

Catatonia and vitamin B12 deficiency – A hidden cause? A review article

N.A. ALHUJAILI

Department of Medicine, Division of Psychiatry, Faculty of Medicine in Rabigh, King Abdulaziz University, Jeddah, Saudi Arabia

Abstract. – This paper aims to broadly overview catatonia and vitamin B12 deficiency and highlight this association as a possible hidden cause.

A review of published articles which examined the association between vitamin B12 deficiency and catatonia was performed. The articles for this review were selected by searching the electronic databases of the MEDLINE from March 2022 until August 2022 using catatonia (and related terms such as psychosis; psychomotor) and vitamin B12 (and related terms such as vitamin B12 deficiency; neuropsychiatry) as keywords. Articles had to be written in English to be included in this review.

The direct relationship between levels of B12 and catatonic symptoms is difficult to confirm, as catatonia has different etiologies and can be triggered under the influence of multifactorial stressors. In this review, few published reports showed the reversibility of the catatonic symptoms once the level of B12 levels increased to more than 200 pg/ml. This could explain the responsibility of deficiency of B12 in the catatonic presentation of the few published case reports.

B12-level screening in cases of catatonia of unclear etiology needs to be considered, particularly in a group at risk of B12 deficiency. Of particular concern is that vitamin B12 can be close to the normal range, which may delay the diagnosis. Detection and treatment of catatonic illness usually result in a rapid resolution of the condition, which, if untreated, can lead to potentially fatal outcomes.

Key Words:

Catatonia, Vitamin B12, Neuropsychiatry, Vitamin B12 deficiency, Psychosis, Psychomotor.

Introduction

Catatonia is a group of motor and psychiatric symptoms which affects the ability of an individual to move in a usual manner. Walther et al¹ stated that catatonia is historically

categorized as a type of schizophrenia, and its symptoms include agitation, restlessness, lack of communication, and movement. Catatonia is presented in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) in three structures: catatonia related to other psychiatric disorders, mental confusion due to another illness, and unknown catatonia². At least three symptoms out of twelve characterize it: catalepsy, waxy flexibility, stupor, agitation, mutism, negativism, posturing, stereotypes, grimacing, echolalia and echopraxia³.

Vitamin B12 is essential for adequately functioning sensory systems and erythropoiesis. Any deficiency in this supplement can, in turn, cause megaloblastic insufficiency and a variety of neuropsychiatric problems⁴. Vitamin B12 deficiency is estimated at 10-15% in an established population aged 60 years or older. However, it is estimated⁵ that 5% and 10% of those recalling a failure state have significant clinical manifestations. Routine non-psychiatric clinical episodes of vitamin B12 insufficiency include macrocytic iron deficiency and spinal cord impairment with decreased vibration and position sense. Gastrointestinal side effects can also be caused by vitamin B12 deficiency, including constipation, decreased hunger, glossitis, and glossodynia⁴. Several psychiatric manifestations associated with vitamin B12 deficiency have been observed⁶. It is not known which specific component of B12 deficiency causes psychiatric symptoms. Depression, psychosis, and mental aggravation, including dementia or drowsiness, are the main psychiatric symptoms of this deficiency⁶.

This paper aims to broadly overview catatonia and vitamin B12 deficiency and highlight the association between catatonia and vitamin B12 deficiency as a possible hidden cause.

Catatonia

In epidemiological studies⁷, the commonness of catatonia in psychiatric patients shifted between 7% and 31%. In the United States, 90,000 individuals are hospitalized every year for catatonia⁸. For instance, in a survey⁹ of people with a mental health condition in the Netherlands, the extent of cases broken down clinically was 2%, and the extent came to by experts with unequivocal scales surpassed 18%.

Catatonia is divided into three types: excited catatonia, akinetic catatonia, and malignant catatonia. Excited catatonia is a type in which a person can move, whereas this is considered impulsive and pointless¹⁰. Moreover, the person with excited catatonia may mimic the gestures and movements of those who try to help him. This person often seems delirious, combative, and agitated. In contrast, akinetic catatonia is referred to as the most common type, and the affected person seems blank most of the time and does not respond when someone tries to speak to him¹¹.

Furthermore, he may respond occasionally but in such a manner that he tends to repeat the statement that was asked of him. The affected person often lies and sits in such a position that he cannot move. According to Mulder et al¹² malignant catatonia is a type associated with continued symptoms, which further lead to other health problems such as drastic changes in body temperature, breathing, heart rate, and blood pressure. This is the last stage of catatonia, and the person who is catatonic for an extended period may experience kidney failure, blood clots, and dehydration.

Common Causes of Catatonia

The common causes that lead to catatonia are stated below:

Neurologic and General Medical Conditions

Catatonia is also associated with neurologic conditions, including frontal lobe disease, bilateral globus pallidus disease, post-encephalitic states, general paresis, parietal and thalamic lobe lesions, and parkinsonism¹³. By means of seizures and developmental disorders, catatonia may be found in children. General medical conditions lead the patients toward catatonia. Certain conditions, such as viral infections (HIV), metabolic disturbances, autoimmune disease, typhoid fever,

endocrinopathies, and heart stroke, are mostly associated with catatonia. Moreover, catatonia is also induced by drug withdrawals and intoxications. Exposure to illicit recreational and antipsychotic drugs, withdrawal from opiate intoxication, dopaminergic drugs, and benzodiazepines are all drug-related conditions¹⁴⁻¹⁶.

Mood Disorder

The greater part of the catatonia was the consequence of mania and depression. Fink et al¹⁷ saw that “as a rule, mental signs compare to hyper and melancholic conditions” like self-irritation. Peralta et al¹⁸ showed that close to half of mental assaults start with a pressure episode, that catatonia and mania are regularly connected, and that patients of praecox with more noteworthy catatonia are bound to foster dementia. Numerous markers partner catatonia with mood disorders. Their outcomes propose that 25% or a more significant number of catatonic patients have adequate mental issues to satisfy a mood disorder diagnosis¹⁹.

Psychosis

When there are no present and past episodes related to mood disorders required in the diagnosis, it is evaluated that approximately 10-15% of catatonic patients meet the schizophrenia criteria. The features such as mutism, catalepsy, posturing, and mannerisms are interlinked with schizophrenic catatonia²⁰.

Vitamin B12 Deficiency

The clinical manifestation of B12 insufficiency is generally variable; it includes macrocytic weakness, which usually occurs early, gastrointestinal indications, and neuropsychiatric manifestations such as neuropathy, myelopathy, dementia, catatonia, and dementia. Neuropsychiatric problems are the main symptoms without associated deterioration or abnormal macrocytosis and address an expressive dilemma⁶.

Causes of Vitamin B12 Deficiency

Vitamin B12 is a very specific resource that the body can consume. The acidic climate of the stomach releases the nutrient from food, which binds to the R protein and enters the small digestive tract. In the small digestive tract, the R protein is contaminated with compounds from

the pancreas, with which the anticancer climate acts. A natural element (IF) secreted by specific gastric cells binds to vitamin B12 in the terminal ileum, where the vitamin B12-IF complex is maintained²¹. Retention occurs through a receptor component in view of calcium supplied by the pancreas and about 1% through the unbranched circulation. The best-known causes of vitamin B12 deficiency are malabsorption problems due to the confusing course of intake rather than nutritional insufficiency. In pernicious anemia, the immune system clears the gastric mucosa, leading to a dual B12 retention problem: reduced acidity, which inhibits clearance of dietary vitamin B12 and antibodies against IF²². This leads to a decrease in IF and thus to the binding of the vitamin B12-IF complex for retention. In the elderly, impaired absorption of vitamin B12 may similarly occur due to reduced gastric corrosion or pancreatic protein deficiency. Various causes include careful emptying of the stomach and small parts of the small digestive system, tropical celiac disease and sprue, pancreatic insufficiency, intoxication, delayed intake of gastric corrosive drugs, and AIDS²³. Less often, in a group of cases, the leading causes of B12 deficiency were the poor intake of B12, like in vegetarians and seniors⁴.

Catatonia and Vitamin B12 Deficiency

Catatonia is seen in a wide range of clinical, neurological, general psychological, drug- and pollutant-related problems, making it difficult to determine the etiological outcome here and there²⁴.

Certainly, psychiatric manifestations can precede the onset of neurological weakness or spikes and can sometimes be found without macrocytosis and with B12 levels that are not very low²⁴. Four cases of vitamin B12 deficiency introduced as catatonia have been reported²⁴.

One case of a postmenopausal lifelong vegetarian woman is presented as catatonia without signs of macrocytosis. Despite extensive hematology and biochemical examinations, the prominent irregularity was low vitamin B12 levels of 150 pg/ml (normal 190-1,190 pg/ml). The patient's catatonic symptoms were remitted entirely with B12 replacement without recurrence for the next four years.

Two cases of pernicious anemia presented with psychiatric symptoms before hematological or neurological manifestations appeared. Low B12 levels and intrinsic factor antibodies were

found^{25,26} by chance. The catatonic episode was successfully treated with lorazepam and adequate doses of cyanocobalamin.

A young woman with the progressive onset of paranoid psychosis and catatonia was found²⁷ to have vitamin B12 deficiency. Catatonic symptoms improved rapidly but partially with benzodiazepines and electroconvulsive therapy. Complete remission was achieved with vitamin B12 replacement.

Current information shows a clinical-organic parallel between psychiatric manifestations and B12 levels^{28,29}. It generally reinforces the way that catatonia can occur even with relatively low levels of vitamin B12. The direct relationship between levels of B12 and catatonic symptoms is difficult to confirm, as catatonia has different etiologies and can be triggered under the influence of multifactorial stressors. In any case, the reversibility deficit by shortening the cut-off times between cyanocobalamin infusions, which leads to an increase in B12 levels of more than (200 pg/ml), explains the responsibility of deficiency of B12 in the catatonic presentation of previous case reports^{28,29}.

Studies by Pavlov et al²⁸ and Benarous et al²⁹ have shown that mental manifestations of B12 insufficiency can occur without a trace of hematologic or spinal cord side effects. Research^{28,29} has also shown that psychological side effects can occur with B12 levels slightly lower than typical levels but still much higher than those associated with the macrocytic disease. This caused much debate about the less "typical" level of vitamin B12 in serum. Some have suggested^{28,29} that the "typical" range of vitamin B12, commonly considered 190 pg/mL to 900 pg/mL, might be correct for hematologic side effects but not for neurologic or non-neurologic side effects.

Catalano et al³⁰ in a comprehensive clinic study with emotional and mental illnesses revealed that 31.3% had B12 levels of 400 pg/ml and 20.6% of follow-up patients could only reach recommended levels in the low range of normal, almost low. Crystal et al³¹ looking at the rate of asymptomatic dementia (with few mental health problems) found that those with moderate vitamin B12 levels (mean 558 pg/mL) had the exact incidence as those with low vitamin B12 levels of 200 pg/mL or less. This suggests that typical low or even moderate to normal levels of vitamin B12 in older people may lead to mental decline. In this way, vitamin B12 levels may not recognize patients who are biased about the psychological consequences of vitamin B12

deficiency. Thus, even though a research facility's conclusion for vitamin B12 deficiency typically includes testing for serum vitamin B12, serum homocysteine, or methylmalonic acid (MMA), it can be used to screen an insufficient condition independently of normal serum vitamin B12 testing³².

Vitamin B12 is not routinely listed as one of the investigations related to catatonia. The deficiency in most reported cases is found by chance. All patients engaged with catatonia should undergo an EEG test to evaluate for other neurological issues³³. Since catatonia can be brought about by a great range of cerebrum imaging and neurological problems, preferably MRI is suggested to detect these issues³⁴. Testing at laboratories ought to incorporate the total count of platelet, creatinine level, blood urea nitrogen, liver, and synthetic muscle substances, blood glucose, electrolytes, and thyroid function tests, to evaluate mental states and causes³⁴.

Catatonia Treatment

The fundamental treatment for catatonia is principally benzodiazepines; however, treating the underlying medical cause is crucial for optimum results. Benzodiazepines follow up on GABA-A receptors and assist with freeing the breakdown from GABA that happens in specific patients with a mental state³⁶. Lorazepam needs to be tested when catatonia is suspected. The response indicates the high possibility of catatonia³⁷. The beginning portion of lorazepam is 2 to 6 mg/day and can be expanded to 12 to 16 mg/day³⁸. With some defense, a response is typically seen within 3 to 7 days; however, the reaction to treatment can sometimes be moderate and slow³⁹.

Electroconvulsive therapy (ECT) is considered the foremost treatment for neurologic leukemia, risky catatonia, and unfortunate catatonia. It is reviewed⁴⁰ that ECT acts by growing the cerebral blood stream to the frontal lobe and parietal cortices, expanding receptor articulation and activity of GABA. It might likewise be an appropriate treatment when treatment with benzodiazepines has been stopped. The reaction rate for catatonia secondary effects while utilizing ECT is around 80-100%⁴¹. It may require some ECT treatments to accomplish ideal outcomes⁴². It might take around six meetings for execution to help⁴⁰. The effect of ECT can be considered as the presence of a total clinical reaction or additional clinical improvement after two successive meetings⁴¹.

Prognosis of Catatonia

Catatonia generally has a reasonable prognosis unless it is detected early, its purpose is addressed, side effects occur, and discomfort persists. In clinical catatonia, metabolic causes might have preferable anticipation over primary mental injury⁴³.

Conclusions

If testing is delayed, B12 insufficiency can be attributed to irreversible side effects. The absence of obvious hematologic symptoms in the early stages of B12 insufficiency may contribute to this delay. Therefore, in catatonia of unclear etiology, B12-level screening may be valuable for early detection and treatment, particularly in a group at risk of B12 deficiency. Detection and treatment of catatonic illness usually result in a rapid onset of the condition. If treated incorrectly, it can lead to potentially fatal seizures, a dangerous neuroleptic condition, and pneumonia embolism. Likewise, clinicians must have undeniable concerns about mental health, especially in patients with severe mental illness.

Conflict of Interest

The author reports there is no conflict of interest to declare.

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ORCID ID

Naseem Abdulmohi Alhujaili: 0000-0002-7131-4811.

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