International Journal of Innovative Research in Medical Science (IJIRMS)
Volume 07, Issue 08, August 2022,
https://doi.org/10.23958/ijirms/vol07-i08/1482

Case Report

Subacute Combined Degeneration of Spinal Cord - The Only Manifestation in an Otherwise "Normal" Vitamin B12 Deficient Patient

Dr Darshankumar Manubhai Raval, MD [1], Nritya Brijesh Trivedi [*2], Shraddha Trivedi [2], Yash Vaghasiya [2], Aditi Parida [5]

[1]Department of Medicine, SSGH, Medical College Baroda, Vadodara, Gujarat, India
[2]Intern, Department of Medicine, SSGH, Medical College Baroda, Vadodara, Gujarat, India

*Corresponding author: Nritya Brijesh Trivedi; Orcid Id: *0000-0003-4727-030X; nritya.p.b@gmail.com*

Received 25 July 2022; Accepted 20 August 2022; Published 30 August 2022

Abstract

Sub-acute combined degeneration (SACD) is a myelopathy associated with vitamin B12 deficiency. Vitamin B12 deficiency may be asymptomatic or present with neurological and/or hematological features - neurological features such as myelopathy, neuropathy, dementia/neuropsychiatric abnormalities and rarely optic atrophy commonly presenting at a later stage than hematological changes. We present a case of a 15-year-old female who presented with ataxia, paresthesia and learning disability but no clinical symptoms or hematological evidence suggesting vitamin B12 deficiency. Our case report highlights the importance of early diagnosis and prompt treatment of vitamin B12 deficiency in a patient having only SACD as the disease's manifestation.

Keywords: ***Vitamin B12 deficiency, SACD, Normal Hemoglobin, No Anemia.***

Introduction

Subacute combined degeneration of spinal cord is a preventable, reversible medical condition reported in upto 14.8% of people having Vitamin B12 deficiency that affects the brain and spinal cord; it is a disease mostly affecting the posterior and lateral columns of spinal cord primarily due to demyelination occurring as a complication of Vitamin B12 deficiency [1,2]. It is estimated that about 40% people suffer from a low vitamin B12 level in developing countries [3]. This percentage of the population is constituted more commonly by the elderly; especially strict vegan diet consumers or those belonging to lower socio-economic strata [3]. Vitamin B12 is a cofactor in a reaction converting homocysteine to methionine. The by-product of this reaction is used in the synthesis of pyrimidine bases of DNA. In B12 deficiency, homocysteine levels will accumulate and pyrimidine bases will not be formed, slowing down DNA synthesis in erythroid precursors causing megaloblastic anemia. Vitamin B12 is also used as a cofactor for the enzyme methyl malonyl CoA mutase, which converts methylmalonyl-CoA to succinyl-CoA. In patients with B12 deficiency, methyl malonic acid (MMA) levels will accumulate, It is hypothesized that elevated levels of MMA and homocysteine contribute to myelin damage, accounting for the neurologic deficits, such as neuropathy and ataxia [4,5].

Vitamin b12 deficiency may produce typical clinical features such as pallor, fatigue, glossitis with occasional neurological symptoms and associated gastrointestinal features. Jaundice may also be a presenting feature in some patients due to hemolysis. In Vitamin B12 deficient individuals, the blood count would show anemia and peripheral smear would show hyper segmented neutrophils. In addition, the mean corpuscular volume (MCV) would be increased to a level greater than 100 [6].

Approximately two-thirds of patients with vitamin B12 deficiency are shown to have hematological abnormalities [7].

However, no particular correlation between hematological and neurological features has been demonstrated in some studies [8]. Thus, we are presenting a case on the same lines of such studies- an adolescent female who presented to us with chief neurological-motor complaints without any other clinical feature suggestive of an underlying B12 deficiency.

Case Report

A 15-year-old adolescent, vegetarian female presented to us with a chief complaint of difficulty in walking since 2 months. The Patient also complained of difficulty in standing up from squatting position and tingling/numbness in both the lower limbs and imbalance while walking since 2 months but had no complaints of bowel or bladder incontinence. There was no complaint of breathlessness, fatigue. Signs of meningeal irritation were also absent. Her teacher complained about her inability to learn as reported by her parents. An elaborate neurological exam was performed.

The patient was well oriented to time, place and person but showed difficulty in concentrating and a delay in following written and spoken commands. She also showed reduced attention span (tested by asking her to perform serial subtraction of numbers) and poor recall (recalled 1 out of 3 objects in 5 minutes). Her mini mental state examination was found to be 18/30 (maximum score = 30; score >25 interpreted as normal). She showed no signs of aphasia

and reported to have no delusions, hallucinations, and delirium or mood changes.

Cranial nerve examination showed no signs of nerve impairment. Motor examination showed bilaterally increases tone on lower limb muscles.

Power of all muscles on examination was found to be normal at all joints.

Deep tendon Reflexes were tested and the result was as follows. (Table 1)

Table 1: Deep Tendon Reflexes

	Biceps	Triceps	Supinator	Patellar	Ankle
Left	+2	+2	+2	+4	+1
Right	+2	+2	+2	+4	+1

Grading of Deep tendon reflexes: 0 = reflexes absent; +1 = reflexes diminished but absent; +2 = normal; +3 = reflexes increased; +4 = clonus present

Superficial reflexes were tested and the recorded results are as follows. (Table 2)

Table 2: Superficial reflexes

	Corneal	Abdominal	Plantar
Left	+2	+2	Extensor
Right	+2	+2	Extensor

Sensory examination was performed and results were recorded as follows. (Table 3)

Table 3: Sensory examination

Parameter	Left	Right
Spinothalamic sensation		
1) Pain	Intact	Intact
2) Temperature	Intact	Intact
3) Pressure	Intact	Intact
Posterior column sensation		
1) Fine touch	Impaired (below knee)	Impaired (below knee)
2) Vibration	Impaired (below knee)	Impaired (below knee)
3) Proprioception	Impaired (below knee)	Impaired (below knee)

Cortical sensations above the knee were intact.

Patient showed positive Romberg test and past-pointing. Laboratory investigations performed were unremarkable with a hemoglobin concentration of 12.1 g/dl (reference range: 11-15 gm/dl), red blood cell count of 3.8 x 10^6/mm^3 (reference range: 3.8-4.8 x10^6/mm^3), mean corpuscular volume (MCV) of 90 fl (reference range: 83-101 fl), mean corpuscular hemoglobin concentration of 31.5 g/dl (reference range: 31.5-34.5 gm/dl), platelet count of 326,000/mm^3 (reference range: 150,000-410,000/mm^3), serum creatinine of 87 micromoles/L (reference range: 52.2-91.9 micromoles/L), and normal fasting plasma glucose level (70-100 mg/dl) and thyroid stimulating hormone levels (reference range: 0.5-5.0 milliIU/L) . Her blood picture revealed no features of vitamin B_{12} deficiency including an absence of hyper segmented neutrophils in peripheral smear and showed normochromic normocytes. However, as the patient showed neurological manifestations consistent with posterior and lateral column degeneration we decided to proceed with further workup and it was consistent with vitamin b12 deficiency with a very low cobalamin level (80pg/ml) {reference range: 160-950pg/ml}, elevated serum homocysteine levels (20 micromoles/L) {reference range: 5-15 micromoles/L} and elevated serum methyl malonic acid levels (0.55 micromole/ml) {reference range: 0.0-0.40 micromole/ml}.

No pallor, icterus, oedema, lymphadenopathy, cyanosis, koilonychia, clubbing was seen. Systemic examination was unremarkable.

MRI spine showed lesions involving the posterior and lateral columns, predominantly in the mid thoracic and lumbar regions [**Figure 1**].

Patient was treated with Inj.Cyanocobalamin 1000 ug (bd) x 7 days. Then she was started on sublingual tablets cyanocobalamin 1500 ug x 3 months. Patient is currently on regular follow up fortnightly and is showing physical signs of improvement since last 1 month.

MRI spine done about 5 months later showed complete resolution [**Figure 2**].

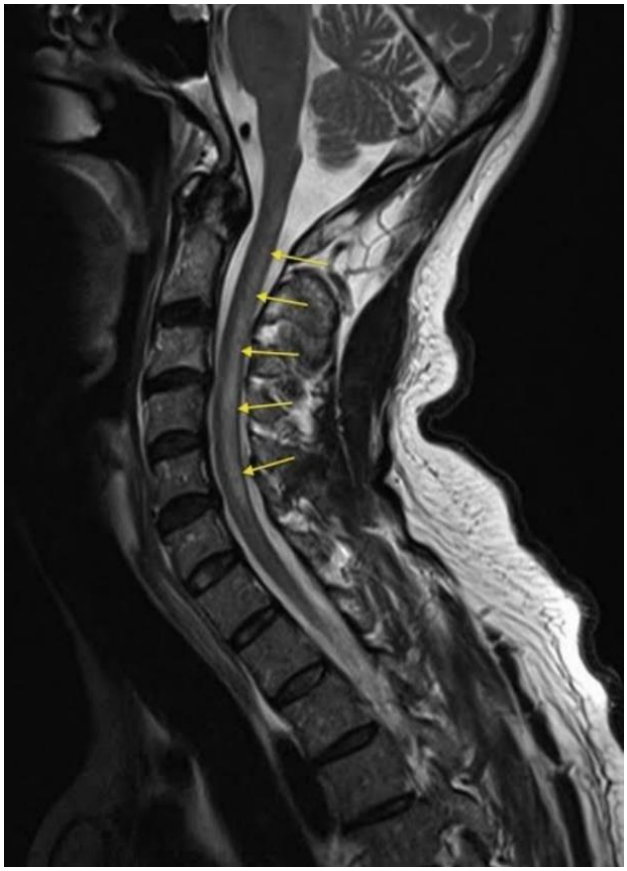

Figure 1

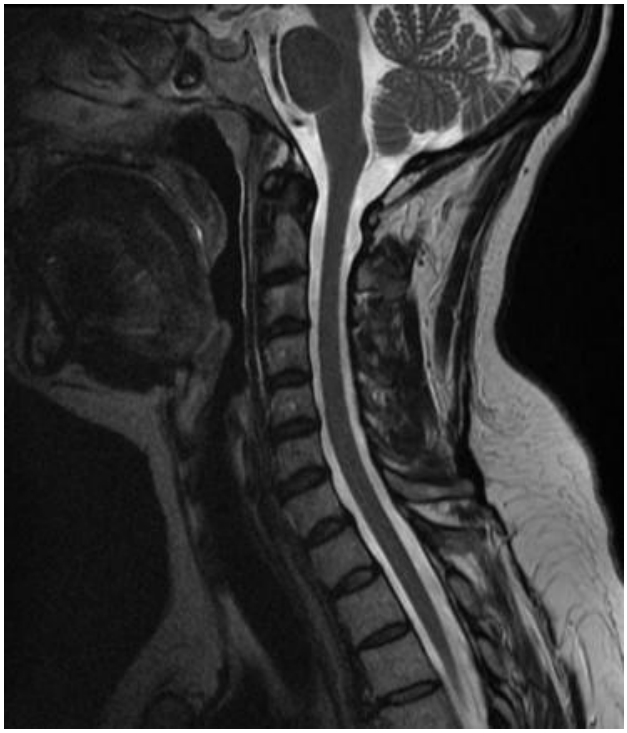

Figure 2

Discussion

Vitamin B12 is needed in biochemical pathways that generate metabolites needed for DNA maturation and myelin stability. As hematopoietic precursor cells are constantly dividing undifferentiated cells, it is expected that the deficiency of B12 would initially disrupt hematopoesis causing megaloblastic changes and low Hemoglobin levels and thereafter if the deficiency continues, would hamper myelin integrity causing neurological changes. SACD is the most frequent manifestation of vitamin B_{12} deficiency,[9] but anemia is a common and leading symptom to the diagnosis of vitamin B_{12} deficiency, and neurological manifestations typically occur after the onset of anemia [10,11]. Our patient presented with features of sensory ataxia, spastic paraparesis, decreased proprioception and vibratory sensation in lower limb and extensor plantar response. Lack of any other presenting symptom (gastrointestinal or hematological) in this patient could make it difficult to narrow down the list of differentials to suspect a vitamin B12 related etiology. Thus, vitamin B12 assessment should be included in the workup of all such similar cases irrespective of hematological signs.

Differential diagnoses of subacute combined degeneration of spinal cord include posterior column involvement seen is copper deficiency; Methotrexate induced myelopathy, vitamin E deficiency. Non traumatic causes of disease localized to spinal cord are transverse myelitis, multiple sclerosis, tabes dorsalis, epidural tumors, cervical spondylosis myelopathy.

Spinal cord involvement in copper deficiency is usually seen in patients who have undergone bariatric surgeries or undergoing excessive zinc chelation therapy for Wilson's disease. Vitamin E deficiency also shows neurological signs and symptoms similar to vitamin B12 deficiency. Pure vegetarian diet, no relevant history of zinc intake, bariatric surgery or a fat malabsorbtion producing condition in the patient can presumptively rule out copper and vitamin E deficiency respectively. Elevated serum methylmalonic acid and serum homocysteine levels and adequate response to cyanocobalamin therapy suggests vitamin B12 deficiency to be the prime etiological factor for sub-acute combined degeneration in this patient.

Methotrexate induced myelopathy and tabes dorsalis (neurological sequela of syphilis) can be ruled out with proper history taking.

Multiple sclerosis generally presents with asymmetric involvement of the spinal cord and can involve numerous areas. Multiple sclerosis is further characterized by neurological symptoms that are distributed over time. Patients also show many other general neurological symptoms, including bowel and bladder involvement and cerebellar involvement. These symptoms are not typical of subacute combined degeneration of the spinal cord [12].

Transverse myelitis, epidural tumors, cervical spondylosis myelopathy produce neurological symptoms similar to vitamin B12 deficiency but proper imaging in the form of MRI should be sufficient to rule out these conditions [12].

Psychiatric manifestations in Vitamin B12 deficiency may also include decreased memory, personality change, psychosis, and rarely delirium or coma, and may be seen in patients without haematological manifestations, or low normal B_{12} levels [11].

Our patient did not show mood changes or psychotic features but presented with learning disability - not attributed to poor vision as cranial nerve examination was unremarkable and there were no ocular complaints suggestive of optic atrophy or neuritis. A possible dietary deficiency was suspected to be the cause of Vitamin B12 deficiency and thus the patient was given cyanocobalamin supplements.

Conclusion

The paucity of clinical symptoms of anemia and hematological changes visible in laboratory reports in a patient showing only neurological manifestations of vitamin B12 deficiency is a rare case entity. It highlights the importance and benefit of harboring a high suspicion about the possibility of such an unusual presentation and prompts the physician to always be on a lookout for the presence of SACD even when no clinical features suggestive of an underlying B12 deficiency are seen. A prompt diagnosis and treatment would result in early reversal of this condition.

Conflicts of Interest disclosure

No conflict of interest

Financial support

There have been no funders for our project. No financial support has been granted to our work to have influenced its result/conclusion.

Key clinical message

The possibility of SACD occurring in a patient with no clinical symptoms of anemia or hematological changes consistent with B12 deficiency is rare. It highlights that a high suspicion index is crucial for diagnosis and treatment of this condition.

References

[1] Qudsiya Z, Jesus O. Subacute Combined Degeneration of the Spinal Cord [Internet]. Ncbi.nlm.nih.gov. 2021 [cited 25 November 2021]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559316/

[2] Jain KK, Malhotra HS, Garg RK, Gupta PK, Roy B, Gupta RK. Prevalence of MR imaging abnormalities in vitamin B12 deficiency patients presenting with clinical features of subacute combined degeneration of the spinal cord. J Neurol Sci. 2014 Jul 15; 342(1-2):162-6.

[3] Allen LH. Folate and vitamin B12 status in the Americas. Nutr Rev. 2004 Jun; 62(6 Pt 2): S29-33; discussion S34.

[4] Oo TH, Rojas-Hernandez CM. Challenging clinical presentations of pernicious anemia. Discov Med. 2017 Sep; 24(131):107-115.
[5] Cavalcoli F, Zilli A, Conte D, Massironi S. Micronutrient deficiencies in patients with chronic atrophic autoimmune gastritis: A review. World J Gastroenterol. 2017 Jan 28;23(4):563-572.
[6] Ankar A, Kumar A. Vitamin B12 Deficiency [Internet]. Ncbi.nlm.nih.gov. 2021 [cited 29 November 2021]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441923/
[7] Clinical significance of low cobalamin levels in older hospital patients. van Asselt DZ, Blom HJ, Zuiderent R, Wevers RA, Jakobs C, van den Broek WJ, Lamers CB, Corstens FH, Hoefnagels WH Neth J Med. 2000 Aug; 57(2):41-9.
[8] McCadden A. Vitamin B12 in neurology and ageing: Clinical and genetic aspects. Biochimie 2013; 95:1066-76.
[9] Lee GR. Pernicious anemia and other causes of vitamin B12 (cobalamin) deficiency. In: Lee GR, Foerster J, Lukens J, Paraskevas F, Greer JP, Rodgers GM, editors. Wintrobe's clinical hematology. 10. Baltimore: Lippincott Williams; 1999. pp. 941–964.
[10] Magnetic resonance imaging findings within the posterior and lateral columns of the spinal cord extended from the medulla oblongata to the thoracic spine in a woman with subacute combined degeneration without hematologic disorders: a case report and review of the literature. Rabhi S, Maaroufi M, Khibri H, Belahsen F, Tizniti S, Berrady R, Bono WJ Med Case Rep. 2011 Apr 27; 5():166.
[11] Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis. Lindenbaum J, Healton EB, Savage DG, Brust JC, Garrett TJ, Podell ER, Marcell PD, Stabler SP, Allen RH N Engl J Med. 1988 Jun 30; 318(26):1720-8.
[12] Saji AM, De Jesus O. Spinal Cord Subacute Combined Degeneration. [Updated 2021 Aug 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560728/