Journal of Nutrition and Food Security
Shahid Sadoughi University of Medical Sciences
School of Public Health
Department of Nutrition
Nutrition & Food Security Research Center

eISSN: 2476-7425 pISSN: 2476-7417 JNFS 2023; 8(2): 158-162 Website: jnfs.ssu.ac.ir

Onset of Mania by Vitamin B12 Injection in a 52-Year Old Patient with Refractory and Resistant Depression

Valentina Artoonian; MD [1], Vajiheh Aghamollaii; MD [2], Azadeh Nadjarzadeh; PhD [3,4] & Reza Bidaki; MD [*5,6]

[1] Department of Psychiatry, Fellowship in Psychotherapy. Tehran University of Medical Sciences, Tehran, Iran; [2] Department of Neurology, Tehran University of Medical Sciences, Tehran, Iran; [3] Department of Nutrition, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran; [4] Nutrition and Food Security Research Center, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran [5] Research Center of Addiction and Behavioral Sciences, Shahid Sadoughi University of Medical Sciences, Yazd , Iran; [6] Fellowship in Neuropsychiatr, Diabetes Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

ARTICLE INFO

CASE REPORT

Article history:
Received:10 Jul 2021
Revised: 28 Dec 2021
Accepted: 28 Dec 2021

****Corresponding author***
Reza.Bidaki111@gmail.com
Research Center of Addiction and Behavioral Sciences, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

Postal code: *8991683316*
Tel: +98 353 2632004

ABSTRACT

Vitamin B_{12} affects and modify the function of multiple organ systems. Its deficiency may cause psychiatric symptoms in addition to hematologic, gastrointestinal, and neurologic manifestations. The present case study aims to report a patient with vitamin B_{12} deficiency who coexisted with resistant and persistent depression, and experienced mania phase after the replacement of vitamin B_{12}. For a patient with refractory and resistant depression and evidence or a risk factor for vitamin B_{12} deficiency, it is required to check plasma levels and monitor psychiatric symptoms during vitamin B_{12} supplementation. There are some manifestations of B_{12} deficiency including bipolar disorder, mood lability, irritability, and psychosis due to deficiency but we didn't find case report about induce of psychiatric presentation follow correction of vitamin B_{12} deficiency .

Keywords: *Refractory depression; Bipolar disorder; Vitamin B_{12} deficiency*

Introduction

Pharmacological induced hypomania or mania should be carefully considered after use of a medicinal agent and mood disorder is suggested according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM 5) (Terao and Tanaka, 2014). Although solitary case reports are not reliable in general, and evidence must be sought from large series and systematic reviews of treated patients matched with control groups, every precise case presentation can contribute new insights and cues for science development.

Vitamin B_{12} or cobalamin, is one of the essential vitamins, affecting various systems of the body. Vitamin B_{12} deficiency leads to psychiatric symptoms and is parallel with hematologic, gastrointestinal, and neurologic manifestations {Murray, 2012 #13}.

This paper should be cited as: Artoonian V, Aghamolaee V, Nadjarzadeh A, Bidaki R. ***Onset of Mania by Vitamin B12 Injection in a 52-Year Old Patient with Refractory and Resistant Depression.*** *Journal of Nutrition and Food Security (JNFS)*, 2023; 8(2): 158-162.

[DOR: 20.1001.1.24767417.2023.8.2.3.1]
[DOI: 10.18502/jnfs.v8i2.12589]

Both vitamin B_{12} and folic acid play roles as cofactors in the neurotransmitter synthesis like serotonin and norepinephrine (Hutto, 1997). Vitamin B_{12} deficiency changes neurotransmitters rate and can predispose to mood disorders (Deana *et al.*, 1977).

This case study aims to report on a patient with vitamin B_{12} deficiency and resistant depression, who experienced mania phase after vitamin B_{12} replacement. The researchers did not find any similar cases. There are some cases with B_{12} deficiency that showed manifestations of bipolar disorder, mood lability, irritability, and psychosis due to deficiency but we didn't find psychiatric presentation follow correction of vitamin B_{12} deficiency.

Case presentation

A 52-year old married, right handed woman with a non-vegetarian diet with the diagnosis of Major Depressive Disorder, despite taking medicine (Sertraline 100 mg/day and Trazodone 50 mg/day), experienced exacerbation in her symptoms. Gradually, paranoia and persecutory overvalue idea were added and increasing Sertraline dose up to 150 mg/day and adding Perphenazine 4 mg/day, were not effective. Moreover, speech volume and rate were reduced and she became progressively isolated from her family and peers. Her attention to personal health care was decreased. Finally, symptoms of oscillatory cognitive disturbance and generalized weakness were recognized. According to these symptoms, she was referred to a neurologist with complaints of "insomnia, depression, anhedonia, agitation, psychomotor retardation, persecutory delusion, generalized weakness, oppositional states, orolinguomandibular dyskinesia, and progression of cognitive impairment without parkinsonism symptoms. In the mental status examination and evaluation showed impaired attention, concentration, reduced working and short-term memory. Her Montreal Cognitive Assessment screening test (MOCA) core was 22.

She was psychotic; therefore, Tab. Quetiapine 25 mg was prescribed. However, worriy and agitation were exacerbated. Her daughter confirmed that these complaints had been obvious and started in the past year. Speech volume and rate had reduced, and she had become progressively isolated from her family and peers. According to previous psychiatric history, she suffered from depression with onset from past 8 years, with a pattern of recurrence and resistance in during last year. She was admitted in psychiatry ward and discharged after full remission of disorder. Drugs included Tab. Serteraline 150 mg/day and Tab. Lorazepam 1 mg at night, anti-diabetic agents (Diabetes known case) and Tab. Cabergoline (because of hypophysis micro adenoma hyper prolactinemia) at that time. In the next episode, she experienced depressive symptoms again. The psychiatrist added the previous medication with Tab. Bupropione. She did not show a suitable response to treatment and was admitted again. In this episode she had suicidal thoughts. She was prescribed Sertraline 200 mg/day, Bupropion 150 mg/day and Trazodone 25 mg/ day and was discharged with partially remission. She passed another two years with this combination of drugs. In her third episode, she was visited by psychiatrist out of our center and was diagnosed with bipolar disorder and was prescribed with Lithium Carbonate which she could not tolerate it due to its side effects. Therefore, she came back to our center, and because there were not found any significant symptoms of bipolar disorder, she was diagnosed depression disorder and was prescribed by Sertraline 100mg/day and Trazodone 50mg/day again and her symptoms got partially remission for another one year.

About premorbid personality, there were extrovert, euthymic, and openness traits and there aren't history of major psychiatric diagnosis include bipolar spectrum, psychotic disorder or postpartum depression. Finally, during the past year, she has used Tab. Serteralin 150 mg/day for treatment of depression, but it has not elevated her mood.

She had a history of refractory depressive disorder and was resistant to treatment with

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psychotic features at the age of 44 years.

Previous medical history included diabetes mellitus, hypothyroidism, hypothesis micro adenoma, and hyper prolactinemia. She did not have GI upset, history of specific dietary regimen and tablet (Metformine and H_2 blockers). Drugs including Tab. Cabergoline and Tab. Donepezil (5 mg/day) were started because of cognitive impairment and hyper prolactinemia by another physician. However, it was suggested that they stop using these medications because that vascular cognitive impairment was more possible diagnosis about this case. Brain imaging showed medial temporal atrophy (MTA), stage 2 based on Shelton score.

Considering some neurologic symptoms and signs like paresthesia and thyroid abnormality, levels of B_{12} and prolactine were assessed. In last laboratory findings, she had low vitamin B_{12} level (109 pg/ml) and plasma prolactin was 54µg/l and MCV was 84 fl. Therefore, Vitamin B_{12} as IM injection was prescribed. After 4 days, she showed an irritable mood and after follow up it was onset of manic episode. Therefore, Vitamin B_{12} as IM injection was prescribed. After 4 days, she showed an irritable mood and in follow ups it was onset of manic episode. Therefore, we started Tab. Sodium Valproate 200 mg BID, Tab. Quetiapine 50 mg twice a day. After one month by raising the dose of sodium Valproate up to 800mg/day and Quitiapine up to 250 mg/day, her mania symptoms disappeared. Moreover, her neurological symptoms like orolinguomandibular dyskinesia and cognitive state was significantly got better 3 months after vitamin B_{12} supplementation. In a sense, her MOCA score was 25 at that time.

Ethical considerations

Written informed consent was taken from the caregiver for publication of this case study. This case was presented in ethical committee of Roozbeh hospital , Tehran and approved with code number IR798933 in Feb 2022.

Discussion

Although adequate vitamin B_{12} concentration and status is essential in all human life, it seems more important in some conditions such as elderly people, women in childbearing ages, and even patients with psychiatric disorder. The patient was middle-aged with atypical and resistant depression, which was nearly late onset, and the medication changed after taking vitamin B_{12}. Therefore, she was a patient with bipolar disorder type III. It is known that the prevalence of bipolar disorder is declined in the elderly (Depp and Jeste, 2004). Therefore, it requires medical evaluation due to the underlying disease.

Therefore, if a new case of bipolar disorder, atypical depression, and resistant depression at middle or old age refer, complete assessment will be necessary because of some organic problems like various type of deficiencies. The level of B_{12} should be assessed based on the history of atypical psychiatric symptoms, treatment-resistant depressive disorders even without presence of risk factors for nutritional deficiency such as alcoholism, elderly age, Tab. Metformin, PPI, H2 blockers, malabsorption, GI surgery or vegetarian diet.

Although mechanism of depression due to vitamin B_{12} deficiency is determined, the effect of vitamin B_{12} on the treatment of mania is unclear. Neurological impairments such as neuropathy, myelopathy, memory impairment, dementia and brain atrophy may happen in cases of low B_{12} status (Vogiatzoglou *et al.*, 2009). Except for brain atrophy and memory impairment, the patient did not have any problems after vitamin B_{12} replacement and mood disorder management. Some studies have shown that metformin and the duration of consumption is associated with level of vitamin B_{12} (Beulens *et al.*, 2015, Ko *et al.*, 2014).

In a case study, a woman who suffered from psychotic depression did not respond to conventional therapy but resolved significantly after replacement of vitamin B_{12} (Milanlıoğlu and Investigations, 2011). Vitamin B_{12} deficiency has shown a significant relationship with chronic recurrent depression especially in a oxidative stress condition (van de Lagemaat *et al.*, 2019).

The studied patient had a dramatically response as euphoric mood and manic state. Dose and

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[DOI: 10.18502/jnfs.v8i2.12589]

prescription of vitamin B_{12}, patient's characteristic, type of depression, brain reserve, and atrophy might be important for type of therapeutic response as non-responder, euthymic, elevated or euphoric mood and even psychosis.

Probiotic-containing fermented foods can change the microbiome and increase the bio-availability of mood-regulating B vitamins crucial to neurotransmitter production. Vitamin D deficiency results in increasing pro-inflammatory cytokines and disrupts mitochondrial function and monoamine production. Magnesium, Vitamin D, and B vitamins deficiency correlate with depression severity. Deficiency of folate also may lead to treatment-resistant depression (Simkin and Arnold, 2020). A mixture of EPA and docosahexaenoic acid has been reported to improve depression and the course of illness in bipolar disorder (Bozzatello *et al.*, 2016).

In the elderly with low vitamin B_{12} plasma level, elevated serum folate concentration was related to acceleration of cognitive decline, but in people with normal vitamin B_{12}, high serum folate level was shown to be protective against cognitive decline (Morris *et al.*, 2007).Folate concentration was not evaluated in this patient. However, it can be mentioned that this condition can affect mood status.

Studies with prospective design, large case series, clinical trial, and systematic review studies which focused on vitamin deficiency or augmentation and outcomes are needed for understanding the role of this vitamin the etiology of similar diseases.

Conclusion

Patients with refractory and resistant depressive disorder, especially middle-aged and elderly, need for checking and replace Vitamin B_{12} with monitoring of psychiatric symptoms.

Acknowledgement

Thanks are owed to the patient's family for participation in this case study.

Conflicts of interest

The authors declare that they have no conflict of interest.

Authors' contributions

Artoonian V and Aghamollaii V interviewed the patient and collected data, Bidaki R wrote primary draft and discussed about it, and Nadjarzadeh A and Bidaki R critically revised and submitted it.

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[DOI: 10.18502/jnfs.v8i2.12589]