

Cobalamin Deficiency Manifested with Seizures, Mood Oscillations, Psychotic Features and Reversible Dementia in the Absence of Typical Neurologic and Hematologic Signs and Symptoms: A Case Report

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ABSTRACT

Cobalamin deficiency is associated with a wide spectrum of hematologic, neurologic, gastroenterologic and psychiatric disorders or symptoms. We report a case of a 50-year-old man with complex partial seizures with secondary generalization, mood oscillations and psychotic symptoms alternating with confusion and reversible dementia secondary to cobalamin deficiency in the absence of typical neurologic and/or hematologic symptoms and signs. Exclusion of epilepsy, acute, atrophic or expansive lesion of central nervous system and usual etiology associated with reversible dementia (infectious diseases, an endocrine etiology and deficiency of vitamins other than cobalamin); finding of cobalamin deficiency only and complete neuropsychiatric recovery after substitution, confirmed etiology. Typical and atypical psychiatric manifestations due to cobalamin deficiency that precede neurologic and/or hematologic signs and symptoms can recover completely after adequate replacement therapy.

Key words: mood oscillations, delusions, auditory hallucinations, dementia, cobalamin deficiency

Introduction

Cobalamin deficiency has long been associated with a wide spectrum of hematologic, neurologic, gastroenterologic and psychiatric disorders or symptoms. Anemia and macrocytosis are the most frequent hematologic manifestation, while combined medullar sclerosis together with peripheral sensory neuropathies is the most common neurologic manifestation of cobalamin deficiency¹⁻³. A wide spectrum of psychiatrically inclined disorders or symptoms have been documented to be associated with cobalamin deficiency. Slow cerebration, confusion, memory disturbances, delirium with or without hallucinations and/or delusions, depression and acute psychotic states are frequently seen, while reversible manic and schizophreniform states rather rarely⁴⁻⁹.

Psychiatric manifestations due to cobalamin deficiency commonly precede neurologic symptoms and/or megaloblastic anemia. The importance of such finding is in the potential for early substitution interventions in patients with psychiatric symptoms due to cobalamin deficiency, but without anemia, macrocytosis or spinal cord symptoms.

Case Report

A 50-year-old male patient presented with seizures, mood oscillations associated with psychotic symptoms (delusions of different type, most prominently paranoid

and auditory hallucinations) and reversible dementia. He had no previous psychiatric or neurological treatment; somatically healthy.

No typical hematologic or traditional neurologic repercussions due to cobalamin deficiency (anemia, macrocytosis, combined medullar sclerosis together with peripheral sensory neuropathies) were found. Folate level was normal. Different known causes associated with reversible dementia (infectious diseases, endocrine etiology, deficiency of vitamins other than cobalamin) were excluded.

Repeated: glycemia, blood analysis (biochemistry, hematology), thyroid function, urine analysis, electrolytes, erythrocyte sedimentation rate, C-reactive protein values and cerebrospinal fluid findings were normal. No parameters of infectious diseases were found. All serology results (including testing to *Borrelia burgdorferi*, important because of patient's profession: forestry worker) were normal. Tumor markers were normal. Endocrine etiology and deficiency of vitamins other than cobalamin were excluded as causes of reversible dementia. Performed ECG records, X-ray of the lungs, repeated inter-nistic and infectologic examinations were normal. Fundoscopy showed normal findings.

Repeated EEG records, performed after seizures and within inter-seizures periods, showed discretely irregular, but normal findings. Repeated NMR findings (three within two-months' period, all normal) excluded acute and/or expansive CNS lesion, as well as cerebral atrophy inadequate for patient's age.

The first neuropsychiatric manifestations due to cobalamin deficiency included three seizures, periods of confusion alternating with periods of almost normal functioning with coexisting: mood oscillations and psychotic symptoms and reversible dementia. All seizures were of complex partial type with secondary generalization. Patient's mood oscillated between depression, euthymia, dysphoria and emotional lability, while the most prominent psychotic features included paranoid delusions (within a wide spectrum of various delusions) and auditory hallucinations. Sleep disturbances (initial and middle insomnia) were part of the clinical picture, too. Finally, reversible dementia was observed with the lowest Mini Mental State Examination (MMSE)¹⁰ sum of 16.

During initial four-months' treatment period, a combination of psychopharmacotherapy (haloperidol 2 mg/daily, diazepam 15 mg/daily and carbamazepine 800 mg/daily) and cobalamin substitution was chosen. Cobalamin replacement therapy had the following scheme: Hydroxycobalamin 1000 ng/day i.m. for 10 days, followed with 1000 ng/once weekly i.m. for next 6 weeks, and, finally, 1000 ng i.m. once monthly and still ongoing. After initial four-months' combined (substitution and psychopharmacs) therapy, only partial neuropsychiatric recovery was achieved. Sleep disturbances were reduced, seizures disappeared, periods of confusion became less frequent, though still present, while periods with coexisting mood oscillations and psychotic symptoms were significantly shortened. Hallucinations disappeared, as did most of delusions, with the exception of paranoid delusions

that persisted, but with a much lower intensity. At the end of the initial four-months' treatment period, the MMSE was an average of 22.

During the next four months, the patient was on replacement therapy only (patient's decision), receiving hydroxycobalamin 1000 ng/monthly i.m. and complete neuropsychiatric recovery was achieved. No confusion, seizures, mood oscillations, psychotic symptoms or cognitive impairments (MMSE sum was 30!) were found. Patient achieved full clinical remission.

Presently, after a one-year follow up, patient is still receiving hydroxycobalamin 1000 ng/once monthly i.m. and is still in complete clinical remission.

Discussion

Cobalamin deficiency is not a rare finding. Typical clinical triade includes: megaloblastic anemia, glossitis and neuropsychiatric symptoms¹⁻³.

In our case, in relatively young patient (without earlier internistic, neurologic and/or psychiatric complaints) cobalamin deficiency manifested itself with atypical neuropsychiatric triade: seizures, confusion periods alternating with episodes with coexisting mood oscillations and psychotic symptoms (delusions of various type, most prominently paranoid and auditory hallucinations) and reversible dementia (MMSE sum increased from 16 to 30 after replacement therapy).

After the initial four-month combined pharmacotherapy (small dose of haloperidol in combination with diazepam and carbamazepine) and cobalamin substitution, only partial therapeutic result was achieved. Seizures disappeared, periods of confusion became less frequent but still present, alternating with periods of less expressed mood oscillations and reduced, but still present, psychotic component: paranoid delusions, while sleep disturbances were partially relieved. An attempt was made to increase the dose of haloperidol, during a three weeks' period, to 4-6 mg/daily (with diazepam 15 mg/day and carbamazepine 800 mg/day, constantly), but no clinically significant improvement was achieved, while the patient reacted with mild extrapyramidal symptoms, which withdrew completely after dosage reduction. Subsequently, during a one-week period risperidone up to 4 mg/daily was prescribed to substitute haloperidol (component of combined pharmacotherapy – with diazepam and carbamazepine), but worsening of psychiatric status ensued. Delusions and confusion periods were more frequent and patient and his family insisted on returning to a small dose of haloperidol. During the second four-month treatment period, patient received cobalamin substitution only, at the end of which complete neuropsychiatric recovery was achieved. Seizures, confusion, mood oscillations, psychotic symptoms and cognitive impairments disappeared.

We speculate that patient developed cobalamin deficiency most probably due to decreased absorption. There was no previous inadequate dietary intake due to psychiatric problems or other reasons that could result in decreased serum cobalamin level.

Discovering of potentially reversible cause of cognitive impairments or even dementia (in our case, associated with seizures, mood oscillations, psychotic symptoms and sleeping disturbances), such as cobalamin deficiency, does not always mean that after adequate replacement therapy the patient will recover completely. In many cases, for only partial recovery, a combination of psychopharmac and substitution therapy is needed. Still, com-

plete recovery is possible. In our case, after an initial combination of psychopharmacotherapy and vitamin replacement, only partial recovery was observed, while after a continued cobalamin replacement therapy only, full neuropsychiatric recovery was achieved. In each single case, an individual treatment strategy should be chosen, always counting with the possibility of complete clinical remission after adequate replacement therapy.

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DEFICIT KOBALAMINA MANIFESTIRAN KONVULZIJAMA, OSCILACIJAMA RASPOLOŽENJA, PSIHOTIČNIM ELEMENTIMA I REVERZIBILNOM DEMENCIJOM U ODSUSTVU TIPIČNIH NEUROLOŠKIH I HEMATOLOŠKIH ZNAKOVA I SIMPTOMA: PRIKAZ SLUČAJA

SAŽETAK

Deficit kobalamina je povezan sa širokim spektrom hematoloških, neuroloških, gastroenteroloških i psihijatrijskih poremećaja i simptoma. Prikazan je slučaj 50-godišnjeg muškarca s krizama svijesti (kompleksne parcijalne sa sekundarnom generalizacijom), oscilacijama raspoloženja i psihotičnim simptomima koji su se izmjenjivali sa smetenošću i reverzibilnom demencijom kao manifestacijama deficita kobalamina, a u odsutnosti tipičnih neuroloških i/ili hematoloških simptoma i znakova. Etiologija je potvrđena isključenjem epilepsije, akutne, atrofične ili ekspanzivne lezije središnjeg živčanog sustava i drugih poremećaja povezanih s reverzibilnom demencijom (infektivne bolesti, endokrina etiologija i deficiti ostalih vitamina), te nađenim izoliranim deficitom kobalamina i potpunim povlačenjem neuropsihijatrijskih simptoma nakon nadoknade kobalamina. Tipične i atipične psihijatrijske manifestacije deficita kobalamina koje mogu prethoditi neurološkim i/ili hematološkim znakovima i simptomima, mogu se u potpunosti povući nakon adekvatne nadomjesne terapije.