



## Correlation of Clinical and MRI Features of Neuropsychiatric Manifestations in Sub-acute Combined Degeneration of Spinal Cord: Neurological Syndrome Associated with Vitamin B12 Deficiency

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### Abstract

Vitamin B12 or cyanocobalamin is an important water soluble vitamin which plays a key role in erythropoiesis, proper nervous system functioning and for the metabolism of carbohydrate, fat and protein. Patients with cyanocobalamin deficiency may present with haematological, gastro-intestinal, oral, dermatological, psychiatric and neurological disturbances. We present a case of sub-acute combined degeneration (SACD) of spinal cord in a forty-nine year old female presenting with one month history of progressive symptoms of lower limb paraesthesia, sensory deficit, psychotic symptoms and postural instability. This case report is unusual as it elucidates the characteristic triad, i.e., haematological, psychiatric and neurological symptoms in sub-acute combined degeneration of spinal cord (SACD) associated with B12 deficiency, correlation of its clinical manifestations, electrophysiological signs, laboratory investigations (especially biomarkers of B12 status) and spinal magnetic resonance (MR) imaging in establishing the diagnosis, treatment outcomes, and potential therapeutic relevance of vitamin B12 replacement therapy in symptoms remission.

**Keywords:** Vitamin B12; Dementia; Neuropathy; Spinal MRI; Sub-acute combined degeneration.

### Introduction

Vitamin B12 or cyanocobalamin is an important water soluble vitamin which plays an important role in erythropoiesis, proper nervous system function and for the metabolism of carbohydrate, fat and protein. Vitamin B12 (cyanocobalamin) is found essentially in animal products including meat, fish, eggs and dairy products. Other dietary sources include B12 containing fortified plant products such as cereals, plant based milks, soy products and fortified yeast extract [1,2]. Patients with cyanocobalamin deficiency may present with haematological, gastro-intestinal, oral, dermatological, psychiatric and neurological disturbances. This case report illustrates the severity of B12 deficiency, causes, clinical manifestations, treatment outcomes, biomarkers of B12 status and potential therapeutic relevance of vitamin B12 replacement therapy. The purpose of this article is to highlight neuropsychiatric symptoms in B12 deficiency associated SACD, correlation of its clinical manifestations, electrophysiological signs, laboratory investigations and spinal magnetic resonance (MR) imaging, high index of suspicion for its early diagnosis as delay in treatment can lead to poor neurological recovery due to this subtle vitamin deficiency.

### Case Presentation

A 49-year-old female was referred to our hospital with two month history of gradual progressive dementia, followed by social withdrawal, mood swings and apathy. One month ago, abrupt onset of tingling in the toes, pins and needle sensation of lower limbs up to trunk started. She also complained of difficulty in walking and progressive postural instability. The patient presented with confusion, mood lability, memory and attention impairment and disorientation in time. The patient's neuropsychological profile revealed impairment of her attentional, reasoning and executive functions along with reduced performance at the delayed free recall of the Rey's list [Rey auditory verbal learning test (RAVLT)]. The score of the Raven's matrices [Raven's coloured progressive matrices (RCPM)], Word fluency test, Weigl's sorting test (WST) and Mini mental state examination (MMSE) was also impaired.

The score of the MMSE was 23. A careful history revealed that psychotic or cognitive symptoms preceded neurological symptoms. (Gradual progression of dementia and irritability started two months ago). The patient did not report any significant past history or family history of psychiatric illness, gastrointestinal symptoms, pre-existing diabetes mellitus, alcohol addiction, any medications which can decrease serum Vit. B12 level or Nitrous oxide exposure. But, the patient revealed strict preference for vegetarian diet and consumed lentils (Kesari). She had no fever, weight loss, visual or bulbar symptoms, sphincter incontinence or pain in the spine or limbs. On systemic examination, vital signs were found to be normal but mild anaemia and glossitis was noticed. Deep tendon reflexes were normal. Sensation and joint position sense of the distal part of lower extremities was impaired. Though power and tone of lower limbs were normal but vibration was impaired over ankle and toes. Romberg's sign was positive but Babinski's sign and Lhermitte's sign were absent. Gait was evaluated as ataxic. All laboratory results were within normal limits except vitamin B<sub>12</sub>, which was extremely low: the patient had a serum level of 30 pg/mL (normal range: 200 to 835 pg/mL). Peripheral blood smear examination showed anisopoikilocytosis with macrocytosis blood picture. Hemoglobin was 11.0 gm/dl with raised MCV (107.5 fl). Random Blood Sugar, TSH, folate, LFT, LDH, creatinine were all normal. HIV and VDRL-TPHA test were negative. Titers of antibodies specific for parietal cells were in the normal range.

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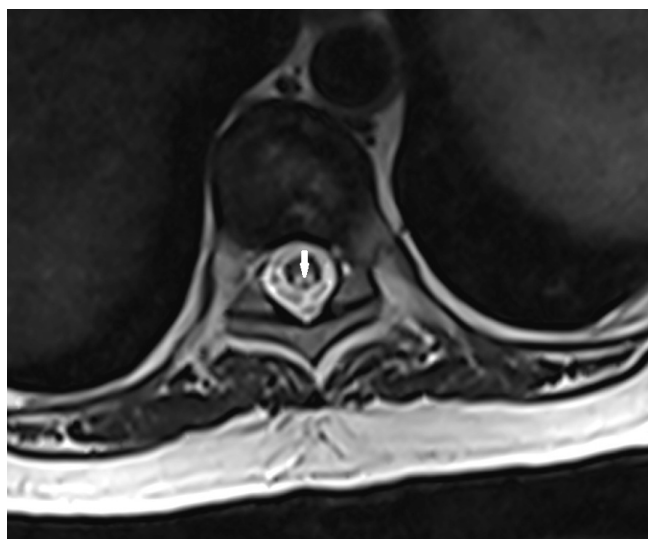
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Genomic investigation did not reveal Methylene tetrahydrofolate (MTHFR) deficiency. Somatosensory evoked potential (SEP) studies disclosed prolonged P40 latency and diminished amplitude. Electromyography was normal. MRI brain imaging was normal. MRI Scan of the Cervicodorsal Spine showed T2 hyperintensity involving posterior column of dorsal spinal cord extending from D2- D9 vertebral level (Figure 1). Thus, correlation of clinical manifestations, laboratory investigations, electrophysical signs and spinal MR imaging studies confirmed the diagnosis of sub-acute combined degeneration (SACD) due to Vitamin B12 deficiency.

Patient was given Injection Vitamin B12 1mg I/M daily for 7 days and weekly for six weeks and other supportive treatment. Follow up after two months, she showed significant improvement in her postural stability and psychiatric manifestations. Neuropsychological symptoms especially lower limb paraesthesia, sensory deficits, dementia, confusion, irritability, mood fluctuations and other negative symptoms were nearly resolved. The patient showed significant improvement in her attentional, reasoning, executive and cognitive functions along with a normal performance in her MMSE score (score value 30), verbal fluency test and the delayed free recall of Rey's 15 words as shown in Table 1.



**Figure 1:** MRI image of the Cervicodorsal Spine showing abnormal T2 hyperintensity involving posterior column of dorsal spinal cord extending from D2- D9 vertebral level.

Domain	Test	Admission	Two months later
General mental status	Mini mental state examination (MMSE)	23/30	30/30
Reasoning and executive functions	Raven's coloured progressive matrices (RCPM)	15/36	24/36
	Verbal fluency (FAS words/min)	16/25	23/25
	Weigl's sorting test (WST)	4/15	8/15
Digit span	Digit span forward	4/5	5/5
	Digit span backward	3/5	5/5
Memory	Rey auditory verbal learning test (RAVLT delay recall)	2/15	9/15
Attention	Months of year backward	7/12	12/12

**Table 1:** Comparison of Neuropsychological tests results at the time of admission and two months after vitamin B12 replacement therapy. Vitamin B12 level increased to over 900 picogram/dl.

## Discussion

Vitamin B12 deficiency may present with haematological (delayed DNA synthesis in rapidly growing hematopoietic cells leading to inefficient erythropoiesis and macrocytic anaemia), gastrointestinal (gastric atrophy due to decreased acid and intrinsic factor production leading to vitamin B12 malabsorption), psychiatric and neurological manifestations (thought to be a result of insufficient availability of S-adenosylmethionine, the principal methyl group donor in cellular metabolism and required for the synthesis of myelin phospholipids, caused by reduced activity of vitamin B<sub>12</sub> dependent methionine synthase (hyperhomocysteinaemia). Second hypothesis states that both myelin sheaths and axons are destroyed mainly in the white matter of the spinal cord due to methylmalonic aciduria toxicity caused by reduced activity of vitamin B12 dependent methylmalonyl-CoA mutase. The laboratory diagnosis is usually based on low serum vitamin B12 levels or elevated mean corpuscular volume (MCV), serum methylmalonic acid, Transcobalamin II and homocysteine levels [3]. In our patient also, vitamin B12 levels are as low as 30 pg/mL (normal range: 200 to 835 pg/mL). Elevated homocysteine is an important marker for vitamin B<sub>12</sub> and/or folate deficiency. Symptoms of vitamin B12 deficiency include anaemia, neuropathy, and neuropsychiatric disorders [4].

Neurologic abnormalities of B12 deficiency include neuropathy, myelopathy, loss of deep tendon reflexes, movement disorders, paraesthesia, dysarthria, sensory deficits, memory impairment, dementia, developmental regression, neuropsychiatric changes and seizures [5-7]. Possible causes of vitamin B12 deficiency include decreased intake, alcoholism, ileocaecal tuberculosis, abnormal absorption, genetic deficiency of methylmalonyl-CoA mutase, defects in vitamin B12 transport and metabolism and other gastrointestinal causes (e.g., Zollinger-Ellison syndrome, Crohn's disease, coeliac disease or chronic pancreatic insufficiency [8]. This patient as described presented with features consistent with SACD of the spinal cord. Herein, in our case patient was strict vegetarian and often consumed lentils (Kesari). The cause for B12 deficiency was considered decreased uptake of vitamin B12 as absence of MTHFR deficiency and normal titres of antibodies specific for parietal cells excludes any genetic cause or pernicious anaemia. Sub-acute combined degeneration (SACD) of the spinal cord, characterised by degeneration of the lateral and posterior columns, is the most serious debilitating neuropsychological complication of cobalamin deficiency and most commonly occurs with macrocytic anaemia [9]. The clinical profile of our patient suggested mild anaemia, confusion, dementia, psychosis followed by paraesthesia and gait disturbance with impairment of position and vibration sense in the lower limbs. Differential diagnoses of abnormal signal lesions in the posterior columns of the spinal cord include infectious or post infectious myelitis, lymphoma and other neoplasm, peripheral neuropathy, radiation myelitis, paraneoplastic myelopathy, cervical spondylosis, multiple sclerosis, sarcoidosis, arterial or venous ischaemia, traumatic cord injury, vascular malformations of the dura and spinal cord, and syringomyelia, metabolic disease (including vitamin E deficiency) and acute transverse myelitis [10]. Various studies documented abnormally increased T2-signal hyper intensity in SACD on spinal MR imaging [11,12]. Axial T2- weighted MR image suggested abnormal increased hyper intense signal in the dorsal posterior column of spinal cord as shown in our case.

**There are various methods of B12 replacement therapy including parenteral (or intravenous) replacement therapy.** Treatment included IM 1mg/day cyanocobalamin injections daily in the first 7-14 days, weekly in the subsequent month, and monthly afterwards, to restore

cyanocobalamin in the body [13]. The follow-up of such patients ranged from 2-12 months.

## Conclusion

The present case report highlights characteristic imaging findings of sub-acute combined degeneration (SACD) of spinal cord diagnosed on spinal magnetic resonance (MR) imaging and correlation of clinical, imaging, electrophysiological signs and laboratory investigations in a 49-year-old woman presenting with neuropsychological symptoms. Early diagnosis and treatment play an important role in the reversibility of neuropsychological deficits; as delay in treatment can lead to poor neurological recovery and may results in irreversible disabling neurological impairment.

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