

Case report

Catatonia and other psychiatric symptoms with vitamin B₁₂ deficiency

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Objective: To study unusual psychiatric manifestation of vitamin B₁₂ deficiency and related issues.

Method: A case study of 52-year-old female and review of relevant literature.

Results: Complete remission of psychiatric symptoms without recurrence for the next 4 years with vitamin B₁₂ as the only specific therapy instituted.

Conclusion: Importance of B₁₂ estimation and replacement in patients with varied psychiatric manifestations.

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Introduction

Vitamin B₁₂ deficiency has been associated with various psychiatric manifestations. The common psychiatric sequelae are depression, agitation or violence and acute paranoid states (1, 2). Depression has been especially associated with B₁₂ deficiency. Recently, a report, the first one of its kind, attributed catatonia to very low levels of vitamin B₁₂ in an elderly patient (3). The most common neuro-psychiatric manifestations are sensory impairment in the form of paresthesias and decreased vibratory and touch sensations, ataxia, organic psychosis, recent memory changes, and delirium with or without delusions and hallucinations (4, 5). The earliest to manifest were symptoms of sensory impairment which were present for a mean duration varying from 4 to 10 months in these studies. The psychiatric symptoms can develop long before anemia or spinal cord symptoms (6–8). In various studies, the neuropsychiatric abnormalities were present in up to 28% of patients in the absence of any change in the hematocrit values or increase in red cell mean corpuscular volume (MCV); the hematological indices most commonly affected by B₁₂ deficiency (4, 5, 9). A study has emphasized that the peripheral blood smear and marrow biopsies should not be regarded as diagnostic of vitamin B₁₂ deficiency (this might be masked by excess folate intake) (8). Here we present a case highlighting some of the above features.

Case report

Mrs M, a 52-year-old postmenopausal, life-long vegetarian, presented to our casualty services with sudden onset of stuporous state for last 10 days. On examination, the patient was found to be mute, having odd motor movements, waxy flexibility, active negativism, perplexed look and incontinent for stool and urine. Her physical examination revealed tachycardia and no abnormality in cardiovascular, respiratory and neurological examinations. She was transferred from a private hospital where she had been administered electroconvulsive therapy twice and Flupenthixol 1 mg twice a day for the last 5 days. The computed tomography (CT) scan there had revealed mild atrophy with normal hemogram, liver, renal, and thyroid function [T₃, T₄ and thyroid stimulating hormone (TSH)] tests. She had no history of fever, head injury or overdose of any drugs prior to the stuporous state. Her past history, revealed symptoms for the last 14 years in the form of lethargy, easy fatigability, excessive worry, hypochondriacal preoccupations along with poor sleep, appetite and constipation for which repeated investigations including a chest X-ray, mantoux, liver, renal and thyroid function tests revealed no abnormality; a B₁₂ level was never performed. She sought a psychiatric consultation 2 years ago when she developed frequent crying spells, marked anxiety about her household, odd motor movements in the form of forcibly closing her eyes, moving her arms purposelessly in supin-

ation and pronation and elementary perceptual changes as if somebody was calling her. She was diagnosed major depression with psychotic features and treated with Trifluoperazine 20 mg/day and Fluoxetine 40 mg/day for 6 months. The hemogram, liver, renal, and thyroid functions were normal; the B₁₂ estimations were not performed. She recovered considerably, although certain neurasthenic symptoms like lethargy, fatigue, constipation persisted until the current presentation when she also developed pervasive sadness, anhedonia, restlessness and suicidal ideas. The investigations after admission into the psychiatry ward were all normal except for a Hb 10.2 gm/dl, low sodium (129 meq/l) and increased potassium (5.2 meq/l) levels and an electroencephalogram (EEG) showing generalized slowing with no epileptiform discharges. The MCV was 86 fL and the peripheral smear showed normocytic normochromic morphology. The physical examination revealed no abnormality including no signs of peripheral neuropathy. The normal serum cortisol and thyroid functions (T₃, T₄ and TSH) ruled out hypothyroidism and Addison's disease and a nephrology consultation ruled out a renal cause for the abnormal sodium and potassium levels. She was kept only on supportive management. In the first 3 weeks, she showed little recovery with spontaneous speech and control of incontinence but had impaired attention span and was disoriented to time, place, and person. She also had recent memory deficits, perseveratory errors, constructional apraxia, impairment of judgement, and conceptual abilities along with depressive symptoms. The Mini-Mental Status Examination (MMSE) scores were constantly low at 8–10 of 30. An estimation of vitamin B₁₂ levels revealed a low value of 150 pg/ml (normal 190–1190 pg/ml). The folate and serum Anti-Nuclear antibody (ANA) levels were normal and an antiparietal cell antibody was negative ruling out pernicious anemia. The patient had no history of tropical sprue, ulcerative colitis, Crohn's disease, ulcer or any surgical intervention. She was given intramuscular cyanocobalamin 1000 mcg on alternate days for 3 days, then weekly for a month along with oral tablets daily. Over the next 4 weeks, there was absence of irrelevant speech, marked decrease in agitation, depressive cognition and improvement in MMSE scores, which persisted at 28–30 of 30. Over the next 6–8 weeks, the patient returned to her premorbid self as was 14 years ago with no neurasthenic symptoms and weight gain of 4–5 kg. She has been asymptomatic for the last 4 years. The estimation of B₁₂ levels performed 3 months later were 1197 pg/ml and a repeat EEG revealed no abnormality.

Discussion

The patient described was seen to have long standing neurotic symptoms and an episode of major depression with psychotic features, who, now presented with catatonic features which on improvement still left her with cognitive dysfunction with depressive symptoms. The only positive findings were generalized slowing on the EEG, mild atrophy on the CT scan and low B₁₂ levels without any hematological or neurological abnormalities. The patient's symptoms remitted completely with reversal of EEG to normal, with B₁₂ replacement without any recurrence for the last 4 years. Any other organic cause was ruled out with relevant investigations. The patient had no premorbid disposition or family history of psychiatric illness. A negative antiparietal antibody ruled out pernicious anemia and there was no risk factor for B₁₂ deficiency except for being a lifelong vegetarian. The case highlights the development of psychiatric manifestations in the absence of hematological or spinal cord abnormalities as repeatedly stressed in previous studies (6–8, 10).

It is important that the B₁₂ deficiency is treated early as the symptoms may be difficult to reverse after a certain duration because of irreversible changes secondary to axonal degeneration (11). Certain studies (12, 13) point out that this narrow window of opportunity is approximately 1 year or even lesser, although there are a few reports of complete remission of very long standing psychiatric symptoms (7). In the present case, although there was complete remission of various longstanding symptoms of 14 years duration but with the above evidence and no previous estimations of B₁₂ available, it is a possibility that the past symptoms were independent of the deficiency. A confounding factor could be the levels of B₁₂ required to predict psychiatric manifestations, which have been postulated as high as 600–1000 pg/ml (14) far higher than the current acceptable levels, based on hematological criteria. The case highlights the fact that severe psychiatric manifestations including catatonia can occur even with moderately decreased B₁₂ levels (150 pg/ml) while in another report of catatonia attributable to B₁₂ deficiency in an elderly male patient on risperidone (3), the levels were markedly lower (1.07 pg/ml) and the authors also discuss a possibility of neuroleptic induced catatonia or malignant syndrome in that case. To the authors, this is the first case with an asymptomatic follow-up period of 4 years with catatonic presentation attributable to moderately decreased B₁₂ levels without any hematological or spinal cord

symptoms that reversed completely with B₁₂ replacement.

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Invited comment

Vitamin B₁₂ deficiency is a commonly overlooked cause of psychiatric morbidity. While many clinicians are aware of the neurological symptoms associated with it, many would be hard-pressed to discuss some of the psychiatric symptoms associated with vitamin B₁₂ deficiency. Psychiatric disturbances of vitamin B₁₂ deficiency include depression, apathy, irritability, dementia, delirium and hallucinations (1). Catatonia has been associated with extreme vitamin B₁₂ deficiency as well (2).

One of the first problems associated with vitamin B₁₂ deficiency is that many clinicians are unaware that the reference ranges that are often described as

the 'normal' range are actually based on hematological indices only (3). In most clinical facilities, the low end of the normal range of vitamin B₁₂ levels is around 200 pg/ml. In order to avoid the development of neuropsychiatric symptoms, the vitamin B₁₂ levels should actually be much higher. Domisse has recommended that every person's vitamin B₁₂ levels should be at least 600 pg/ml, and should actually be over 1000 pg/ml to maximize mental functioning (4). An increased mean corpuscular volume (MCV) cannot be used as a substitute for an evaluation of a patient's vitamin B₁₂ level. While it is true that a patient with an increased MCV will often have decreased vitamin B₁₂ levels, this has been found to be incorrect 28% of the time (5).

Another problem associated with vitamin B₁₂ deficiency is that many clinicians are unaware of how commonly this clinical entity is present. In a longitudinal study of non-demented elderly patients, 8.5% had a vitamin B₁₂ level of 200 pg/ml or less (6). In another study of depressed outpatients, 12% were found to have vitamin B₁₂ levels of 200 pg/ml or less (7). Finally, in a study of patients in a general medical hospital with mood and cognitive disorders, 31.3% of those with a mood disorder and 20.6% of those with a cognitive disorder were found to have vitamin B₁₂ levels less than 400 pg/ml (8).

Finally, there needs to be an increase in the urgency in the treatment of vitamin B₁₂ deficiency. While some clinicians may wish to undertake a lengthy work-up to find the cause of the deficiency, one must also remember that vitamin B₁₂-induced psychiatric illness must be corrected within 12 months or the damage may become irreversible (9). It is felt that the most robust response occurs if the patient's vitamin B₁₂ deficiency is corrected within the first 6 months (9).

'Catatonia and other Psychiatric Symptoms with Vitamin B₁₂ Deficiency' is a very important case for a number of reasons (10). First, the patient developed catatonia with only a mild decrease in her vitamin B₁₂ level. In the previous case of vitamin B₁₂-deficiency-induced catatonia (2), the patient developed catatonia with a vitamin B₁₂ level of 1.07 pg/ml. In this case, symptoms occurred with only a moderately decreased vitamin B₁₂ level (150 pg/ml). Also, another important aspect is that while the patient had both mood and psychotic symptoms, all her symptoms resolved without the use of psychotropic medications. Her condition responded to vitamin B₁₂ level supplementation only. This is extremely important, because if vitamin B₁₂ deficiency is found to be the cause of a patient's catatonia, then the patient

can be spared prolonged treatment with dopamine-blocking agents and antidepressant medications. Hopefully, this case will make more clinicians aware of the ramifications of untreated vitamin B₁₂ deficiency, and open the eyes of mental health professionals to the importance of evaluating vitamin B₁₂ levels in psychiatric patients.

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