation, and Nutrient Deprivation. Cham: Springer International Publishing; 2018. p. 1-30.