It is illegal to post this copyrighted PDF on any website. Late-Onset Psychotic Symptoms Associated With Vitamin B₁₂ Deficiency in a Patient With Celiac Disease

Tomás Teodoro, MD, MSc^{a,b,c,d,*}

utritional psychiatry is an emerging field, ranging from dietary strategies to the study of gut microbiota and immune dysregulation and their impact on prevention and treatment of psychiatric disorders.^{1,2} Cobalamin (vitamin B_{12}) deficiency has been consistently associated with several neuropsychiatric symptoms including seizures, peripheral neuropathy, depression, dementia, and psychosis.^{3,4} Schizophrenia-like symptoms may present due to other conditions.^{5–8} Here, a case of chronic hallucinatory psychosis associated with cobalamin deficiency and celiac disease is presented.

Case Report

A 75-year-old woman was admitted to an acute inpatient unit after presenting with auditory hallucinations, persecutory delusions, thought broadcasting, and insomnia. She described several voices commenting on her actions and occasionally insulting her as well as thought echo. She attributed these voices to neighbors and started believing they were conspiring against her and accessing her thoughts. At presentation, timing of symptom onset was unclear but was estimated to have resulted in functional impairment at least 1 month before presentation. The physical and neurologic examination was unremarkable, and there was no recent history of sensory or motor abnormalities. Her Mini-Mental State Examination (MMSE)⁹ score was 30/30. Laboratory investigations detected mild anemia (hemoglobin: 11.6 mg/dL) and cobalamin deficiency (<125 pg/mL) but were unremarkable for other causes of psychosis (including brain computed tomography, infectious serologies, and thyroid function).

^aEarly Intervention and First Episode Psychosis Unit, Department of Psychiatry, Centro Hospitalar Psiquiátrico de Lisboa, Lisbon, Portugal ^bAdult ADHD and Neurodevelopmental Disorders Outpatient Service, Centro Hospitalar Psiquiátrico de Lisboa, Lisbon, Portugal

*Corresponding author: Tomás Teodoro, Department of Psychiatry, Centro Hospitalar Psiquiátrico de Lisboa, Avenida do Brasil 53, 1749-002 Lisbon, Portugal (tomasteodoro.md@gmail.com).

Prim Care Companion CNS Disord 2023;25(3):22cr03405

To cite: Teodoro T. Late-onset psychotic symptoms associated with vitamin B₁₂ deficiency in a patient with celiac disease. Prim Care Companion CNS Disord. 2023;25(3):22cr03405.

To share: https://doi.org/10.4088/PCC.22cr03405

© 2023 Physicians Postgraduate Press, Inc.

Clinical records revealed that she first developed psychotic symptoms at age 68 years, with 2 previous admissions since then and discharge diagnoses of delusional disorder and schizoaffective disorder (ICD-10). During her previous admissions, no mood symptoms were described, and the MMSE scores and neuropsychological assessment were within normal limits. Investigations did not include vitamin levels. Since her first admission, she was on monotherapy with risperidone 4 mg/d with partial remission but with periods of poor adherence. Until her first admission for psychosis, she had past psychiatric history of recurrent depressive disorder (ICD-10) with 2 previous mild-moderate depressive episodes but no admissions or psychotic symptoms. Data regarding past antidepressant pharmacologic treatment were unavailable. She had not undergone antipsychotic psychopharmacologic treatment until her first psychiatric admission to the best of our knowledge. Past general medical history included celiac disease diagnosed at age 50 years, and she had been on a gluten-free diet since then. There was no family history of psychiatric disorders.

During this admission, she was treated with a D₂ antagonist (olanzapine titrated to 15 mg/d) and intramuscular cyanocobalamin. After starting olanzapine and cobalamin replacement, she had a good clinical response with full remission of delusions in 5 days. Although auditory hallucinations persisted for another week, there was a marked decrease in volume and frequency of these phenomena, with the patient quickly developing insight. She was discharged with her psychotic symptoms in full remission and with good insight. She remained symptom free at several follow-up assessments with her community mental health team and maintained normal cobalamin levels as monitored by her primary care team.

Discussion

The patient's presentation is consistent with the historical syndromes of systematized paraphrenia and the French concept of chronic hallucinatory psychosis.^{10,11} In current classification systems (DSM-5 and ICD-11), these concepts have been incorporated in schizophrenia and the controversial category of schizoaffective disorder.¹² Secondary psychotic syndromes are part of the differential diagnosis of any condition presenting as schizophrenia-like psychosis.¹³ The definite diagnosis of secondary psychosis (organic psychoses) has always been problematic in part due to the challenges in establishing causality and the lack of pathognomonic symptoms.¹⁴ Several non-neurologic autoimmune and gastrointestinal conditions, in particular

^cPsychiatry Emergency Department, Hospital São José, Centro Hospitalar Universitário Lisboa Central, Lisbon, Portugal

^dCHRC—Comprehensive Health Research Centre, NOVA University Lisbon, Lisbon, Portugal

For reprints or permissions, contact permissions@psychiatrist.com. • © 2023 Copyright Physicians Postgraduate Press, Inc. Prim Care Companion CNS Disord 2023;25(3):22cr03405 PSYCHIATRIST.COM e1

Tomás Teodoro

It is illegal to post this copyrighted PDF on any websites celiac disease, have shown a positive association with in absence of or preceding hematologic abnormalities.

psychosis.^{15,16} Although the patient presented here adhered to the recommended dietary restrictions, it has been reported that deficiencies of cobalamin may persist with a gluten-free diet.^{17–19} Several vitamin deficiencies have been linked to psychosis.^{20–24} Cobalamin deficiency, albeit rarely, has also been associated with isolated psychotic symptoms either

Whether there is a direct causal relationship between nutritional deficits and psychosis, or these are epiphenomena with modulatory effects on their complex pathophysiology, clinicians need to be aware of their relevance and include a nutritional assessment as part of the diagnostic workup of new-onset psychotic symptoms at any age.

Published online: May 23, 2023.

Relevant financial relationships: None. Funding/support: None.

Patient consent: Consent was received from the patient to publish the case report, and information has been de-identified to protect anonymity. ORCID: Tomás Teodoro: https://orcid. org/0000-0002-4603-3946

REFERENCES

- 1. Firth J, Gangwisch JE, Borisini A, et al. Food and mood: how do diet and nutrition affect mental wellbeing? *BMJ*. 2020;369:m2382.
- Teasdale S, Mörkl S, Müller-Stierlin AS. Nutritional psychiatry in the treatment of psychotic disorders: current hypotheses and research challenges. *Brain Behav Immun Health*. 2020;5:100070.
- Green R, Miller JW. Vitamin B₁₂ deficiency. In: Vitamins and Hormones. Vol 119. Elsevier; 2022:405-439.
- Sahu P, Thippeswamy H, Chaturvedi SK. Neuropsychiatric manifestations in vitamin B₁₂ deficiency. In: *Vitamins and Hormones*. Vol. 119. Elsevier; 2022:457–470.
- Teodoro T, Oliveira R. Fahr's syndrome and neuropsychiatric symptoms: differential diagnosis in neuropsychiatry. *Acta Med Port*. 2019;32(7-8):558.
- Endres D, Matysik M, Feige B, et al. Diagnosing organic causes of schizophrenia spectrum disorders: findings from a one-year cohort of the Freiburg Diagnostic Protocol in Psychosis (FDPP). *Diagnostics (Basel)*. 2020;10(9):691.
- Endres D, Leypoldt F, Bechter K, et al. Autoimmune encephalitis as a differential diagnosis of schizophreniform psychosis: clinical symptomatology, pathophysiology, diagnostic approach, and therapeutic considerations. Eur Arch Psychiatry Clin Neurosci. 2020;270(7):803–818.

- Arora S, Jolly AJ, Suhas S, et al. Subacute sclerosing panencephalitis masquerading as schizophrenia: an example of diagnostic overshadowing in neuropsychiatry. *Prim Care Companion CNS Disord*. 2022;24(3):21cr02997.
- Folstein MF, Folstein SE, McHugh PR. "Minimental state": a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975;12(3):189–198.
- Chabrol H. Chronic hallucinatory psychosis, bouffée délirante, and the classification of psychosis in French psychiatry. *Curr Psychiatry Rep.* 2003;5(3):187–191.
- Ravindran AV, Yatham LN, Munro A. Paraphrenia redefined. *Can J Psychiatry*. 1999;44(2):133–137.
- Jäger M, Haack S, Becker T, et al. Schizoaffective disorder–an ongoing challenge for psychiatric nosology. *Eur Psychiatry*. 2011;26(3):159–165.
- Skikic M, Arriola JA. First episode psychosis medical workup: evidence-informed recommendations and introduction to a clinically guided approach. *Child Adolesc Psychiatr Clin N Am.* 2020;29(1):15–28.
- Keshavan MS, Kaneko Y. Secondary psychoses: an update. World Psychiatry. 2013;12(1):4–15.
- Cullen AE, Holmes S, Pollak TA, et al. Associations between non-neurological autoimmune disorders and psychosis: a metaanalysis. *Biol Psychiatry*. 2019;85(1):35–48.
- Colijn MA. The co-occurrence of gastrointestinal symptoms and psychosis: diagnostic considerations. *Prim Care Companion CNS Disord*. 2022;24(3):22nr03236.
- Vici G, Belli L, Biondi M, et al. Gluten free diet and nutrient deficiencies: a review. *Clin Nutr.* 2016;35(6):1236–1241.
- Theethira TG, Dennis M, Leffler DA. Nutritional consequences of celiac disease and the glutenfree diet. *Expert Rev Gastroenterol Hepatol*. 2014;8(2):123–129.
- 19. Caruso R, Pallone F, Stasi E, et al. Appropriate

nutrient supplementation in celiac disease. *Ann Med*. 2013;45(8):522–531.

- Gama Marques J. Pellagra with casal necklace causing secondary schizophrenia with Capgras syndrome in a homeless man. Prim Care Companion CNS Disord. 2022;24(2):21cr03014.
- Evans DL, Edelsohn GA, Golden RN. Organic psychosis without anemia or spinal cord symptoms in patients with vitamin B₁₂ deficiency. *Am J Psychiatry*. 1983:140(2):218–221.
- Silva B, Velosa A, Barahona-Corrêa JB. Reversible dementia, psychotic symptoms and epilepsy in a patient with vitamin B₁₂ deficiency. *BMJ Case Rep.* 2019;12(5):e229044.
- Kimoto K, Shibasaki B, Tamura N, et al. A case of vitamin B₁₂ deficiency with various psychiatric symptoms and cognitive impairment. *Prim Care Companion CNS Disord*. 2020;22(1):19102490.
- Prakash R, Aggarwal N, Jose N. A crosssectional study of serum folate and vitamin B₁₂ levels in psychiatric inpatients. *Prim Care Companion CNS Disord*. 2019;21(5):19m02464.
- Lindenbaum J, Healton EB, Savage DG, et al. Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis. *N Engl J Med.* 1988;318(26):1720–1728.
- Lachner C, Šteinle NI, Regenold WT. The neuropsychiatry of vitamin B₁₂ deficiency in elderly patients. *J Neuropsychiatry Clin Neurosci.* 2012;24(1):5–15.
- Nichols NA, Naqvi NF, Munjal S, et al. Cobalamin deficiency and acute-onset auditory and visual hallucinations in an elderly man. J Acad Consult Liaison Psychiatry. 2021;62(1):131–139.
- Slade TB, Bharadwaj RS. A case of acute behavioral disturbance associated with vitamin B(12) deficiency. *Prim Care Companion J Clin Psychiatry*. 2010;12(6):PCC.10100968.