



Case Report

Psychiatric Adverse Reaction to Triple Therapy for *Helicobacter Pylori*: A Case of Reversible Clarithromycin-Induced Psychosis

Anupam Dutta¹

¹Department of Medicine, Assam Medical College and Hospital, Dibrugarh, Assam, India.

*Corresponding author:

Anupam Dutta,
Associate Professor,
Department of Medicine,
Assam Medical College and
Hospital, Dibrugarh, Assam, India.
dranupamdutta80@gmail.com

Received: 01 September 2025

Accepted: 10 November 2025

Epub Ahead of Print:

25 March 2026

Published: ** ** ** **

DOI

10.25259/ABMH_41_2025

Quick Response Code:



ABSTRACT

Standard *Helicobacter pylori* (*H. pylori*) eradication regimens, commonly consisting of a proton pump inhibitor (PPI) combined with clarithromycin and amoxicillin, are widely regarded as safe and effective. However, clarithromycin has been rarely implicated in neuropsychiatric side effects, including acute psychosis. The onset of such adverse events can pose diagnostic dilemmas, particularly in patients without any pre-existing psychiatric history. We present a case of clarithromycin-associated transient psychosis in an otherwise healthy adult male, occurring shortly after initiation of triple therapy for *H. pylori*. A 35-year-old man presented with upper abdominal discomfort and was diagnosed with *H. pylori*-induced gastritis via upper gastrointestinal endoscopy and biopsy. He was started on standard triple therapy: clarithromycin 500 mg twice daily, amoxicillin 1 g twice daily, and pantoprazole 40 mg twice daily. Within 36 hours of starting treatment, he developed acute-onset behavioral disturbances, including paranoia, auditory hallucinations, disorganized speech, and psychomotor agitation. There was no history of psychiatric illness, substance abuse, or concurrent medication use. Laboratory evaluations, including metabolic panels, thyroid function, liver and renal parameters, were unremarkable. Computed tomography (CT) brain imaging was normal, and no signs of systemic infection were present. A provisional diagnosis of drug-induced psychosis was made. The eradication therapy was immediately discontinued, and the patient received supportive care with low-dose risperidone. Complete resolution of symptoms occurred within 48 hours of withdrawal, and the patient remained asymptomatic at 4-week follow-up. Clarithromycin is known to penetrate the blood-brain barrier and may exert neurotoxic effects through Gamma-Aminobutyric Acid (GABA) ergic modulation or proinflammatory cytokine release. Although rare, acute psychosis associated with clarithromycin has been reported in several case studies, typically with a rapid onset and full recovery following drug discontinuation. Awareness of this potential adverse effect is crucial to prevent misdiagnosis and unnecessary psychiatric treatment. Clinicians should maintain a high index of suspicion for antibiotic-induced neuropsychiatric events, especially with macrolides like clarithromycin. Early recognition and prompt withdrawal can lead to rapid recovery without long-term sequelae.

Keywords: Antibiotic-induced psychosis, Case report, *Clarithromycin*, *H. pylori*, Neuropsychiatric adverse effect, Psychosis

INTRODUCTION

Helicobacter pylori (*H. pylori*) infection remains a pervasive global health concern, implicated in chronic gastritis, peptic ulcer disease, and gastric malignancies. Standard eradication regimens typically include a proton pump inhibitor (PPI) combined with antibiotics such as clarithromycin and amoxicillin (or metronidazole) — a protocol referred to as “triple therapy”.^[1] Although this regimen is generally well tolerated, it has been associated, in rare instances, with neuropsychiatric adverse effects.

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, transform, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

©2026 Published by Scientific Scholar on behalf of Academic Bulletin of Mental Health

Clarithromycin, a macrolide antibiotic, is sometimes implicated in causing central nervous system side effects. These include dizziness, confusion, insomnia, irritability, and in very uncommon cases, severe neuropsychiatric syndromes such as psychosis or mania (often described in the literature under the term “antibiomania”).^[2] The pathophysiology remains unclear, but the drug’s ability to cross the blood-brain barrier and modulate neurotransmitter systems (e.g., GABA-A receptors) has been hypothesized as a possible mechanism.^[2]

Case-based evidence has demonstrated that clarithromycin can provoke acute psychotic reactions even in otherwise healthy individuals. For instance, a 49-year-old woman developed an abrupt onset of hallucinations, delusions, and disorganized behavior 24 hours after commencing clarithromycin as part of triple therapy, with full recovery occurring within days of discontinuation.^[3] Similarly, additional reports have confirmed psychosis and manic symptoms in younger healthy adults following clarithromycin administration, usually resolving rapidly once the antibiotic was stopped.^[4,5]

Beyond individual case reports, population-level data have also highlighted a short-term elevation in risk for neuropsychiatric events associated with *H. pylori* eradication therapy containing clarithromycin. In a self-controlled case series study involving over 66,000 patients, the incidence of acute neuropsychiatric symptoms, including psychosis and cognitive impairment, was observed to be approximately four times higher during the initial two weeks of clarithromycin-based therapy, compared to baseline periods; risk returned to baseline after the treatment period ended.^[6] The absolute risk remained low (~0.12 events per 1,000 courses), but the temporal clustering strongly supports a causal association.^[6]

Although other components of triple therapy (such as amoxicillin or PPIs) have occasionally been considered, the evidence overwhelmingly implicates clarithromycin as the most likely agent responsible for such reactions.^[6] Clinicians must therefore recognize that, while rare, these neuropsychiatric complications can affect patients without any prior psychiatric history, usually presenting within days of initiation and resolving quickly upon cessation.

Awareness of this potential adverse effect is critical to avoid misdiagnosis, unnecessary psychiatric hospitalization, and inappropriate long-term treatment. Prompt identification and withdrawal of the offending agent often leads to complete recovery within one to three days.^[3,4,6] Here, we describe a case of a 35-year-old man who developed acute psychosis shortly after starting *H. pylori* triple therapy and achieved full resolution following therapy cessation—a presentation that closely mirrors previously published cases yet remains underrecognized.

CASE REPORT

A 35-year-old Indian male, with no prior medical, psychiatric, or substance use history, presented to the outpatient department with complaints of upper abdominal discomfort, early satiety, and intermittent epigastric pain for three weeks. His physical examination was unremarkable, and there were no signs of systemic illness. Vital signs were within normal limits.

Routine hematological and biochemical investigations, including complete blood count, liver and renal function tests, fasting blood glucose, thyroid-stimulating hormone serum electrolytes, and urine analysis, were all within normal limits. Viral serologies (Hepatitis B virus, Hepatitis C virus and Human Immunodeficiency Virus) were negative. Abdominal ultrasonography was normal.

An upper gastrointestinal endoscopy revealed mild antral erythema and gastric mucosal congestion. A rapid urease test and histopathological examination of antral biopsy confirmed active *H. pylori* infection. The patient was initiated on standard first-line *H. pylori* triple therapy comprising: clarithromycin 500 mg twice daily, amoxicillin 1 g twice daily, and pantoprazole 40 mg twice daily.

Approximately 36 hours after initiating therapy, the patient developed acute behavioral changes characterized by agitation, paranoia, insomnia, and auditory hallucinations. He exhibited incoherent speech, persecutory delusions, and inappropriate laughter. There were no accompanying fever, headache, seizures, or focal neurological deficits. The family denied any history of substance use or recent stressors. There was no previous or family history of psychiatric disorders.

On presentation to the emergency department, the patient was alert but severely disoriented and responding to internal stimuli. The glasgow coma scale was 15/15. Neurological examination was non-focal. Laboratory investigations—including serum ammonia, blood glucose, renal panel, electrolytes, and arterial blood gas—were normal. Electrocardiogram and non-contrast computed tomography brain showed no abnormalities. A urine toxicology screen was negative. Cerebrospinal fluid analysis was not performed due to the absence of meningeal signs and stable vitals.

Given the temporal correlation, a diagnosis of clarithromycin-induced acute psychosis was considered. The triple therapy was discontinued immediately. The patient was managed supportively with a low-dose atypical antipsychotic (risperidone 1 mg twice daily), intravenous hydration, and observation in a monitored inpatient setting. Over the next 48 hours, his psychotic symptoms resolved completely, and

risperidone was gradually tapered off.

At four-week follow-up, the patient remained asymptomatic with no recurrence of psychiatric symptoms. He was advised alternative *H. pylori* eradication with a probiotic capsule containing *Lactobacillus reuteri* DSMZ 17648 (Pylopass TM) 100 mg (equivalent to NLT 10 Billion *Lactobacillus reuteri* cells) for 28 days. On follow-up endoscopy after four weeks, there was *H. pylori* eradication, documented by upper gastrointestinal endoscopy.

DISCUSSION

This case illustrates an acute psychotic reaction temporally linked to *H. pylori* triple therapy—most likely mediated by clarithromycin. Although rare, increasing literature demonstrates that macrolide antibiotics, particularly clarithromycin, may trigger neuropsychiatric syndromes in susceptible individuals.^[3]

A comprehensive literature review identified 38 adult cases of clarithromycin-induced neurotoxicity, with ages ranging from 19 to 87 years (mean ~51 years), and a slight female dominance (52.6%).^[7] The most frequent presentations included delirium, acute psychosis, mania, seizures, and non-convulsive status epilepticus, with onset typically within 1–10 days (mean ~5 days) after initiating therapy.^[7] In line with these data, our patient developed pronounced psychotic features within approximately 36 hours of starting clarithromycin-based therapy.

The pathophysiology underlying clarithromycin-associated neuropsychiatric effects remains under investigation, but several plausible mechanisms have emerged. Clarithromycin and its active metabolite 14-hydroxyclearithromycin can cross the blood-brain barrier, antagonizing GABA_A receptors and potentially lowering seizure threshold, while also modulating glutamatergic neurotransmission.^[8] Inhibition of cytochrome P450 3A4 may elevate endogenous cortisol and prostaglandins.^[3] Additionally, macrolides may induce oxidative stress and endoplasmic reticulum dysfunction, impairing neuronal homeostasis.^[9] These neurotoxic effects appear independent of dose severity, having occurred at both low and moderate doses.^[10]

Although many reported individuals had no renal or hepatic comorbidities, chronic kidney disease may impair the metabolism and clearance of clarithromycin, increasing neurotoxicity risk.^[8] Concomitant use of CYP3A4-inhibiting agents (e.g., fluoxetine, antifungals, calcium channel blockers) may likewise lead to elevated drug concentrations.^[7] In our patient, no co-medication or metabolic derangement was evident, highlighting that such reactions can occur in otherwise healthy individuals.

The abrupt onset of psychiatric symptoms necessitates a broad differential, including primary psychotic disorders, metabolic encephalopathy, central nervous system (CNS) infection, toxic/metabolic derangements, or structural lesions. In the present case, neuroimaging (non-contrast CT brain), metabolic panels (electrolytes, glucose, ammonia), toxic screens, and vital signs were unremarkable, effectively excluding central nervous system pathology or systemic causes. This pattern mirrors previously published cases in which discontinuation of clarithromycin led to rapid resolution, strongly supporting a drug-induced etiology.^[3]

Although Electroencephalogram (EEG) was infrequently reported in earlier series—performed in only four of 38 cases—it may be especially informative in suspected seizure-related presentations or non-convulsive status epilepticus.^[7] However, in our patient, the absence of clinical seizures and rapid recovery following drug withdrawal rendered an EEG unnecessary. If prolonged or atypical symptoms occur, an EEG should be considered.

A key prognostic feature of clarithromycin-induced neurotoxicity is reversibility upon cessation. In the review cohort, neuropsychiatric symptoms resolved in nearly all patients after discontinuing the antibiotic, often within 1–3 days. Approximately 58% required short term neuroleptic or benzodiazepine therapy.^[7] Our patient's symptoms subsided within 48 hours of stopping the regimen and initiating low-dose risperidone. No recurrence was noted on follow-up at one and four weeks.

Klain *et al.* described a 49-year-old female who developed acute psychosis within 24 hours of clarithromycin initiation as part of triple therapy; dramatic remission occurred within two days of drug cessation, mirroring our timeline.^[3] A younger adult case (19 F) following IV clarithromycin for tonsillitis required longer hospitalisation and antipsychotic therapy, though eventual recovery was complete.^[6] A more complex scenario of 'antibiomania' mimicking limbic encephalitis occurred in a 64-year-old woman who experienced psychosis and seizures after *H. pylori* eradication; recurrent episodes only resolved following permanent cessation of clarithromycin.^[2]

This case and supporting literature alert clinicians to the potential for clarithromycin to precipitate acute neuropsychiatric reactions even in patients without prior psychiatric pathology. Awareness is crucial to avoid misdiagnosis of primary psychiatric disorder and consequent inappropriate long-term psychotropic treatment. In particular, psychiatrists and gastroenterologists prescribing triple therapy should counsel patients regarding rare neuropsychiatric side effects, monitor early cognitive or behavioral changes, and evaluate adjunctive risk factors (e.g.,

renal impairment, drug interactions).

Given the infrequency of reported cases, the true incidence of clarithromycin-induced psychosis remains uncertain and likely under-recognized. Prospective pharmacovigilance or registry-based studies could better quantify incidence rates, elucidate pharmacogenomic susceptibility, and evaluate dose-response relationships. Rigorous mechanistic studies, including EEG, neurochemistry, and imaging, may further clarify central nervous system pathways affected by clarithromycin and its metabolites.

CONCLUSION

In summary, clarithromycin associated acute psychosis is a rare but real adverse effect. Temporal correlation, symptom resolution on drug withdrawal, and supportive previous case reports reinforce a likely causal relationship. Our patient's presentation, onset within two days, rapid improvement, and absence of other causative factors, matches previous descriptions and underlines the need for vigilance when prescribing clarithromycin-based regimens.

Authors' contributions: AD: Collected data and prepared the manuscript.

Ethical approval: Institutional Review Board approval is not required.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given consent for clinical information to be reported in the journal. The patient understands that the patient's names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship: Nil

Conflict of interest: There are no conflict of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation: The author confirms that they have used ChatGPT for

editing the manuscript.

REFERENCES

1. Hu Y, Zhu Y, Lu NH. Novel and effective therapeutic regimens for *Helicobacter pylori* in an era of increasing antibiotic resistance. *Front Cell Infect Microbiol.* 2017;7:168.
2. Trzebiatowska I, Barwina M, Waldman W, Sein Anand J. Psychosis caused by the treatment with clarithromycin: a case report. *Przegl Lek.* 2011;68:560–1.
3. Klain V, Timmerman L. Comment on the dangers of gastritis: a case of clarithromycin-associated brief psychotic episode. *J Nerv Ment Dis.* 2015;203:481.
4. Kouvelou E, Pourzitaki C, Aroni F, Papazisis G, Kouvelas D. Acute psychosis induced by clarithromycin in a healthy adult? *J Clin Psychopharmacol.* 2008;28:579–580.
5. Abba-Aji A, Mulligan O. Psychosis? Beware – case series of clarithromycin and psychosis. *Ir J Psychol Med.* 2007;24:79–80.
6. Wong AY, Wong IC, Chui CS, Lee EH, Chang WC, Chen EY, *et al.* Association between acute neuropsychiatric events and *Helicobacter pylori* therapy containing clarithromycin. *JAMA Intern Med.* 2016;176:828–34.
7. Kogan Y, Elias N, Paz A, Odeh M. Acute delirium associated with levofloxacin. *J Clin Med Res.* 2018;10:725–7.
8. Nightingale SD, Koster FT, Mertz GJ, Loss SD. Clarithromycin-induced mania in two patients with AIDS. *Clin Infect Dis.* 1995;20:1563–1564.
9. Meszaros EP, Stancu C, Costanza A, Besson M, Sarasin F, Bondolfi G, *et al.* Antibiomania: a case report of clarithromycin and amoxicillin-clavulanic acid induced manic episodes separately. *BMC Psychiatry.* 2021;21:399.
10. Bandettini di Poggio M, Anfosso S, Audenino D, Primavera A. Clarithromycin-induced neurotoxicity in adults. *J Clin Neurosci.* 2011;18:313–8.

How to cite this article: Dutta A. Psychiatric Adverse Reaction to Triple Therapy for *Helicobacter Pylori*: A Case of Reversible Clarithromycin-Induced Psychosis. doi: 10.25259/ABMH_41_2025