CASE REPORT

# Reversible dementia, psychotic symptoms and epilepsy in a patient with vitamin $B_{12}$ deficiency

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## SUMMARY

Vitamin $B_{12}$ deficiency is a common condition, typically associated with megaloblastic anaemia, glossitis and neuropsychiatric symptoms. We report the case of a patient presenting with progressive cognitive and functional deterioration, psychosis and seizures, later found to be secondary to pernicious anaemia. Importantly, the diagnosis of pernicious anaemia was only established 5 years after symptom onset and was overlooked even when the patient was under medical care, in part due to the lack of classic neurological and haematological signs associated with the condition. The patient had a remarkable neuropsychiatric recovery after vitamin replacement and psychopharmacological management. We discuss similar presentations of vitamin $B_{12}$ deficiency found in the literature, symptom reversibility and the importance of its early recognition and treatment.

## BACKGROUND

Vitamin $B_{12}$ deficiency is a common condition, typically associated with megaloblastic anaemia, glossitis and neurological and psychiatric symptoms.[1] The most common neurological findings are subacute combined degeneration of the spinal cord and peripheral sensory neuropathies, but epileptic seizures have also been reported.[2–4] Psychiatric manifestations include depression, irritability, cognitive slowing, memory disturbances, dementia, psychosis and delirium.[5] In vitamin $B_{12}$ deficiency, neuropsychiatric symptoms may develop even in the absence of anaemia or macrocytosis[6]—in a published series of 141 consecutive cases with neuropsychiatric symptoms, 40 patients (28%) had a normal haematocrit, normal mean corpuscular volume or both.[7] The absence of classic haematological and neurological signs can delay the diagnosis, with severe consequences since neuronal damage is likely to be irreversible if treatment is delayed.[1] We describe a patient presenting with progressive cognitive and functional deterioration, severe psychosis and seizures, later found to be secondary to pernicious anaemia, in the absence of classic signs. Despite the prolonged deficit, the patient had a remarkable recovery after vitamin replacement. We discuss similar presentations of vitamin $B_{12}$ deficiency found in the literature, symptom reversibility and the importance of early recognition and treatment.

## CASE PRESENTATION

A 61-year-old woman, with no relevant neuropsychiatric or medical history, was referred for neuropsychiatric evaluation by her attending neurologist due to altered behaviour. She was brought in by her sister, who provided most of the history because the patient did not speak Portuguese. She had been born in Cape Verde, and since her husband's death had been living there alone for 12 years. During the last 5 years, her relatives had noticed a gradual change in her behaviour: she walked the streets naked and sometimes appeared to be talking to people who were not present. Her house was unkempt, she no longer cooked and she neglected her hygiene, prompting her sister to bring her to Portugal. Few months after her arrival, her sister witnessed a sudden loss of consciousness followed by tonic-clonic movements and brought the patient to the local emergency department. At admission, she was fully conscious with no apparent cognitive impairment—although no formal cognitive assessment was carried out due to the language barrier. Apart from psychomotor retardation, neurological examination was unremarkable. Workup revealed a normal complete blood count, glycaemia, C-reactive protein, ionogram and kidney, liver and thyroid function. Head CT scan showed no structural abnormalities. She was medicated with carbamazepine 400 mg two times per day and referred to a neurology outpatient clinic. An interictal electroencephalogram (EEG) study showed generalised slowing compatible with diffuse brain dysfunction, with no epileptiform activity. She went on to have another tonic-clonic seizure, but seizures stopped after her family started managing her medication and ensuring compliance. Despite adequate seizure control, she continued to have psychotic symptoms and poor global functioning, prompting referral for psychiatric evaluation. According to her sister, she continued talking and shouting about the spirits of dead relatives whom she could see clearly and who told her not to take her medication. She feared that her family would poison her and refused to share meals with them. She had trouble remembering things and seemed to be very distracted. She could not go outside alone as she would get lost and be unable to return home without help. The mental status examination was limited by the language barrier. The patient was conscious but disoriented in time and space. Her speech was slurred and, according to her sister, sometimes incomprehensible. Auditory and visual hallucinations and persecutory delusions were inferred from her observed behaviour. Her mood was overall euthymic, but the affect was blunted.

## INVESTIGATIONS

Initial workup revealed a vitamin $B_{12}$ deficiency (<117 pmol/L) and hyperhomocysteinaemia (15.3 $\mu$mol/L), with normal red blood cell count, haemoglobin and mean corpuscular volume. Reversible causes of dementia, including infectious diseases, endocrine dysfunction and deficiency of other vitamins, were excluded. The subsequent study showed positive anti-intrinsic factor and antiparietal cell antibodies. Brain MRI showed only discreet and unspecific white matter abnormalities in the frontal region and mild cortical and subcortical atrophy. A complete neuropsychological evaluation proved impracticable due to the linguistic barrier. She was referred to gastroenterology for gastric endoscopy, which revealed signs of nonerosive gastritis. Subsequent histologic analysis showed chronic atrophic gastritis, with marked atrophy of the oxyntic component of the gastric mucosa, mild inactive chronic inflammation and complete intestinal metaplasia without dysplasia in about 60% of the glandular component of the sample.

## DIFFERENTIAL DIAGNOSIS

Our patient presented with progressive cognitive and functional deterioration, psychotic symptoms (visual and auditory hallucinations and persecutory delusions) and seizures. The differential diagnosis thus included degenerative dementia, primary or secondary epilepsy, primary psychotic disorders and affective disorders with psychotic symptoms. Epilepsy could either be secondary to dementia or a primary process. Psychotic symptoms could also be secondary to dementia or epilepsy (interictal psychosis) or a primary psychiatric disorder. As such, reversible causes of dementia were investigated first, as were other causes of epilepsy. The investigation revealed no other alterations apart from vitamin $B_{12}$ deficiency, associated with positive anti-intrinsic factor and antiparietal cell antibodies, compatible with the diagnosis of pernicious anaemia.

## TREATMENT

Olanzapine 10 mg once a day was initially used to alleviate psychotic symptoms. When the diagnosis of pernicious anaemia was established, the patient was treated with parenteral cyanocobalamin, 1 mg administered daily in the first 6 days, weekly in the following 6 weeks and monthly after that. Carbamazepine was maintained at 400 mg two times per day.

## OUTCOME AND FOLLOW-UP

Psychotic symptoms responded favourably to olanzapine. At the subsequent revaluation, there were no reports of aggressive behaviour and the persecutory delusions and hallucinations had stopped. The patient remained disoriented, disabled and incoherent. After initiating parenteral cyanocobalamin, the patient's cognitive status improved dramatically. She became oriented in time and space, her speech became coherent and logic, and her functional status returned to what her relatives considered to be normal. She could now cook, help around the house, go out shopping and be entirely independent in daily activities. Nine months after resolution of psychotic symptoms, we successfully stopped olanzapine. However, after another 6 months, the psychotic symptoms recurred, with prominent visual hallucinations and persecutory delusions. Because the patient was found to have increased fasting glucose, paliperidone 9 mg once a day was started, due to the more favourable metabolic profile compared with olanzapine. The patient responded favourably, with complete remission of the psychotic symptoms. During this period, she also had another tonic-clonic seizure after stopping carbamazepine treatment on her own initiative, so we advised her to maintain carbamazepine 400 mg two times per day indefinitely. She has remained seizure-free since then. Currently, the patient remains on parenteral cyanocobalamin, 1 mg monthly.

## DISCUSSION

The combined presentation of progressive cognitive and functional deterioration, psychosis and seizures is uncommon in vitamin $B_{12}$ deficiency, with only one published case so-far, to the best of our knowledge.[2] The authors reported full remission of symptoms under vitamin replacement therapy, even after discontinuation of antipsychotic and antiepileptic drugs. In the present case, psychotic symptoms and seizures recurred after discontinuation of antipsychotics and antiepileptic medication, despite continuous cyanocobalamin replacement treatment. This may be due to the significant delay in diagnosis, as it has been suggested that cerebral neurons with destroyed myelin sheaths secondary to protracted vitamin $B_{12}$ deficiency are more susceptible to the excitotoxic effects of glutamate and thus more prone to suffer irreversible axonal damage associated with psychotic symptoms and epilepsy.[8] Notwithstanding this, cognitive and functional recovery was still possible after vitamin $B_{12}$ replacement began, showing that patients with prolonged vitamin $B_{12}$ deficiency can still partly recover from their neuropsychiatric deficits with adequate treatment, even in the presence of persistent neuropsychiatric sequels.

This case illustrates that psychosis, reversible dementia and seizures can be dissociated from the classic textbook haematological and neurological signs associated with vitamin $B_{12}$ deficiency. We suggest that vitamin $B_{12}$ deficiency should be considered in the differential diagnosis of patients presenting with atypical psychosis or seizures, especially when associated with cognitive decline. Since serum vitamin $B_{12}$ levels have been shown to have low sensitivity[9] and specificity,[10] we recommend that serum homocysteine should be determined in cases where cobalamin deficiency is a possibility but where the full-blown textbook manifestations are absent, and serum $B_{12}$ levels are normal or low normal. Clinicians should bear in mind that concomitant treatment with antiepileptic drugs and exposure of the blood sample to room temperature for more than 2 hours may give rise to false positives.[11] Finally, our case suggests that dementia associated with vitamin $B_{12}$ deficiency can still be reversed with vitamin replacement therapy, even after a prolonged deficit status.

### Learning points

- Vitamin $B_{12}$ deficiency is a common condition, typically associated with megaloblastic anaemia, glossitis and neurological and psychiatric symptoms.
- Psychiatric manifestations, cognitive decline and seizures can be dissociated from the typical neurological and haematological signs.
- Vitamin $B_{12}$ status should be routinely assessed in patients presenting with atypical psychosis or seizures.
- Vitamin replacement therapy can be useful even after a prolonged deficit status, especially in reversing cognitive decline. Some conditions, such as psychosis and epilepsy, may become irreversible.

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