

## Case Report

## B12 Deficiency as a Cause of Neutropenic Sepsis

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## Abstract

A 34-year-old Afro-Caribbean lady with a history of epilepsy presents with increased frequency of seizures. She was found to be febrile and pancytopenic, with undetectably low B12 levels and was anti-parietal cell antibody positive. B12 deficiency is most commonly caused by pernicious anemia and this case highlights the relatively rare complication of bone marrow suppression and neutropenic sepsis.

**Keywords:** B12 deficiency; Pernicious anaemia; Neutropenic sepsis

## Introduction

Cobalamine (B12) deficiency is relatively common in the Western population, with rates of up to 20% in older people, [1] despite the fact it is readily available in an average diet. B12 deficiency can affect multiple body systems, leading to a range of clinical manifestations. This could make it difficult to diagnose in a patient presenting with unusual symptoms. If treated appropriately, the complications are fully reversible with B12 replacement; however, delay in treatment could lead to permanent deficits.

## Case Presentation

A 34-year-old Afro-Caribbean lady with a background of partial-seizure epilepsy presented with increased frequency and duration of seizures. She complained of recurrent seizures over the last few days, each episode lasting 30 seconds where she experienced clenching of her jaw and could not speak. She remained fully aware of her surroundings throughout the episodes and subsequently felt lethargic for 30 minutes. She usually gets a similar seizure every 6 months which lasts a maximum of 10 seconds, and is associated with an aura.

She takes 400mg lamotrigine BD for epilepsy, which she has taken since her early teenage years after she sustained a traumatic head injury from a fall. She was otherwise healthy and not taking any further medications, supplements or recreational drugs. There was no significant family history. She held an office-based job and had no concerns at work. Her last trip abroad had been to Jamaica over a year prior to presentation. She claimed to eat a balanced diet; however, she confessed she did not eat sufficient fruit or vegetables – occasionally a piece of fruit per day.

On examination, she looked well overall and had conjunctival pallor. Chest and abdominal examinations were normal and there was no neurological deficit. There were no palpable lymph nodes or organomegaly. A digital rectal examination was conducted due to her blood test results and no abnormality was found.

She had a temperature of 38.5 degrees Celsius and observations were otherwise within normal limits.

## Investigations

Blood tests showed pancytopenia with the following: haemoglobin -33 g/L, mean corpuscle volume (MCV) -112.4fL, white cell count (WCC) -3.01 x 10<sup>9</sup>/L, neutrophils -0.59 x 10<sup>9</sup>/L, platelet count

(PLT) -47 x 10<sup>9</sup>/L, international normalised ratio (INR) -1.09, C-reactive protein -27 x 10<sup>9</sup>/L, calcium -2.34 mmol/L, B12 <100 pg/mL, intrinsic factor anti-parietal antibodies >100 (normal range 0-5), anti-nuclear antibody (ANA) screen positive (titre 300; speckled pattern), immunoglobulin (Ig) G -16.12 g/L (normal range 7-16), IgA -1.20 g/L (normal range 0.7-4), IgM -0.26 g/L (normal range 0.4-2.3).

Folate, iron profile, electrolytes, liver function tests, anti-neutrophil cytoplasmic antibody (ANCA) screen and complement protein C3 and C4 were within normal limits except for a bilirubin of 24 micromol/L. Urine dipstick showed a trace of blood and protein only. A blood film revealed red cell anisopoikilocytes and true thrombocytopenia and no blast cells were seen. Blood cultures did not grow microorganisms. Chest X-ray showed a marginally globular heart with no consolidation or lung pathology.

## Differential diagnoses

The increased seizure frequency was attributed to neutropenic sepsis. Differential diagnoses for pancytopenia included malignancy, lamotrigine-induced dyscrasia and B12 deficiency.

This presentation was likely due to B12 deficiency – it was unlikely to be an adverse effect of medication because she had taken lamotrigine for over 20 years and as she was asymptomatic with no organomegaly/lymphadenopathy imaging for malignancy was not indicated.

## Management

She was given 2 units of packed red cells on admission and 1 mg B12 replacement intramuscularly on alternate days for 2 weeks. Neutropenic sepsis was treated with IV tazobactam/piperacillin, following local hospital microbiology guidelines, and she was transferred into a side room for isolation measures.

She remained stable and was discharged when she stopped spiking temperatures, with a final WCC of 6.15 and PLT of 297. Although she was asymptomatic throughout her admission, her blood tests initially became more deranged – PLT fell to 32 and WCC to 2.76. This was despite her B12 levels normalising after the first 2 doses of treatment, however, correction of hematology results has been reported to take up to 10 days [2].

## Discussion

B12 is a co-factor in DNA methylation, essential for cell

replication. An average diet which incorporates meat, fish and dairy, provides sufficient intake of B12 [2]. However, B12 deficiency remains relatively common, with a prevalence of up to 20% in the elderly Western population, and higher rates seen in Africa and Asia [1].

Absorption of B12 is dependent on intrinsic factor-mediated selection for uptake across the terminal ileum. Intrinsic factor is produced in gastric mucosa and levels can be reduced in pernicious anaemia, which is the leading cause of B12 deficiency [3].

There are multisystem complications of B12 deficiency: skin manifestations include glossitis and hyper pigmentation; neurological effects include sensory neuropathies, sub acute combined degeneration of the spinal cord and mood disturbances; and bone marrow suppression can result in a macrocytic anaemia, thrombocytopenia and neutropenia [2]. Deficiency is treated with parenteral hydroxocobalamin with complete resolution of symptoms and normalisation of blood tests if treated promptly.

In conclusion, this case of neutropenic sepsis emphasises the less common, yet severe hematological complications of B12 deficiency.

### Learning Points

- Consider B12 deficiency in patients presenting with haematological abnormalities.
- B12 deficiency can be associated with pancytopenia complicated with neutropenic sepsis.
- Correction of haematological parameters may take up to 10 days of treatment with B12 replacement.

### References

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