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Vitamin B12 deficiency manifesting as reversible leukoencephalopathy and ataxia

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Abstract

We present here a 52 years old man with rapidly progressive cognitive decline and ataxia. Brain MRI showed confluent white matter changes and spinal MRI showed posterior column changes. The patient had vitamin B12 deficiency from pernicious anemia. There was clinical and radiological improvement by vitamin B12 replacement. There is no previous report of pernicious anemia causing reversible leukoencephalopathy and ataxia.

Keywords: Vitamin B12, pernicious anemia, leukoencephalopathy, ataxia, white matter changes, SACD

INTRODUCTION

Vitamin B12 deficiency causing anemia and neurological complications like ataxia, peripheral neuropathy, optic neuropathy and cognitive impairment have been well described in the literature. MRI showing abnormalities in the posterior column of the spinal cord is also well documented in vitamin B12 deficiency, but brain imaging showing extensive white matter changes is rarely described.[2] We report here a patient presented with rapidly progressive cognitive decline and ataxia with confluent white matter changes on brain MRI and posterior column changes on spinal cord MRI, due to vitamin B12 deficiency from pernicious anaemia. There was also clinical and radiological improvement by vitamin B12 replacement.

This case describes the importance of vitamin B12 deficiency as a cause of reversible rapidly progressive dementia, ataxia with extensive white matter changes on MRI brain along with changes in spinal cord MRI.

CASE REPORT

A 52-year-old vegetarian male with no comorbidities working as a peon, presented to our clinic with subacute onset behavioural changes followed by a rapidly progressive cognitive decline for 4 months. Initially, patient had behavioural changes in the form of aggressiveness, religious delusion, disorganized thought process, and apathy. A progressive loss of recent memory and visuospatial problems followed this. The patient gradually became apathetic and stopped taking initiative in doing both motor and cognitive tasks. After 2 months of symptom onset, the patient developed gradually worsening imbalance while walking with the tendency to fall following which he started using a walking stick and stopped going to work. After another one month patient had further deterioration in mentation with episodes of irrelevant talking and eventually developed incontinence of urine and stools.

On examination, patient had pallor. Mini Mental State Examination (MMSE) score at presentation was 7/30. Cranial nerves including fundus was normal. Motor examination showed an increased tone in all limbs with normal power and deep tendon reflexes. Joint position and vibration were impaired below the knees, Romberg's sign was positive and he had extensive sensory ataxia. His haemoglobin was 9.6 g/dL with mean corpuscular volume 104 fL. Peripheral smear showed macrocytes and anisocytosis. Vitamin B12 level was low, 83.0 pg/mL. Serum anti-parietal cell antibody and anti-intrinsic factor antibody were positive by immunofluorescent assay. Plasma homocysteine level was 45μmol/L. The autoimmune profile and the heavy/ trace metal's screen was negative. Cerebrospinal fluid examination was normal. Liver, renal, thyroid

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function tests, HIV and ANA, ds DNA, ANCA, RA factor were all negative. Visual evoked potential showed prolonged P100 bilaterally. Nerve conduction velocity was normal.

MRI Brain revealed confluent T2/FLAIR white matter hyperintensities involving deep and periventricular white matter of bilateral frontal, parietal and posterior temporal region (Figure 1 a, b and c). MRI spinal cord showed long segment T2 hyperintensity involving the posterior column of cord from C5/C6 to D11/D12 level suggestive of subacute combined degeneration of the cord (Figure 1 d and e). PET brain showed hypometabolism in bilateral frontal, parietal and temporal lobes.

Patient was started on intramuscular injections of methylcobalamin 1000 μgm daily for 7 days followed by weekly injections for a month, followed once a month for 6 months and 6 monthly thereafter. Within 2 weeks of initiating treatment patient had noticeable improvement in his sensorium and MMSE improved by 7 points to 14/30 and to 17/30 in 4 weeks. There was a substantial improvement in imbalance, gait and patient had become continent for bowel and bladder by 4 weeks of treatment. He was under regular follow up and continued to improve. At 1.5 year of follow up, the patient was in a normal state of health with an MMSE score of 29/30 and no neurological deficit. His haemoglobin was 13mg/dl and vitamin B12 level was 1050 pg/mL. Follow-up imaging after 18 months showed regression of signal changes in brain white matter and resolution of posterior column signal changes in spinal cord (Figure 2 a to e).

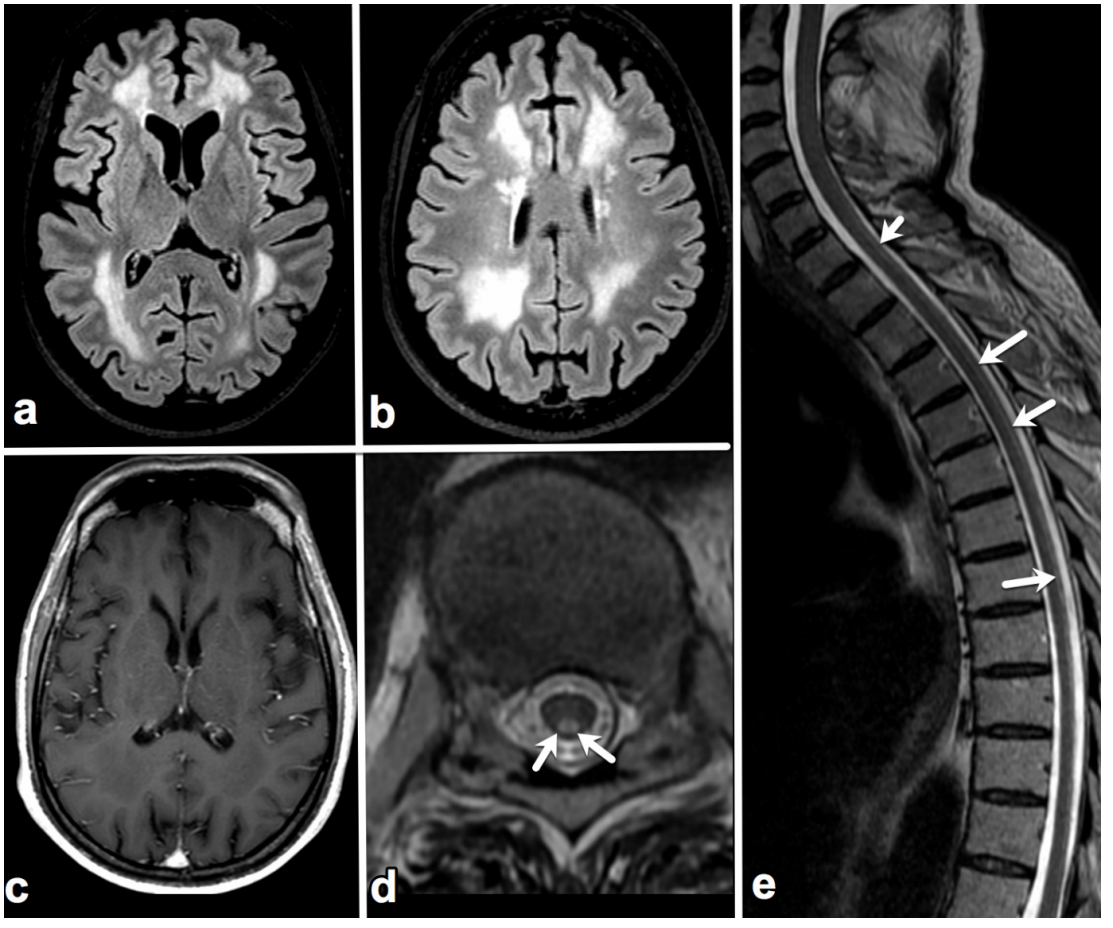

Figure 1. MRI Brain: Axial FLAIR images show bilateral fairly symmetrical hyperintensities in deep and periventricular white matter of frontal, parietal and posterior temporal regions (a, b). Axial post-gadolinium contrast enhanced T1-weighted image show no enhancement in corresponding hypointense areas (c). Axial (d) and sagittal (e) T2-WI of spine show symmetrical posterior column hyperintensities, giving the appearance of "inverted v sign" (arrows) on axial images (d).

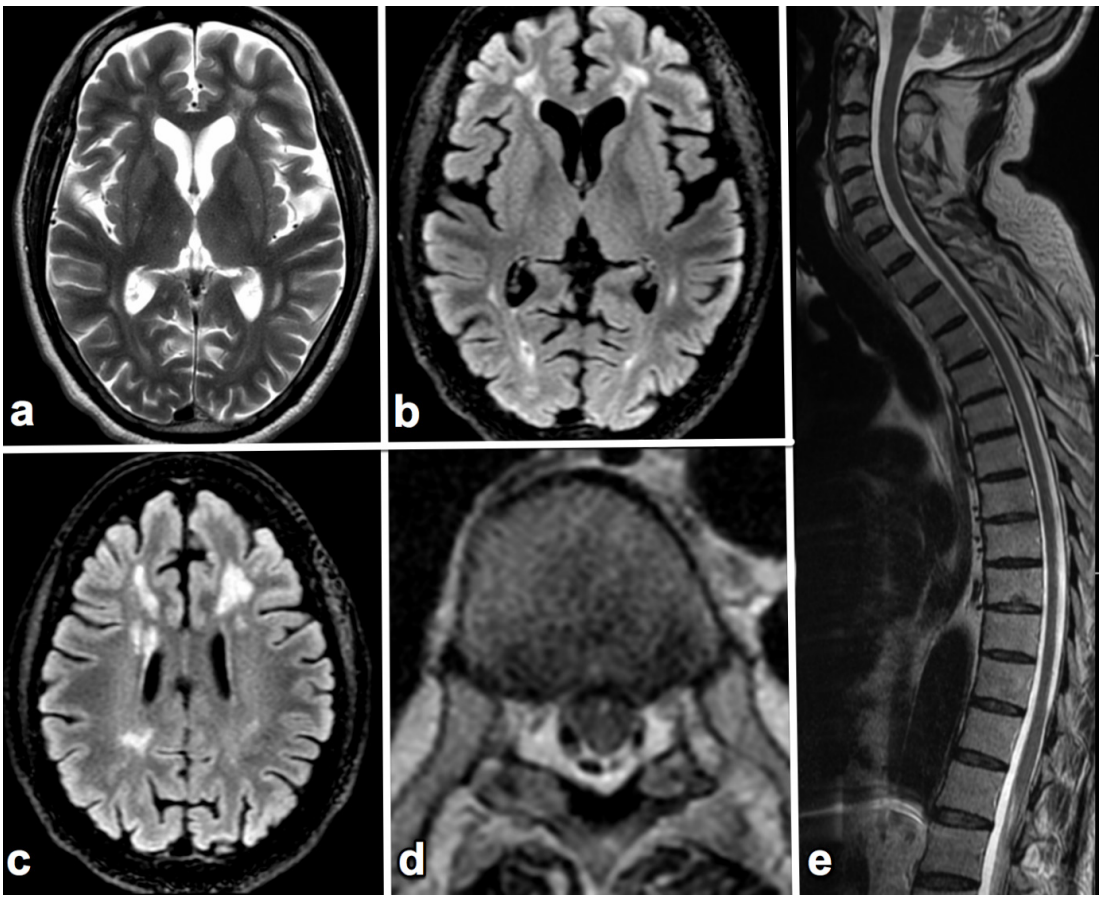

Figure 2. Follow imaging after 18 months. MRI Brain: Axial T2 (a) and FLAIR (b, c) images show partial resolution of T2/FLAIR hyperintensities with volume loss in deep and periventricular white matter of bilateral frontal, parietal and posterior temporal region. MRI spine show complete resolution of posterior column hyperintensities on axial (d) and sagittal (e) T2- weighted image

DISCUSSION

Vitamin B12 deficiency can present as a wide variety of clinical manifestations including megaloblastic anemia and neurological complications such as ataxia, peripheral neuropathy, subacute combined degeneration of the cord, optic neuropathy and cognitive impairment.[1,3] Pernicious anemia, an autoimmune disease associated with anti-gastric parietal cell and anti-intrinsic factor antibodies, is the most common cause of vitamin B12 malabsorption. Our patient had these antibodies leading to pernicious anemia and neurological manifestations. Hematological manifestations of vitamin B12 include anemia, leukopenia, thrombocytopenia, macrocytosis, and hypersegmented neutrophils.4 Rannelli *et al*. reported that the severity of anemia was inversely proportional to the severity of neurological manifestations, the reason for which was not clear. They attributed neurological complications to the fact that deficiency in vitamin B12 led to an accumulation of methylmalonic acid and homocysteine due to enzymatic defects which caused direct insult to the nervous system responsible for neuropsychiatric disturbances.[5]

Our case initially presented with psychiatric and behavioural manifestations that rapidly progressed to frank cognitive dysfunction and later followed by ataxia after 8 weeks. His MRI brain had confluent T2/FLAIR hyperintensity involving the deep and periventricular white matter of bilateral frontal, parietal and the posterior temporal region with a picture suggestive of leukoencephalopathy. Tangney *et al*. have described white matter hyperintensities and reduced total brain volume and correlated it with vitamin B12 deficiency which may contribute to cognitive decline.[6] The differential diagnosis we considered in this patient were toxin induced leukoencephalopathy, HIV encephalopathy,

paraneoplastic leukoencephalopathy and vascular dementia. Based on imaging findings adult onset leukodystrophy was also kept as a possibility, and we were able to exclude all these differentials after investigations. In our patient we found extensive white matter hyperintensities in brain as well as in spinal cord, as a consequence of pernicious anaemia which were reversible, and have not been described previously. Graber *et al*. have reported one case of vitamin B12 responsive leukoencephalopathy syndrome with autonomic dysfunction, where the patient had elevated homocysteine and methylmalonic acid levels but normal vitamin B12 levels.[7] After starting the patient on intramuscular vitamin B12 injections, he showed dramatic improvement in his MMSE scores, gait ataxia, and psychiatric manifestations.

It is important to have a high index of suspicion of vitamin B12 as a cause of dementia when the patient has associated anemia. As pernicious anemia is treatable cause it must be kept in mind as a differential diagnosis in such cases in order to start prompt treatment with good recovery. It is also important to note that radiological improvement can lag behind the clinical improvement as in the case of this patient.

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DISCLOSURE

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