

# Clinical Reasoning: An Unusual Case of Acute Psychosis and Tetraparesis in a Young Zambian Man

Stanley Zimba, MBChB, MMED, STP, Lorraine Chishimba, MBChB, Mashina Chomba, MBChB, and Deanna Saylor, MD, MHS

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## Correspondence

Stanley Zimba  
stanpaulzimba@yahoo.co.uk

## Section 1

A 27-year-old Zambian man presented to the neurology clinic with a 1-month history of mental status changes and a 5-day history of visual and auditory hallucinations, paranoia, and difficulty walking. Notably, a month before presentation, he became increasingly withdrawn and was diagnosed with depression in a psychiatry clinic. His medical history was also significant for an anal fissure with hematochezia and severe anemia (hemoglobin 4 g/dL) 6 months prior. Examination revealed a thin patient responding to auditory and verbal hallucinations who accused the examiner of trying to harm him. He had a spastic tetraparesis with 2/5 power in all limbs, hyperreflexia with clonus, and a palpable bladder and was unable to walk. Sensory examination was unreliable because of the patient's mental state.

### Questions for Consideration:

1. What is the localization for his presentation?
2. What is the differential diagnosis for the etiology of his presentation?

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From the Department of Internal Medicine (S.Z., D.S.), University Teaching Hospital; Lusaka, Zambia; Department of Internal Medicine (L.C., M.C., D.S.), University of Zambia School of Medicine, Lusaka, Zambia; and Department of Neurology (D.S.), Johns Hopkins University School of Medicine, Baltimore, MD.

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## Section 2

The patient's presentation suggests 2 possible localizations. The altered mental status along with visual and auditory hallucinations suggests diffuse cortical involvement, whereas the spastic tetraparesis, hyperreflexia with clonus, a palpable bladder, and inability to walk suggest either bihemispheric lesions or a spinal cord lesion. It is unfortunate that a reliable sensory examination could not be obtained to localize within the spinal cord, both lengthwise and in cross-section. Although the sensory level could not be determined, the presence of upper extremity weakness indicates involvement of the corticospinal tract within or above the cervical

spinal cord. Potential differential diagnosis would include, but not limited to, infectious (e.g., neurosyphilis, disseminated tuberculosis, and HIV-associated infections), inflammatory (e.g., systemic lupus erythematosus, neurosarcoidosis, acute disseminated encephalomyelitis, and multiple sclerosis), toxic (e.g., nitrous oxide), and metabolic (e.g., vitamin B12, vitamin E, copper, and folate) etiologies.

### Questions for Consideration:

1. What information can help to narrow the differential diagnosis?
2. What are the appropriate diagnostic tests?

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## Section 3

Among the important investigations indicated in this case are infectious, autoimmune, and metabolic serologic tests. Testing for serum folate, methylmalonic acid, vitamin B1, vitamin B12, vitamin E, copper, heavy metals, and thyroid-stimulating hormone is also indicated. Determination of immune status, especially HIV status in the Zambian setting, is also essential for honing the differential diagnosis, and urine toxicology could also be useful to investigate potential toxic etiologies. MRIs of both the brain and spinal cord are also indicated, as are CSF studies, to evaluate for inflammatory and infectious etiologies.

However, because this case was occurring in a resource-limited setting, some investigations were inaccessible because of local unavailability or expense. As such, a stepwise diagnostic approach was taken in which available investigations expected to be the highest yield based on our patient's history were obtained first. Our patient was HIV uninfected, which made infections associated with immunosuppression such as CMV, disseminated VZV, and others, unlikely. He also had no history of any recent exposure to nitrous oxide through either procedural sedation or recreational use and was not a vegetarian and had not been on medication such as proton-pump inhibitors, which would put him at particular risk of vitamin B12 and/or other nutritional deficiencies. However, the additional history of anal fissure with anemia and concern for possible inflammatory bowel disease makes a multisystemic process a unifying diagnosis. Crohn disease, which can cause ulceration throughout the gastrointestinal tract including the terminal ileum, can result in malabsorption.<sup>1</sup>

Full blood count was obtained and showed anemia (hemoglobin 10 g/dL and mean corpuscular volume 106 fL), a rapid plasma reagin test for syphilis was negative, and the vitamin B12 level was <60 pg/mL (normal: 190–950 pg/mL). CSF studies showed no pleocytosis, normal protein and glucose, negative Gram stain, negative cryptococcal antigen, negative PCR for *Mycobacterium tuberculosis*, and negative bacterial and acid-fast bacilli cultures. 1.5 T MRI of the brain was normal. However, MRI of the cervical and thoracic spine was of limited utility, as it was obtained on a 0.23 T MRI and was severely degraded by motion artifact. However, expense prevented this study from being repeated and additional laboratory investigations from being obtained.

Based on these investigations, the diagnosis of vitamin B12 deficiency was made given the profoundly low vitamin B12 level and compatible clinical history and examination. The patient was commenced on supplementation with vitamin B12 1,000 micrograms IM daily for 1 week while in admission at our hospital followed by weekly injections for 4 weeks and monthly injections thereafter in our outpatient clinic. Mental status was markedly improved within a week and normal after 2 months. Upper limb strength also improved significantly within 2 months, but lower limb symptoms persisted. After 6 months, his strength had markedly improved, although he remained

nonambulatory because of spasticity. Unfortunately, although medications for spasticity are available in private pharmacies in Zambia, their cost prohibited their use in this patient. Inpatient rehabilitation facilities are largely unavailable in Zambia even for individuals with ample means to pay for them. Even outpatient physiotherapy sessions for this patient were limited to twice per week for less than a month because of cost and transportation limitations. Despite these circumstances, he was ambulatory without support within 1 year after his initial presentation. Unfortunately, workup for pernicious anemia and inflammatory bowel disease has yet to be completed because of the patient's financial limitations, so parenteral vitamin B12 supplementation is being continued indefinitely because no reversible cause of vitamin B12 deficiency was identified.

## Discussion

Vitamin B12 deficiency is often associated with neurologic disorders, of which subacute combined degeneration (SACD) is a common manifestation. SACD is characterized by degeneration of the posterior and lateral columns of the spinal cord and clinically presents with sensory symptoms, ataxia, and spastic paraparesis or tetraparesis.<sup>2,3</sup> MRI of the spine may show abnormal signal intensity in the dorsal column on T2-weighted images.<sup>3</sup> Although it usually presents as a subacute to chronic myelopathy, this case illustrates that more acute presentations of myelopathic symptoms are also possible.

Although an uncommon complication, vitamin B12 deficiency has been reported to cause acute psychosis. In fact, 1 of the first reports of neurologic symptoms due to vitamin B12 deficiency was that of acute psychosis, and it was initially coined as “megaloblastic madness.”<sup>4</sup> Acute psychosis from vitamin B12 deficiency can occur with or without other features of deficiency such as SACD.<sup>5</sup>

Neuropsychiatric manifestations of vitamin B12 deficiency usually present with chronic, nonspecific symptoms such as fatigue, apathy, irritability, cognitive slowing, and forgetfulness.<sup>5</sup> As a result, vitamin B12 deficiency is often part of the standard workup for dementia. However, as our case demonstrates, vitamin B12 deficiency should also be considered as the cause of a broad range of neuropsychiatric symptoms. Acute psychosis is an uncommon but reported complication of vitamin B12 deficiency. The earliest report was from multiple case series, which showed that neurologic and psychiatric symptoms preceded the onset of anemia and described a great variety of neuropsychiatric manifestations. In addition, they stressed the extreme variability of these symptoms, emphasizing that anything from a mild mood disorder to grossly psychotic behavior (megaloblastic madness) may be encountered.<sup>4</sup>

Treatment response of vitamin B12 deficiency seems to be dependent on the underlying etiology and related to the chronicity and severity of the disease, with those with shorter

symptom duration showing greater recovery. Our case also demonstrates this principle as, despite severe neuropsychiatric and myelopathic symptoms, our patient made nearly a complete recovery as he had symptoms for less than a month before vitamin B12 supplementation was begun.

This case also demonstrates an important aspect of practicing as a neurologist in a resource-limited setting. Although this workup may be considered “incomplete” in many settings, limited local availability of investigations in combination with an acute awareness that patients and their families are usually paying out of pocket for investigations is essential. Therefore, once a presumptive diagnosis can be made based on available results with a compatible clinical history and examination, treatment is often begun. The rapid improvement in the patient’s mental status and eventual near-complete resolution of symptoms with vitamin B12 supplementation supports the diagnosis of vitamin B12 deficiency even in the absence of a “complete” workup. Furthermore, this case highlights the postdischarge challenges for patients with neurologic disorders in our setting. Namely, virtually every patient is discharged directly home where those with functional impairments are entirely dependent on informal caregivers (usually family members) and have limited access to rehabilitation services that could speed their recoveries.

In summary, although SACD of the cord and macrocytic anemia are common presentations of vitamin B12 deficiency, physicians should be aware of acute psychosis as a rare but potentially reversible complication. This case also illustrates the importance of a prioritized differential diagnosis, stepwise approach to investigations, and initiation of empiric therapy in response to a reasonable diagnosis with subsequent monitoring of treatment response in all patients, but especially in resource-limited settings.

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### Appendix Authors

Name	Location	Contribution
<b>Stanley Zimba, MBChB, MMED, STP</b>	Department of Internal Medicine, University Teaching Hospital, Lusaka, Zambia	Drafting/revision of the manuscript for content, including medical writing for content; and study concept or design
<b>Lorraine Chishimba, MBChB</b>	Department of Internal Medicine, University of Zambia School of Medicine, Lusaka, Zambia	Study concept or design
<b>Mashina Chomba, MBChB</b>	Department of Internal Medicine, University of Zambia School of Medicine, Lusaka, Zambia	Study concept or design
<b>Deanna Saylor, MD, MHS</b>	Department of Internal Medicine, University Teaching Hospital, Lusaka, Zambia; Department of Internal Medicine, University of Zambia School of Medicine, Lusaka, Zambia; Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD	Drafting/revision of the manuscript for content, including medical writing for content; and analysis or interpretation of data

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