

# The First Case of Ceftazidime-Induced Antibiomania: A Case Report and Literature Review

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## Abstract

Antibiomania is a rare type of secondary mania caused by antibiotics. Here, we describe the first case report of antibiomania in a peritoneal dialysis patient caused by ceftazidime, a cephalosporin antibiotic. Manic symptoms were noted in the patient described here a few days after starting the antibiotic and worsened over the course of a few weeks of antibiotic treatment. There is a close temporal relationship between the start of antibiotics and the onset of manic symptoms in this case. Antibiotics from various groups have been implicated as the causative agents in a few case reports of antibiomania. Several hypotheses have been postulated regarding the underlying mechanism of antibiomania. The authors of this article highlight the importance of recognizing the psychiatric side effects of antibiotics early and formulating effective management options to prevent detrimental effects on a patient's clinical condition.

**Categories:** Neurology, Infectious Disease, Nephrology

**Keywords:** antibiotic induced psychosis, quinolone induced mania, macrolide induced mania, cephalosporin induced mania, clarithromycin induced mania, mania psychosis peritoneal dialysis, antibiotic psychosis, antibiotic induced mania, ceftazidime toxicity, antibiomania

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## Introduction

Antibiomania is a term first introduced in 2002 [1]. It is a type of secondary mania induced by antibiotics and a relatively rare condition given the widespread use of antibiotics and the few reported cases. Mania can occur with different somatic conditions or the use of medications in patients with or without a history of affective disorder. In the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), these cases are best classified as "substance/medication-induced bipolar and related disorders." The worldwide use of antibiotics has increased by 36% between 2000 and 2010, with broad-spectrum penicillin being the most used antibiotic in 2010, followed by cephalosporins, macrolides, and quinolones. To date, macrolides (such as clarithromycin), quinolones (such as ciprofloxacin and ofloxacin), and antitubercular drugs are the most common causative agents of antibiomania reported [2]. A few cases are associated with several other antibiotics.

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## Case Presentation

A 55-year-old male with a past medical history of end-stage kidney disease (ESKD) due to diabetes and hypertension on peritoneal dialysis (PD) and a history of stable depression without medications for over a year with no other psychiatric illness presented to the PD clinic with abdominal pain, and the workup revealed PD-related peritonitis (Table 1). He was started on intraperitoneal (IP) ceftazidime for gram-negative rods as culture showed Capnocytophaga, and his peritonitis improved with a reduction in white blood cell count. On day 12 of treatment, changes in his behavior were noted, including agitation, anxiety, and tearfulness. Psychiatry was consulted and recommended starting sertraline for depression. The patient was sent home to finish the three weeks of ceftazidime.

### How to cite this article

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|-----------------------|-----------------|-------------------|-------------------|--------------------|--------------------|
| Color                 | Yellow          | Light yellow      | Light yellow      | Colorless          | Light yellow       |
| Appearance            | Clear           | Cloudy            | Clear             | Clear              | Cloudy             |
| Nucleated cells       | < 300/micL      | 2694              | 630               | 214                | 7251               |
| Red blood cells       | < 2000/micL     | < 2000            | < 2000            | < 2000             | < 2000             |
| Neutrophils           | < 25%           | 78                | 52                | 49                 | 95                 |
| Lymphocytes           | 20 – 80%        | 3                 | 4                 | 14                 | 1                  |
| Monocytes/Macrophages | 20 – 80%        | 15                | 43                | 35                 | 3                  |
| Eosinophils           | < 25%           | 1                 | 1                 | 1                  | 1                  |
| Mesothelial cells     | 20 – 80%        | 3                 | 1                 | 1                  | 1                  |
| Culture sensitivity   | No growth       | Capnocytophaga    | No growth         | E. cloacae complex | E. cloacae complex |

**TABLE 1: Peritoneal fluid analysis during the first and second peritonitis episodes**

He was readmitted four weeks later due to disruptive behavior with delusions, agitation, elevated mood, reduced sleeping hours, and increased energy. Psychiatry diagnosed him with mania due to ceftazidime and started him on divalproex sodium. PD fluid showed a recurrence of peritonitis with 7251 WBCs, 95% neutrophils, and *Enterobacter cloacae* on culture. He was treated with cefepime, but due to abdominal pain and increasing WBC, the PD catheter was removed. He transitioned to hemodialysis and completed two weeks of IV cefepime. His mental status was monitored while on divalproex sodium. After a year of therapy with antipsychotics, his mood remained stable, and he has switched back to PD.

## Discussion

The patient presented here had developed symptoms of mania after the administration of the antibiotic IP ceftazidime for PD-related peritonitis. Peritonitis is a common complication in peritoneal dialysis patients that is associated with significant morbidity [3]. His symptoms are characterized by disruptive behavior with delusions, irritability, and agitation. In antibiomania, a close temporal relationship is usually present between the initiation of the antibiotic and the onset of manic symptoms, as witnessed in this case. The underlying psychiatric condition may or may not always be present. Remission of manic symptoms with discontinuation of the causative agent has only been reported in one-third of cases; hence, treatment with antipsychotics may be required.

Several hypotheses have been postulated regarding the underlying mechanism of antibiomania [1]. Gamma-aminobutyric acid (GABA) neurotransmission is inhibited by antagonizing its receptor, which is involved in the manifestation of CNS toxicity with beta-lactam antibiotics such as ceftazidime [4]. GABA neurotransmission, the predominant inhibitory neurotransmitter in the CNS, acts to reduce neuronal excitability [5]. Among penicillins, piperacillin and tazobactam appear to be most associated with neurotoxic events, with several reported cases. Hoigne's syndrome is an acute psychotic, toxic, nonallergic reaction most commonly associated with procaine penicillin [6]. Patients with advanced renal failure are particularly at increased risk. Quinolones can cross the blood-brain barrier (BBB) [7] and competitively inhibit the binding of GABA to their receptor sites [8].

Isoniazid, an antitubercular drug, also crosses the BBB and decreases GABA concentration by inhibiting glutamic acid decarboxylase (GAD), an enzyme that catalyzes the decarboxylation of glutamate to GABA and CO<sub>2</sub> [9]. Clarithromycin, a macrolide antibiotic, antagonizes postsynaptic GABA-A receptors in neurons and increases neuron excitability [10-14]. Several case reports of secondary mania induced by clarithromycin have been published in the past [15-17].

## Conclusions

As far as we are aware, this is the first case report of antibiomania in a peritoneal dialysis patient caused by the antibiotic ceftazidime. This case report highlights the importance of recognizing the psychiatric side effects of antibiotics early and formulating effective management options to prevent detrimental effects on a patient's clinical condition. Antibiomania should be strongly considered as a differential diagnosis in patients presenting with manic symptoms after the initiation of ceftazidime.

## Additional Information

### Disclosures

**Human subjects:** Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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Dr. Wadhwa contributed equally to the work and should be considered co-first author.

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