

Cobalamin deficiency triggering *de novo* status epilepticus

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Received October 11, 2013; Accepted February 07, 2014

ABSTRACT – Cobalamin deficiency is included in the spectrum of very uncommon underlying causes of status epilepticus (SE) and the literature contains very few such cases. We herein report a case of unusual presentation of cobalamin (vitamin B12) deficiency with *de novo* SE with the intention to bolster the argument that a *de novo* manifestation of SE due to cobalamin deficiency might not be that uncommon. We also support the importance of prompt identification and treatment of the underlying causes of SE, particularly those which are uncommon.

Key words: epilepsy, status epilepticus, trigger, etiology, cause, cobalamin deficiency

Status epilepticus (SE) is typically characterised by acute onset of continuous convulsive or non-convulsive seizures for at least 30 minutes, or by 30 minutes of intermittent seizures without full recovery of consciousness between seizures (Tan *et al.*, 2010). SE is a neurological emergency with a high morbidity and mortality, and the underlying cause is ranked among the most critical determinants of its prognosis. Common causes of SE include cerebrovascular disorders, brain trauma or tumour, encephalitis, and decreased levels of antiepileptic drugs in patients with epilepsy (Trinka *et al.*, 2012).

However, SE can also be induced by a number of uncommon causes, *i.e.* causes with a frequency of less than 1% in the epidemiological literature (Tan *et al.*, 2010). We herein report a case of unusual presentation of cobalamin (vitamin B12) deficiency with *de novo* SE.

Case study

An 80-year-old, white Caucasian male presented to the emergency department of our hospital with an episode of generalised tonic-clonic seizures which occurred two hours earlier. At the time of initial referral, he was fully oriented and had no acute focal neurological deficit. However, while still being under investigation, he developed a typical generalised convulsive SE (GCSE). During the GCSE, he manifested with four recurrent seizures without regaining consciousness between seizures, within a time period of 30 minutes between first and last seizure. There was no evidence of focal elements. The duration of discrete episodes did not exceed two minutes.

The patient had no history of epilepsy, although his medical history was significant for hypertension which was treated with manidipine. Two weeks before this incident,

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he had also been diagnosed with cobalamin deficiency, with 140 pg/mL serum vitamin B12 (normal range: 220–950 pg/mL). Despite medical advice, he received no replacement therapy.

The patient eventually responded to acute benzodiazepines and infusion of antiepileptic drugs as follows. Acute iv diazepam at 20 mg was given, and 15 minutes later, another 10 mg of diazepam was infused. He was also loaded with phenytoin infusion at a dose of 15 mg/kg (50 mg/min), however, since seizures persisted, levetiracetam load at a dose of 50 mg/kg iv (100 mg/min) was also commenced. Moreover, cobalamin replacement therapy (1,000 µg im daily) was started.

Blood counts showed decreased haemoglobin (11.4 g/dL) and red blood cell count (3.4 million cells per µL). Platelets were also decreased (125 K/µL), mean corpuscular volume was at the highest point within the normal range (95 fL), and mean corpuscular haemoglobin concentration was normal (33 g/dL). A serum cobalamin assay performed before the initiation of replacement therapy revealed 163 pg/mL and folate was 5.0 (normal range: 4.6–18.7 ng/mL). Other biochemical tests were essentially normal.

Brain CT showed mild cerebral atrophy without any evidence of focal cerebral lesion. CSF analysis was not performed. Bifrontal synchronous spike-wave activity was seen on EEG that was performed 24 hours after the resolution of GCSE. The epileptiform activity disappeared on control EEG performed five days afterwards, and there were no additional findings on the control brain CT. Clinically, the patient fully recovered in the following 72 hours after the initiation of cobalamin replacement therapy, while the treatment with levetiracetam was stopped. At this time point (on recovery), neurological examination revealed suppressed ankle jerks and mild proprioception abnormalities, distally. There was no evidence of any other neurological deficit. Plantar reflexes were flexors. Two months after the initial manifestation of GCSE, he was seizure-free with normal serum cobalamin levels.

Discussion

It is well known that cobalamin deficiency commonly induces neuropsychiatric manifestations, including subacute combined degeneration of spinal cord, depression or psychosis, dementia, and ataxia (Lachner *et al.*, 2012). Cobalamin deficiency is included in the spectrum of relatively uncommon underlying causes of SE (Tan *et al.*, 2010). Available data on the pathogenic mechanism of epileptogenesis due to cobalamin deficiency are scarce. It has been previously shown *in vitro* that myelin synthesis of cortical neurons is dependent on normal methylcobalamin levels. Moreover, it has been demonstrated

that deficiency is able to evoke central demyelination, potentially leading to epileptogenesis due to increased susceptibility of cortical neurons to the cytotoxic effects of glutamate (Akaike *et al.*, 1993).

The literature contains two case reports of SE due to cobalamin deficiency, mostly presenting with seizures associated with psychotic phenomena or other CNS symptoms (Aguglia *et al.*, 1995; Kumar, 2004). Kumar *et al.* (2004) reported a case of vitamin B12 deficiency with multiple neuropsychiatric manifestations, such as dementia, psychosis, recurrent seizures, and myeloneuropathy, while Aguglia *et al.* (1995) reported a case that developed a partial complex epileptic confusional status (ECS), unresponsive to acute iv diazepam. To our knowledge, our case is the second reported case (to that of Aguglia *et al.* [1995]) to present *de novo* epileptic confusional status in a patient with cobalamin deficiency and no history of epilepsy.

With this report, we bolster the argument that a *de novo* manifestation of SE due to cobalamin deficiency might not be that uncommon. We suggest that our report is clinically significant because it highlights an uncommon cause of SE that may be increasing in frequency due to the overall aging of the world population and the resulting increasing frequency of cobalamin deficiency, which is much more common in the elderly. As such, the importance of prompt identification and treatment of the underlying causes of SE, particularly those which are uncommon, is supported by our case. On clinical grounds, it is advised to check cobalamin levels in all adults, particularly the elderly, who present with unexplained SE, and not only those with other neurological signs/symptoms that may suggest vitamin B12 deficiency. □

Disclosures.

None of the authors have any conflict of interest to disclose. The preparation of this report, including the decision to submit, was not supported by a funding source.

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