

## Antibiomania: A Case Report of Amoxicillin Clarithromycin and Metronidazole Induced Manic Episode

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## Abstract

## Case Report

**Introduction:** Antibiomania is characterized by the onset of a manic episode in response to antibiotic use. Although relatively rare, this type of adverse effect is increasingly documented and primarily occurs in patients without a history of bipolar disorder. Several dozen cases have been reported in the literature, showing the emergence of manic symptoms following antibiotic administration, notably clarithromycin, which is one of the most frequently involved antibiotics.

**Clinical Case:** We report the case of a 56-year-old patient who experienced a manic episode after receiving triple antibiotic therapy to eradicate *Helicobacter pylori* in the context of a gastroduodenal ulcer. Two days after starting treatment, behavioural disturbances appeared, characterized by irritability, aggressiveness, logorrhoea, insomnia, and a mystical delirium. Upon hospitalization, the patient exhibited acute delirious symptoms congruent with manic mood, such as grandiosity and psychomotor agitation. Brain magnetic resonance imaging (MRI) was normal. Antibiotic treatment was immediately discontinued, and treatment with sodium valproate (1,5g/day) and olanzapine (10 mg/day) was initiated. A rapid clinical improvement was observed, with the resolution of delusional ideas within a week. The patient returned to a euthymic state, and his treatment was maintained for preventive purposes.

**Discussion:** This clinical case raises several questions: Are there predictors of Antibiomania? Is there a risk of recurrence of mood episodes after an episode of Antibiomania? What are the pathophysiological mechanisms that would explain this reaction? In all identified cases, discontinuation of antibiotics has been a determining factor. However, the introduction of psychotropic treatment and its duration remain uncertain. First, longitudinal follow-up would allow for the evaluation of this variable. Second, the presence of personal psychiatric history is not clearly established as a predictor of Antibiomania. Finally, several hypotheses can be proposed to explain this phenomenon: competitive inhibition of GABAergic receptors, epileptic phenomena mimicking psychiatric symptoms, or disruption of the intestinal microbiota by antibiotics, indirectly affecting the central nervous system's functioning. The explanatory model of Antibiomania remains unknown and requires further research.

**Keywords:** Mania, clinical case, amoxicillin, clarithromycin, metronidazole, antibiotics, adverse effects.

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### INTRODUCTION

Antibiomania is characterized by the onset of a manic episode in response to antibiotic use. The term "Antibiomania" was introduced by Abouesh *et al.*, in 2002 [1]. Although relatively rare, this type of side effect is observed in an increasing number of cases and primarily occurs in patients without a history of bipolar disorder. Several dozen cases have been reported, showing the emergence of manic symptoms following antibiotic use. Recent studies suggest that clarithromycin is one of the antibiotics most frequently implicated in these manic episodes [2]. Several hypotheses regarding the underlying mechanism, including pharmacokinetic interactions and interactions with neurotransmitters of the central nervous system (CNS), have been proposed.

We will present the case of a patient who developed a manic syndrome following the administration of triple antibiotic therapy in the treatment of a gastroduodenal ulcer caused by *Helicobacter pylori*. We will then put forward explanatory hypotheses for this phenomenon.

### CASE PRESENTATION

Mr. D is a 56-year-old patient hospitalized for a manic episode with psychotic symptoms congruent to his mood. Clinical investigation during hospitalization suggested the responsibility of antibiotic therapy as a triggering factor. In April 2024, Mr. D received treatment with triple therapy against *H. pylori*, prescribed by his gastroenterologist for a gastroduodenal ulcer. This treatment included amoxicillin (2g/day),

clarithromycin (1g/day), and metronidazole (1,500 g/day). Two days after the antibiotic prescription, family members noted a progressive change in his behaviour, characterized by unusual logorrhoea, irritability, increased physical activity, an elevated mood, excessive charity, and insomnia.

During our first psychiatric evaluation, the patient reported that during the night following the introduction of antibiotics, he felt a sense of imminent death and expressed multiple plans, along with grandiose and mystical delusional statements, claiming that God had removed his heart, purified him of his sins, then replaced it, and that he had been chosen for a special mission so that people could practice their religion correctly. The psychiatric examination revealed a familiar attitude, increased psychomotor activity, irritability, logorrhoea, an elevated mood, difficulty sleeping, and mystical-religious delusions congruent with his mood. The Young Mania Rating Scale (YMRS) score at the time of evaluation was 32, indicating a manic episode.

Investigations were conducted, including blood tests (biochemistry, blood count, coagulation, syphilis serology, HBV, and HCV), as well as a brain MRI (performed to rule out a neurological cause due to the late onset of symptoms) and an electroencephalogram. None of the results revealed abnormalities. Given the normal results of the complementary tests, the patient's age, the absence of a history of mood disorders, and the close temporal relationship between the administration of clarithromycin and amoxicillin and the symptomatology, in addition to the rapid improvement after cessation of treatment, the case was recognized as an antibiotic-induced manic episode, a diagnosis of exclusion. Antibiotic treatment was immediately discontinued, and olanzapine (10 mg/day), combined with sodium valproate (2 g/day) and a tapering benzodiazepine, was introduced to treat the psychomotor agitation.

Since the patient was 56 years old, had no psychiatric history, and given the close temporal relationship between clarithromycin use and the manic episode, along with rapid improvement after discontinuation of clarithromycin, the diagnosis of a manic episode in the context of a substance-induced bipolar disorder (antibiotic therapy: amoxicillin, metronidazole, clarithromycin) was retained as a diagnosis of exclusion. One week after discharge, during the follow-up psychiatric evaluation, the patient reported a subjective impression of slight elevation of mood and loquacity, with a YMRS score of 3, equivalent to a euthymic state.

## DISCUSSION

Antibiomania, defined as the emergence of manic episodes following antibiotic treatment, has garnered increasing interest in the field of psychiatry.

Although rare, this condition highlights the importance of interactions between pharmacotherapy and psychiatric symptoms, particularly in patients without a history of mood disorders. Macrolides, such as clarithromycin, as well as quinolones and certain antituberculosis antibiotics, are often implicated in these manic manifestations, thus demonstrating the need for heightened vigilance among healthcare professionals when prescribing these medications [3].

In a review of reports, it was observed that 27.6% of cases of Antibiomania were attributed to clarithromycin, with an average patient age of 40 years, two-thirds of whom were male [1, 4]. The average duration of symptoms induced by clarithromycin was three days, an observation corroborated by previous studies [1]. Mr. D's case clearly illustrates this phenomenon, with the rapid onset of psychiatric symptoms following antibiotic administration and a swift resolution after the cessation of the suspected treatments.

The relationship between antibiotics and psychiatric disorders may be complicated by the underlying infection. For example, *Helicobacter pylori* infection, responsible for most gastric ulcers, is often treated with antibiotics that have psychiatric side effects [5].

From a pathophysiological standpoint, several mechanisms have been proposed to explain Antibiomania. One of the main mechanisms is related to a high plasma concentration of the antibiotic, due either to high dosing or drug interactions affecting the metabolism of macrolides via cytochrome P450. This could lead to increased diffusion of the antibiotic across the blood-brain barrier, with competitive inhibitory effects on GABAergic receptors, thus explaining the manic symptoms [1, 6]. Moreover, recent studies have highlighted links between the intestinal microbiota and psychiatric pathologies, suggesting that antibiotic-induced modifications of the microbiota could affect neurochemical signalling and contribute to the emergence of psychiatric symptoms [7-10].

The management of episodes of Antibiomania primarily relies on the discontinuation of the responsible antibiotics and, in some cases, the administration of psychotropic treatments such as neuroleptics or benzodiazepines. Medication strategies vary, but symptomatic treatment has been reported in 58% of cases, indicating a proactive approach to managing acute symptoms [6]. However, the current literature does not provide sufficient information on the long-term evolution of patients who have experienced episodes of Antibiomania.

## CONCLUSION

The diagnostic challenges posed by drug-induced manic episodes necessitate particular attention

during the assessment of psychiatric symptoms in patients receiving antibiotics. This is especially relevant in emergency services, where rapid management is crucial. Future research should delve deeper into the underlying mechanisms of Antibiomania.

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