



> THE PATIENT

21-year-old woman

> SIGNS & SYMPTOMS

- Anxiety tied to fear of falling
- Fatigue
- Difficulty concentrating

CASE REPORT

ONLINE EXCLUSIVE

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The authors reported no potential conflict of interest relevant to this article.

> THE CASE

A 21-year-old college student was referred to us by the counseling center at our university for a psychiatric evaluation after 11 psychotherapy sessions over 3 months had failed to reduce her feelings of anxiety and panic.

During our evaluation, the patient described feeling “not quite right” for many months. She had been experiencing mental fogging, fatigue, and worsening concentration/memory. Her anxiety, which had been gradually increasing, was the result of being unsure about her gait. She first noticed this while walking down some bleachers; she felt dizzy, was afraid of falling, and couldn’t walk down without assistance. All episodes of “panic” occurred in situations where she experienced disequilibrium, unsteady gait, and fear of falling. She grew fearful of driving or going anywhere without assistance.

The patient had celiac disease that was well controlled with a gluten-free diet. She had no personal or family psychiatric history and no history of substance abuse.

THE DIAGNOSIS

Physical exam and lab studies, including a complete blood count, comprehensive metabolic panel, and thyrotropin and folate levels, were normal. Her homocysteine level was 11.8 $\mu\text{mol/L}$ (reference range, 5.4-11.9 $\mu\text{mol/L}$) and vitamin B₁₂ level was 292 pg/mL (reference range, 200-1100 pg/mL). Her lab report included a note that read, “Although the reference range for vitamin B₁₂ is 200 to 1100 pg/mL, it has been reported that between 5% and 10% of patients with values between 200 and 400 pg/mL may experience neuropsychiatric and hematologic abnormalities due to occult B₁₂ deficiency; <1% of patients with values >400 pg/mL will have symptoms.”

Based on this vitamin B₁₂ level, the patient’s symptoms, and her borderline high homocysteine level, we diagnosed vitamin B₁₂ deficiency.

DISCUSSION

There are no recommendations by the US Preventive Services Task Force or any other major US medical society for routine vitamin B₁₂ screening.¹ In Canada, the Medical Services Commission of the British Columbia Ministry of Health recommends B₁₂ screening for patients who present with macrocytic anemia or unexplained neurologic symptoms (eg, paresthesia, numbness, poor motor coordination, memory lapses, or cognitive or personality changes).²

Vitamin B₁₂ deficiency can be caused by numerous conditions, including those that cause malabsorption (such as gastric bypass). It can also be caused by diseases such as human immunodeficiency virus infection or Crohn’s disease, long-term adherence to a vegetarian or vegan diet, or by any other lack of dietary intake.¹ The condition can cause hematologic-relat-

➤ **Some evidence suggests B₁₂ supplementation may improve symptoms of depression and anxiety.**

ed signs and symptoms such as megaloblastic anemia, fatigue, and syncope. It also can have neurologic manifestations, including paresthesia, weakness, motor disturbances (including gait abnormalities), vision loss, and a wide range of cognitive and behavioral changes.¹ Anemia is uncommon because since 1998, the US Food and Drug Administration has required fortification of all enriched grain and cereal products with folic acid; thus, vitamin B₁₂ deficiency may proceed without anemia revealing its presence.¹

■ **A controversial topic.** Vitamin B₁₂ deficiency is a complicated and controversial subject. Specifically, there is uncertainty about the clinical importance of lower serum levels of vitamin B₁₂ (200-400 pg/mL), their impact on well-being, and the need for treatment. In addition to measuring a patient's serum B₁₂ level, testing a second biomarker (such as homocysteine or methylmalonic acid) can be helpful in establishing a diagnosis of B₁₂ deficiency.¹ Levels of each of these are elevated in patients with B₁₂ deficiency.¹

Although vitamin B₁₂ deficiency has been well studied in older patients,³ little has been published about the condition in young adults. National Health and Nutrition Examination Survey (NHANES) data from 2000 to 2004 shows that almost 40% of people ages 19 to 30 years have a B₁₂ level <400 pg/mL.¹ How many of these individuals are at risk of complications of B₁₂ deficiency is unknown.

B₁₂ supplementation might improve depression, anxiety

B₁₂ supplementation is inexpensive and has no significant adverse effects.¹ It can be administered orally, parenterally (intramuscularly or subcutaneously), or intranasally.¹ A common oral regimen is 1 mg/d; parental regimens vary widely, but might include a 1-mg injection once a week for 8 weeks, then once a month for life.¹

Some evidence suggests B₁₂ supplementation may improve symptoms of depression and anxiety. A Pakistani study randomized 73 patients with depression and "low normal" B₁₂ levels (190-300 pg/mL) to an antidepressant only (equivalent to imipramine 100-

250 mg/d or fluoxetine 20-40 mg/d) or an antidepressant plus parenteral B₁₂ (1000 mcg once a week).⁴ At 3 months follow-up, 100% of the treatment group showed at least a 20% reduction in their Hamilton Depression Rating Scale (HAM-D) score, compared to 69% in the control arm (*P*<.001).⁴

A Swedish study analyzed the effects of several B vitamins, including 0.5 mg/d of B₁₂ vs placebo on mood in 65 celiac patients on a gluten-free diet who had borderline/low normal B₁₂ levels (>191 pg/mL).⁵ Patients who scored low on a measure of psychological well-being at the beginning of the study and who received B₁₂ experienced significant improvements in anxiety and depressed mood compared to those who received placebo.

Our patient

Because neurologic and psychiatric symptoms require assured compliance and urgent treatment, our patient received vitamin B₁₂ parenterally as cyanocobalamin 1 mg/mL. She was given this dosage intramuscularly once a day for 5 days, then once a week for 4 weeks. She will continue to receive it once a month indefinitely.

The patient was advised that if she wished to switch to oral therapy, she could do so after several months of parenteral treatment, as long as she had close follow-up with frequent B₁₂ measurements to assure that she was absorbing oral therapy. Her anxiety and mood symptoms resolved within one month, and her disequilibrium was almost entirely resolved within 3 months of treatment.

THE TAKEAWAY

Although more common in older patients, vitamin B₁₂ deficiency can also affect younger patients. "Low normal" B₁₂ levels (200-400 pg/mL) may affect psychological well-being.

Consider testing serum B₁₂ and a second biomarker—such as homocysteine or methylmalonic acid, if indicated—in patients who present with depressed mood, anxiety, cognitive symptoms, and/or fatigue. Vitamin B₁₂ supplementation can be administered orally and has no major adverse effects. **JFP**

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