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

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Section 1

A 27-year-old Zambian man presented to the neurology clinic with a one-month history of mental status changes and five-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 Notably, a month before presentation, he became increasingly withdrawn and was diagnosed with depression in a psychiatry clinic.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 past medical history was also significant for an anal fissure with hematochezia and severe anemia (hemoglobin 4 g/dL) six 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, a palpable bladder, and was unable to walk. Sensory examination was unreliable due to the patient's mental state.

Questions for consideration

What is the localization for his presentation?

What is the differential diagnosis for the etiology of his presentation?

Section 2

The patient's presentation suggests two possible localizations. The altered mental status along with visual and auditory hallucinations suggest diffuse cortical involvement, while the spastic tetraparesis, hyperreflexia with clonus, a palpable bladder, and inability to walk suggest either bi-hemispheric lesions or a spinal cord lesion. It is unfortunate that a reliable sensory exam could not be obtained to localize within the spinal cord, both lengthwise and in cross-section. Although

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

What information can help to narrow the differential diagnosis?

What are the appropriate diagnostic tests?

Section 3

Among the important investigations indicated in this case are infectious, autoimmune and metabolic serological 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. Magnetic resonance images (MRI) of both the brain and spinal cord are also indicated as are cerebrospinal fluid (CSF) studies to evaluate for inflammatory and infectious etiologies.

However, because this case was occurring in a resource-limited setting, some investigations were inaccessible due to 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 multi-systemic process a unifying diagnosis. Crohn's disease, which can cause ulceration throughout the gastrointestinal tract including the terminal ileum, can result in malabsorption.¹

Full blood count was obtained and showed anemia (hemoglobin 10 g/dL, mean corpuscular volume 106 fL), a rapid plasma reagin test for syphilis was negative, and 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 0.23T 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 1000 micrograms intramuscularly daily for one week while in admission at our hospital followed by weekly injections for four weeks and monthly injections thereafter in our outpatient clinic. Mental status was markedly improved within a week and normal after two months. Upper limb strength also improved significantly within two months, but lower limb symptoms persisted. After six months, his strength had markedly improved, although he remained non-ambulatory due to spasticity. Unfortunately, while 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 due to cost and transportation limitations. Despite these circumstances, he was ambulatory without support within one year after his initial presentation. Unfortunately, workup for pernicious anemia and inflammatory bowel disease has yet to be completed due to the patient's financial limitations, so parenteral vitamin B12 supplementation is being continued indefinitely since no reversible cause of vitamin B12 deficiency was identified.

DISCUSSION

Vitamin B12 deficiency is often associated with neurological 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.^{2,3} MRI of the spine may show abnormal signal intensity in the dorsal column on T2-weighted images.³ While it usually presents as a subacute to chronic myelopathy, this case illustrates that more acute presentations of myelopathic symptoms are also possible.

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

Neuropsychiatric manifestations of vitamin B12 deficiency usually present with chronic, non-specific symptoms like fatigue, apathy, irritability, cognitive slowing and forgetfulness.⁵ 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 neurological 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.⁴

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. While 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 post-discharge challenges for patients with neurological 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, while 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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