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Vitamin B12 Deficiency Associated with Depression, Psychosis, and Violent Suicidality in an Older Woman

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Abstract

Background: Vitamin B12 deficiency is prevalent among the elderly population and can present with a range of neurologic and psychiatric symptoms, including cognitive decline, mood disturbances, psychosis, and behavioral changes. **Case Presentation:** In this report, we describe a female in her sixties who was hospitalized in a psychiatric unit following a violent suicide attempt in which she forcefully slashed multiple appendages, parts of the torso, and the neck with a steak knife, causing severe superficial and deep tissue damage. History revealed a recent development of paranoid psychosis where she felt she was being controlled by others and surveilled in her apartment and on her phone. Examination revealed severe depressive symptoms with constant suicidal ideation, paranoid psychosis, and significant psychomotor retardation. Laboratory results were only remarkable for a low vitamin B12 level of 170 pg/mL (reference range 232 pg/mL - 1245 pg/mL). MRI demonstrated significant cerebral cortical and cerebellar atrophy, not typical for her age. She received a five-day course of intramuscular B12 1000 units, along with venlafaxine 75 mg extended release for the depressive symptoms. The patient's mood and psychomotor retardation drastically improved during the first several days of B12 replacement, with full resolution of suicidal ideation. Some paranoia continued, and aripiprazole 5 mg was then added. **Conclusion:** This case adds to the literature and suggests a constellation of symptoms, including paranoid psychosis, severe depression, and violent behavior associated with vitamin B12 deficiency. It also emphasizes the importance of obtaining vitamin B12 levels in psychiatric patients, especially those with new-onset depression, psychosis, or violent behavior.

Keywords

Vitamin B12 Deficiency, Psychosis, Major Depressive Disorder, Aggression

1. Introduction

Vitamin B12 is an essential vitamin that is a critical cofactor for two enzymatic reactions, the conversion of homocysteine to methionine and the conversion of methylmalonyl-CoA to succinyl-CoA, which are essential for DNA synthesis, mature red blood cell formation, and the development, myelination, and proper functioning of the central nervous system [1]-[3].

Deficiency of cobalamin among the elderly may be the result of food-cobalamin malabsorption, pernicious anemia, dietary deficiency, and malabsorptive disorders [4]. Vitamin B12 deficiency affects more than 20% of the elderly population, with females between the ages of 60 - 70 years at higher risk. Patients are often asymptomatic and go untreated for many years [4]-[7]. The insidious nature of B12 deficiency is especially concerning given its association with delirium, depression, psychosis, dementia, irritability, and abrupt personality changes [8]. Additionally, a correlation has been identified between vitamin B12 deficiency and bizarre, violent behavior in patients that was not consistent with their premorbid picture and completely resolved following B12 replacement [8]. A case series of 15 patients with B12 deficiency revealed that the most common symptoms were depression, paranoia, and violence [9].

Persons aged 60 and above in the United States have the highest suicide rate [10] [11]. Suicide by gunshot has remained the leading method among older men, while non-firearm methods such as poisoning, hanging, and suffocation have remained the leading methods among older women [12]. Stabbing as a suicide method among elderly women is so rare as not to be mentioned in studies of suicide methods [13]-[15].

In this report, we discuss the case of an older woman with vitamin B12 deficiency suffering from new-onset, violent suicidality with psychotic depression, which improved rapidly and did not recur following B12 replacement. This adds to the literature on a notable association of depression, paranoid psychosis, and violence in vitamin B12 deficiency.

2. Case Report

A female in her sixties was hospitalized in a psychiatric unit following a violent suicide attempt. With witnesses present, she used a large knife from the kitchen and ran outside, slashing multiple appendages, parts of the torso, and neck. She would not stop despite a witness screaming at her and physical intervention by responders. Some lacerations caused by this incident were so severe that deep tissue damage, including the severing of multiple tendons, had occurred. She was appropriately treated in a local hospital prior to transfer to the psychiatric facility.

Neurological exam documented by the hospital family medicine physician did not note any neurologic abnormalities.

Past psychiatric history revealed one previous inpatient psychiatric admission three years earlier due to depression without suicidal ideation or psychosis. No prior history of suicide attempts or violence was reported. She had followed up with psychiatry on an outpatient basis until this hospitalization. Family described the patient as calm, reporting no history of agitation, verbal or physical aggression, and said this drastic change in behavior was unlike anything they had ever witnessed in the patient's life. They mentioned that in her prior depressive episodes, she did not demonstrate any violent behavior. However, the family reported that the patient had become increasingly paranoid, with delusions of being monitored and controlled in her apartment and by her phone for several months prior to admission. Medical history revealed hypothyroidism, asthma, and Meniere's disease.

On initial examination, the patient had obvious bandaged lacerations on her wrists and elsewhere on her body. Severe psychomotor retardation was observed on physical examination. Initially, the patient refused to participate in the evaluation by the mental hygiene commissioner and hid underneath a blanket. She eventually removed the blanket and told the evaluator about her suicidality. The patient endorsed feelings of guilt, low energy levels, and spoke of a "stalker," with feelings of intense paranoia. She reported a multi-decade history of depression treated with vilazodone and diazepam. The patient noted that she had not been taking the vilazodone as prescribed because it suppressed her appetite. The family was contacted and corroborated that the patient had suffered from depression for more than twenty years, but was not aware of any previous suicide attempts. Major depression with psychotic features was the primary differential diagnosis. The patient was started on 75 mg of venlafaxine daily for depressive symptoms.

Further investigation was conducted, and the patient was found to have a significantly low serum vitamin B12 level of 170 pg/mL (N = 232 - 1245 pg/mL). The psychiatric hospitalization three years prior was at a different location and there was no access to this record, so it is unknown if vitamin B12 levels had previously been checked or not. As far as the patient and her family knew, she had never been diagnosed with B12 deficiency before. Following the discovery of her low vitamin B12 level, she was started on a five-day course of intramuscular 1000 U vitamin B12 injection replacement. After the 2nd injection, partial improvement of psychomotor retardation, mood, and psychosis was observed. Dramatic improvement was noted after one week of treatment with both vitamin B12 and venlafaxine 75 mg. She was much more active and animated, with an improvement of both her energy and mood. She denied both suicidal and homicidal ideation. Daily venlafaxine was continued and B12 replacement was changed to oral vitamin B12, 1000 mcg twice daily. Approximately two weeks after admission and supplementation with B12, the patient's serum B12 level measured >2000 pg/mL (N = 232 - 1245 pg/mL). The patient still had some paranoia with delusions of staff conspir-

ing against her. She was started on 5 mg oral aripiprazole for treatment of psychosis and eventually increased to 10 mg with resolution of delusions. MRI of the brain was ordered to assess for other causes of symptoms.

Brain MRI indicated significant cortical and cerebellar atrophy that was not consistent with age (Figure 1).

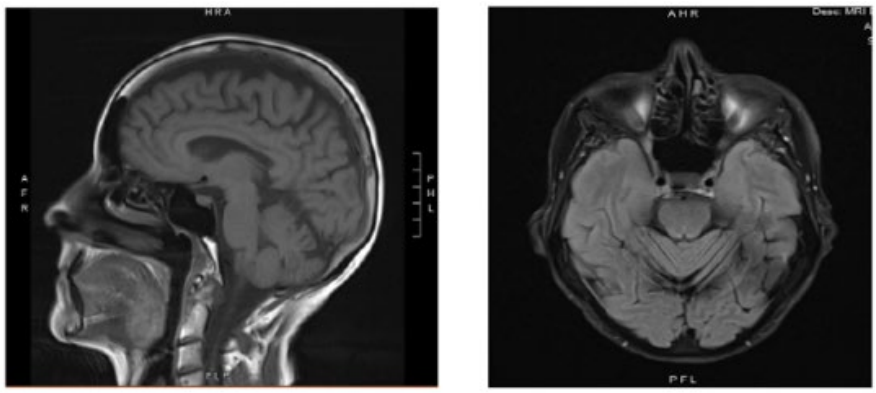

Figure 1. Patient's brain MRI in the sagittal view (left) and axial view (right).

She continued to improve, with resolution of depressive symptoms and psychosis. She reported her mood was "really good" and had no suicidal ideations. She had no deficiencies on tasks relevant to attention, language, memory, visuospatial/executive functioning, abstraction, or orientation. After one month of hospitalization, the patient was deemed stable for discharge.

3. Discussion

According to the Vitamin B12 Health Professional Fact Sheet published by the National Institutes of Health in 2018, approximately 20% of individuals over 60 years of age were diagnosed with vitamin B12 deficiency in the United States. Of this population, elderly women were found to be at higher risk of vitamin B12 deficiency than men [16] [17]. Excess vitamin B12 is stored in the liver for several years, making deficiency unlikely until hepatic stores are depleted. As a result, the various hematologic, neurologic, and psychiatric symptoms associated with B12 deficiency often do not arise until cobalamin stores are markedly depleted, at which point neurological damage is often irreversible [16]. A series of case reports discussed the psychiatric manifestations of vitamin B12 deficiency, including depression, organic psychosis, and dementia [18]. One case discussed involved an 89-year-old female who presented to a psychiatric hospital with paranoid psychosis and was diagnosed with vitamin B12 deficiency. Her paranoia and withdrawn behavior began nine months prior to hospitalization and improved following vitamin B12 replacement [18]. The authors reported a similar occurrence of organic psychosis in a 64-year-old female who presented in a psychotic state with loss of orientation, anxiety, restlessness, incoherent speech, and rapidly fluctuating delusions of persecution. Her psychosis was attributed to underlying hyperthyroidism,

but following treatment for this, the patient remained psychotic. It was later discovered that the patient's vitamin B12 level was low, and following replacement therapy, her psychosis disappeared [18]. In a 1998 publication by Tardiff with the Psychiatric Clinics of North America, the case of a 64-year-old woman was discussed who had no prior history of psychiatric disorders and was admitted after she was found wandering the streets. She had experienced immense paranoid and persecutory delusions, one of which was that her brother was trying to kill her. The patient violently attacked him and left his house immediately after the attack. During hospitalization, she did not respond to antipsychotic treatment, but following five days of vitamin B12 replacement, her delusions markedly improved [8]. A series of patients with vitamin B12 deficiency revealed common symptoms of depression, psychosis, and violence [9]. Our case shares similarities of depression, psychosis, and violence, suggesting a notable association in those with psychiatric symptoms associated with vitamin B12 deficiency. However, our case is the only one where the violence was directed toward oneself, in a violent suicide attempt rather than violence toward others.

The case discussed in this report is noteworthy, as the patient's rather dramatic and violent suicide attempt is discordant with what is known from the literature regarding suicidality in elderly females, who generally opt for guns, poisoning, hanging, or suffocation [10] [11] [19]. One important distinction to make is between that of forcefully stabbing and cutting, the latter of which is a commonly implemented form of nonsuicidal self-injury (NSSI) among younger women [20]. While cutting as a form of NSSI is defined as lacking suicidal intent, the patient discussed in this report had clear suicidal intentions. It is because the patient had a multi-decade history of depression with no prior suicide attempts before the age of 62, and that her first attempt was conducted in such an unusual, violent manner for her age and sex, that her case is particularly noteworthy.

In addition to the patient's unusual suicide method given her age, sex, and medical history, another remarkable finding from this case is that the patient's suicidal ideations, psychomotor retardation, and mood improved within days following vitamin B12 replacement, similar to how some of the psychiatric symptoms in the reviewed cases above resolved following B12 supplementation [2] [3] [18]. While the patient was also on venlafaxine 75 mg for those several days, it would be unlikely that several days of low-dose venlafaxine would have improved the symptoms so dramatically. However, venlafaxine remains a potential confounding factor, and we cannot fully exclude the possibility that the effects of this antidepressant contributed to her improvement or acted synergistically with vitamin B12 replacement to drastically improve her symptoms. While incidents of depression in older women related to vitamin B12 deficiency have been reported [2] [3] [18], the only case report we found that involved B12 deficiency and suicidality was in a 16-year-old adolescent male with psychotic features and passive suicidal ideations [21]. Although suggestive, we cannot know if the vitamin B12 deficiency causes the psychotic depression. Further studies would be helpful to examine the prevalence of vitamin B12 deficiency among elderly females who have attempted

suicide.

Another noteworthy aspect of this case to consider is the patient's history of depression, a risk factor associated with completed suicides among the elderly [22]. While the correlation between B12 deficiency and suicidality has scarcely been studied, numerous studies exist that assess the association between vitamin B12 deficiency and depression. In one such study published by Khosravi *et al.* in 2020, researchers expanded on the fact that poor diet is often linked to depression by specifically exploring the roles that folate (vitamin B9) and cobalamin (vitamin B12) contribute to depression. Their results showed that increased serum folate and cobalamin, obtained from healthy dietary patterns, provide protective effects against depression [23]. Similar results were obtained in a 2008 study that found the incidence of late-life depression (65 years) could be predicted by lower serum levels of folate and cobalamin [24]. While it is impossible to definitively establish the interplay between our patient's depression, suicidality, and vitamin B12 deficiency, the results provided by these studies broaden our understanding of the relationship between cobalamin deficiency and depression.

Another severe and potentially irreversible effect of vitamin B12 deficiency is brain atrophy. Results from a randomized controlled trial conducted by Smith *et al.* found that homocysteine is a risk factor for brain atrophy, cognitive impairment, and dementia [25]. Further results from their study demonstrated that the rate of brain atrophy in older patients with mild cognitive impairment can be slowed by treatment with B-vitamins that lower homocysteine levels [25]. According to a separate article published by Deng *et al.*, the brain regions found to be most affected by vitamin B12 deficiency were the left middle temporal pole and the left insula. The authors noted that these two regions are essential for emotional regulation [26]. Our patient had significant cerebral cortical and cerebellar atrophy on brain MRI. While this atrophy could certainly be related to prolonged B12 deficiency, the chronicity of both the deficiency and neurologic atrophy is not fully known. Thus, other age-related or independent pathological processes cannot be ruled out as contributing factors, especially without prior imaging for comparison. While the previously mentioned publications exhibit that the process of brain atrophy can be slowed with homocysteine-lowering agents, there is little known about the reversibility of atrophy with vitamin B12 replacement in elderly individuals. Conversely, a 2020 case report discussed a vitamin B12-deficient infant who presented to the hospital with severe encephalopathy. CT/MRI imaging showed generalized atrophy of the infant's brain. After vitamin B12 replacement, outpatient oral B12 supplementation, and dietary modifications, radiologic normalization was observed after 7 months [27]. The results from this case support the reversal of atrophy with vitamin B12 supplementation in infants, but without research specifically geared toward the elderly population, conclusions regarding atrophy reversal with vitamin B12 are limited. This emphasizes the importance of future research on this topic that should utilize radiographic imaging of the brain to better understand the extent of atrophy attributable to vitamin B12 deficiency,

and if this atrophy could be reversed in the elderly.

Existing literature reveals a strong association between brain atrophy and psychosis. One proposed explanation for the atrophy observed in psychotic spectrum disorders is aberrant myelination in conjunction with reduced neurites [28]. Given the fact that proper serum levels of vitamin B12 are necessary for proper development, myelination, and function of the central nervous system, it is conceivable that a deficiency of vitamin B12 could lead to brain atrophy, psychosis, cognitive impairment, and/or dementia. An interesting finding regarding this case is that the patient's psychosis did not fully improve alongside her other psychiatric symptoms and only appeared to improve with antipsychotic treatment. Given that the patient and family reported no prior history of psychosis with previous depressive episodes, it is possible that the vitamin B12 deficiency could have either triggered the psychotic episode, requiring treatment with both B12 replacement and an antipsychotic, or that the vitamin B12 deficiency could have unmasked a vulnerability to psychosis. Researchers have reported that vitamin B12 appeared to be an effective adjunct therapy to facilitate the antipsychotic effects of the second-generation antipsychotic quetiapine in Alzheimer's disease [29].

This case report is one of the first to investigate the contribution of vitamin B12 deficiency to the acute onset of violent suicidality in an older female. Future research utilizing radiographic brain imaging is necessary in order to understand the extent of atrophy attributable to vitamin B12 deficiency and whether or not this atrophy can be reversed with repletion. The results of this case, in conjunction with these future directions of research, could be useful for inpatient psychiatric care of elderly women presenting with new-onset suicidality. Furthermore, these results could contribute to greater awareness of the severe and often irreversible consequences of vitamin B12 deficiency among the elderly.

4. Conclusion

This case report is one of the first to explore the possible relationship between vitamin B12 deficiency and new-onset violent suicidality in elderly females. It adds to the literature, suggesting a constellation of symptoms including depression, psychosis, and violence in patients with vitamin B12 deficiency. However, future cases and research are necessary to establish a definitive correlation between vitamin B12 deficiency and suicidality in elderly women. This case, along with the future directions of research proposed, has the potential to provide useful information regarding the management of inpatient psychiatric care of elderly women presenting with new-onset violent suicidality. Further, these results could contribute to greater awareness of the severe and often irreversible consequences of vitamin B12 deficiency in the elderly. This case supports the importance of a full diagnostic workup in cases of new-onset suicidality and psychosis in elderly patients.

Data Availability

The data used to support the findings of this case study are included within the

article.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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