

# A 62-Year-Old Woman with New-Onset Mania

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A 62-year-old woman with a medical history significant for end-stage renal disease (ESRD) on hemodialysis, retinitis pigmentosa with legal blindness, type 2 diabetes, and no known past psychiatric illness was admitted to the medical service for altered mental status of a few days in duration.

One week prior to this emergency department presentation, the patient was admitted to an outside hospital for altered mental status in the setting of a urinary tract infection (UTI). She was diagnosed with delirium secondary to the UTI and she was started on ciprofloxacin. Her delirium resolved with treatment and days later she developed increased energy, irritable mood,

pressured speech, delusions, and insomnia. While still experiencing irritable mood and paranoia, she discharged herself from the outside hospital against the medical advice of her treatment team after getting into a verbal disagreement with

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them. Her symptoms continued after discharge, which prompted family members to bring her into our emergency department a few days later. She was medically admitted to determine the etiology for her new-onset manic symptoms.

Full medical testing was ordered to rule out any organic causes for her presentation. No organic causes were identified with a urine analysis and culture, testing for metabolic/electrolyte abnormalities including her kidney and thyroid function, or computed tomography of her brain. A drug screen was negative. Her medications on admission are shown in **Table 1**, but they were

not thought to be contributing to her presentation.

After her admission, psychiatry was consulted. An evaluation revealed that she was alert and oriented to person, place and time, and had irritable affect, pressured speech, tangential thought process, grandiose and paranoid delusions, and recent worsening of chronic insomnia. She also had poor insight into her symptoms. There was no evidence of delirium on examination. She had no psychiatric diagnoses or hospitalizations before these recent events. The patient and family denied prior episodes of affective disturbances. She was prescribed a low dose of temazepam for chronic sleep issues by her primary care provider months prior, which she had not been taking due to intolerable side effects. She had been compliant with her dialysis and taking her home medications. She denied substance abuse issues.

However, a review of her chart did reveal that the patient had a similar presentation of altered mental status to our emergency department 3 years prior. At that visit, all laboratory tests, computerized tomography of the brain, as well as follow-up magnetic resonance imaging of the brain were normal. The patient's

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*Disclosure: The authors have no relevant financial relationships to disclose. doi:10.3928/00485713-20171108-02*

TABLE 1.

List of Patient's Medications on Admission

| Medication           | Dose  |
|----------------------|---|
| Acetaminophen        | 500 mg every 4 hours as needed for pain     |
| Ciprofloxacin        | 200 mg daily                                |
| Prochlorperazine     | 5 mg every 6 hours as needed for nausea     |
| Quetiapine           | 25 mg nightly (started at outside hospital) |
| Acetylsalicylic acid | 81 mg daily                                 |
| Sevelamer carbonate  | 3,200 mg 3 times daily                      |
| Cinacalcet           | 30 mg daily                                 |
| Furosemide           | 80 mg daily                                 |
| Levothyroxine        | 25 mcg daily                                |
| Pantoprazole         | 20 mg daily                                 |

history at that time revealed she had recently been diagnosed with a UTI by her primary care physician and started on ciprofloxacin. No other medication changes were noted. She had been discharged home from the emergency department and advised to follow up with her primary care physician for a possible neurodegenerative process. Her mental status eventually returned to baseline days less than 1 week later without further intervention.

**DIAGNOSIS**

**Antibiotic-Induced Mania**

Her new-onset manic symptoms were thought to be secondary to the recent start of ciprofloxacin given the temporal relationship between the two events. In addition, this was consistent with her presentation to the emergency department 3 years prior, when she also had been taking ciprofloxacin and experienced

similar signs and symptoms of mania.

The psychiatry department recommended discontinuing her ciprofloxacin and changing to another non-fluoroquinolone antibiotic to treat her UTI, so she was prescribed amoxicillin. With the diagnosis of a manic episode secondary to fluoroquinolone, she was prescribed 0.5 mg of risperidone twice daily and 5 mg of melatonin nightly for sleep. Her symptoms improved over the next 2 days. She slept through the nights and there was no further mention of delusions. The patient was discharged home as she was psychiatrically stable. All psychotropic medications were discontinued on discharge.

**DISCUSSION**

Manic reactions as a side effect of antimicrobial administration are infrequent, and the literature about it is restricted to case reports. Since the introduction of newer antibiotics and the increase in frequency at which they are

prescribed, reports of manic episodes have increased.<sup>1</sup>

The available literature provides some evidence that certain patients might be at an increased risk of developing mania while being treated with antimicrobials, and this is thought to be an idiosyncratic adverse effect.<sup>1</sup> In both published and unpublished case reports, the most common class of antibiotics associated with the onset of manic symptomatology was the fluoroquinolones.<sup>1</sup> Fluoroquinolones are used worldwide for the treatment of several infectious diseases due to their broad spectrum of activity, high bioavailability, and good safety profile.<sup>2</sup> They are well absorbed orally and have long elimination half-lives. They have relatively poor cerebral spinal fluid penetration into uninflamed meninges, but in the presence of inflammation there is moderate penetration of selective quinolones, including ciprofloxacin.<sup>3</sup>

The most common adverse effects of the quinolones are gastrointestinal disturbances, neurotoxicity, blood disorders, renal disorders, metabolic disturbances, QTc interval prolongation, and hypersensitivities.<sup>3</sup> Regarding the neurologic and psychiatric adverse reactions to quinolones (such as in this case report), mania is the most reported event.<sup>3</sup> However, mania is not included in the summary of product characteristics of quinolones.

Hypotheses describing potential mechanisms for the neuropsychiatric adverse effects of fluoroquinolones include the

pharmacokinetics of the antimicrobial agent, such as possible interactions with other medications. For example, an increase in the serum level of an antibiotic could possibly increase its central nervous system concentration in relation to its relative ability to penetrate the blood-brain barrier, inducing mania.<sup>4</sup> Ciprofloxacin is a known inhibitor of CYP1A2 and CYP3A4 in human hepatic microsomes, and an interaction may be responsible for the neurotoxicity of this quinolone.<sup>1</sup> However, no such pharmacokinetic interactions were observed in the reported case. We must also consider patients with underlying medical conditions, such as our patient's ESRD, which may affect pharmacokinetics because ciprofloxacin is renally excreted. In the case presented here, the patient's ESRD and hemodialysis were stable without clear pharmacokinetic implications given the prescribed medications.

In all reviewed case reports, and in the case of our patient, withdrawal of the antibiotic resulted in rapid attenuation of manic symptoms.<sup>1</sup> In the case presented here, manic symptoms also reoccurred upon reintroduction of the offending agent, suggesting a causal relationship.<sup>1</sup>

Patients who present with a first episode of mania while receiving antimicrobial agents likely will not require long-term neuroleptization or mood stabilization, if any.<sup>6</sup> Instead, they may require the minimal use of a psychotropic agent to con-

trol their symptoms, and then discontinue them once resolved.<sup>6</sup> Our patient began to improve after receiving risperidone for only 2 days, and a review of available literature demonstrates that most patients can simply be observed until symptoms resolve, as dramatic corrections to baseline mental functioning were demonstrated simply by discontinuing the antibiotic.<sup>7</sup>

### CONCLUSION

This case illustrates that new-onset mania in adult patients with no previous history of mental illness should prompt a clinician to search for reversible causes of the mania. In the case presented here, this secondary cause of mania appears to be the introduction of the fluoroquinolone, ciprofloxacin. Our patient had no previous psychiatric history or signs of infection, delirium, seizures, or encephalitis. Metabolic abnormalities along with other acute organic conditions or substance abuse that might account for the acute onset of mania were ruled out. There was a clear relationship between the onset of her psychiatric symptoms and treatment with ciprofloxacin, and signs of recovery once the medication was discontinued. In addition, this was the second such episode experienced by our patient after a trial of a ciprofloxacin; she had no known manic symptomology without ciprofloxacin. Reports of mania are increasing with the in-

troduction of newer antibiotics and the frequency with which they are prescribed. It is not possible, given the current literature, to determine whether one antimicrobial agent is more likely than another to cause mania, and we cannot predict the effects of one antimicrobial agent on an individual person.<sup>8</sup> Further research is needed on this topic to help answer this important clinical question.

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