

# Recurrent mania consequent to quinolones exposure: A case report and review of literature

Swapnajeet Sahoo<sup>1</sup>, Jitender Aneja<sup>2</sup>, Debasish Basu<sup>1</sup>

<sup>1</sup>Department of Psychiatry, Post Graduate Institute of Medical Education and Research, <sup>2</sup>Department of Psychiatry, Government Medical College and Hospital, Chandigarh, India

### ABSTRACT

Antibiotics are the one of the most commonly used group, of drugs, in general medical and surgical practice. The quinolone antibiotics can lead to a range of adverse neuropsychiatric effects with most of the reports due to ciprofloxacin and ofloxacin. Here, we report an interesting and rarely described psychiatric manifestation of recurrent mania following the use of quinolone antibiotics, and briefly review the available literature.

**Keywords:** Antibiotics, mania, quinolones

### Introduction

Quinolones, one of the commonly used broad spectrum antibacterials, are frequently associated with neuropsychiatric adverse effects.<sup>[1]</sup> These may range from dizziness, headache, and sleep disturbances being the frequent ones, anxiety, suicidal ideations, delirium, hallucinations, agitation, confusion, psychosis, and catatonia being the other severe adverse events.<sup>[2,3]</sup> Psychiatric adverse events in the form of manic reactions due to quinolones had been mostly reported to the Food and Drug Administration (FDA) and the World Health Organization (WHO) without sufficient clinical details, as well as validity of their diagnosis.<sup>[3,4]</sup> Mania secondary to typhoid, dengue, and other febrile conditions have also been reported in literature.<sup>[5-7]</sup> Typhoid fever has been shown to be associated with a range of neuropsychiatric manifestations with delirium being the most common presentation anteceding or occurring concomitantly with the fever mania is reported rarely.<sup>[8-10]</sup> We report a case of recurrent mania, which developed each time, the patient was exposed to quinolone antibiotics.

**Address for correspondence:** Dr. Jitender Aneja,  
Department of Psychiatry, Government Medical College and  
Hospital, Sector - 32, Chandigarh, India.  
E-mail: anejajitender@gmail.com

### Case Report

Ms. AD is a 34-year-old homemaker, who previously, had two manic episodes with no family history of mental illness/bipolar affective disorder. She was not treated for the first episode and remitted within 1 month of the treatment with olanzapine 10 mg/day, and lithium carbonate 600 mg/day for the second episode. The index episode started in February 2014 when she developed fever, nausea, and vomiting acutely. She took paracetamol 500 mg orally with which fever subsided for once, but it recurred after 2 days and did not remit despite taking antipyretics further. She consulted a physician after 1 week of onset of fever (10<sup>th</sup> day) who diagnosed her with typhoid fever on the basis of serological investigations only (Widal test positive; titers for agglutinin O > 1:160 and agglutinin H > 1:160); prescribed her oral ciprofloxacin 500 mg twice a day for a week. Fever subsided within the next 2 days, and she was asymptomatic for the next 5 days when vomiting and diarrhea recurred along with headache. Ciprofloxacin was continued for 1 more week. Though above mentioned symptoms remitted in the next 2 days, new set of symptoms appeared on the day 10 of treatment with ciprofloxacin. She was noted to get up early in the morning;

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

**How to cite this article:** Sahoo S, Aneja J, Basu D. Recurrent mania consequent to quinolones exposure: A case report and review of literature. J Family Med Prim Care 2016;5:163-5.

#### Access this article online

##### Quick Response Code:



Website:  
www.jfmpc.com

DOI:  
10.4103/2249-4863.184654

would bath early and then start doing household chores. She became more active, indulged herself into multiple tasks at the same time, and left them incomplete. Her family reported her to be very cheerful, amusing, and jocular which was unlike her previous self. She talked in excess at a faster pace and difficult to interrupt. She increasingly participated in religious activities, indulged in unnecessary buying of clothes and jewellery. She took ciprofloxacin for 4 more days in that week. Despite stopping the medication, thereafter no improvement was noted. In the next 2 weeks, her symptoms further worsened. There was no history of altered sensorium, disorientation, and any perceptual abnormalities. As she became unmanageable, so she was brought to our center. Her general physical examination did not reveal any abnormality suggestive of either metabolic disorder or cerebrovascular disease. Her metabolic parameters were within a normal range including thyroid function test. Neuroimaging study of brain in the form of computed tomography was normal. She was not receiving any other medications nor did she abuse any psychotropic substances such as cocaine or amphetamines. She was treated with olanzapine 10 mg and lithium carbonate 600 mg/day which was later on increased to 800 mg/day to achieve optimum serum lithium level. She achieved complete remission within 6 weeks.

In her past, she had suffered from gastroenteritis at 4–5 occasions but sought treatment only on two occasions. These two episodes of gastroenteritis, which occurred 10 and 8 years back, were treated with ciprofloxacin and ofloxacin, respectively, but prescriptions were not available. On both occasions, she developed similar set of mental symptoms as in the index episode characterized by elated mood, decreased need for sleep, increased goal-directed activity, increased religiosity, over-talkativeness, and increase in goal-directed activities though severity were less. Hence, the diagnosis of medication-induced recurrent mania as per diagnostic and Statistical Manual of Mental Disorders Fifth Edition<sup>[11]</sup> was kept. After she had achieved remission, all the psychotropics were gradually tapered and stopped. The patient and family members were cautioned for the use of quinolones in future as these were implicated as etiological in her mental illness. She has been followed up regularly and was in remission until March 2015.

## Discussion

Krauthammer and Klerman<sup>[12]</sup> gave the concept of mania occurring in association with physical disorders, medications, and drugs of abuse which was labeled as secondary mania. An analogy to medical syndromes of multiple etiologies such as hypertension (essential vs. secondary) and Parkinsonism (idiopathic vs. secondary) have also been drawn. Although the etiological dichotomy and validity of manic syndromes into primary versus secondary have been given on the basis of (1) close temporal association with an organic insult, (2) onset at a later age, (3) predominantly negative family history, and (4) negative premorbid history but we are still far from exact neurobiological etiology. Since the work of Krauthammer and

Klerman, there have been many reports of secondary mania due to various etiologies. Without going into literature review of secondary mania, we here give the common causes of this syndrome which include medications (corticosteroids, isoniazid, levodopa, antibacterials, thyroxine, sympathomimetic drugs, chloroquine, baclofen, captopril, amphetamine, phencyclidine, and various anti-depressants), infectious diseases (such as viral encephalitis), metabolic (hemodialysis), intracranial neoplasms (meningioma), temporal lobe epilepsy, and head injury.

The occurrence of mania has been reported in typhoid fever as well as with the use of a range of antibiotics, quinolones being the most notorious. However, typhoid fever as an etiological factor for manic reactions is not very commonly reported. In one of the previous case reports of mania in typhoid fever, the patient was afebrile at the time of onset of manic symptoms but was receiving ciprofloxacin,<sup>[5]</sup> while in other case there were many other confounding factors, thus making it difficult to tease out the causative agent for hypomanic symptoms.<sup>[6]</sup> In a retrospective review of the neuropsychiatric manifestations in 959 patients with typhoid fever, no case of mania was reported.<sup>[13]</sup>

On the other hand, mania in relation to antibiotics has been reported more commonly. In a review of antimicrobial-induced mania, 103 cases were found in un-/published literature with the quinolone group of antibacterials being implicated as the causative agent in 48 (46.7%) cases.<sup>[4]</sup> In another recent review of adverse drug reactions of quinolones, mania was reported most frequently and in association with the use of ciprofloxacin probably due to its wider use.<sup>[3,4]</sup> Both of these reviews relied on the data provided by the FDA and WHO, which in turn reported these adverse drug reactions during postmarketing surveillance. Although the mechanism of antibacterials leading to mania is unclear, the proposed hypothesis is their interactions with neurotransmitters, but competitive inhibition of gamma-aminobutyric acid receptors and induced epileptogenic neurotoxicity is suggested with reference to quinolones.<sup>[3,4]</sup> The management includes identifying and suspending the suspected antibiotic.

In the index case, there was temporal relationship of onset of mania with use of quinolones in all the episodes and in addition to typhoid fever for the current episode. For the first two episodes, there was no fever, and information of the use of quinolones was only available from the caregiver. In addition, there are no reports of mania in gastroenteritis. However, in the current episode both the laboratory evidence of typhoid fever and prescription of ciprofloxacin were medically documented. By the time, the patient developed mania her fever had subsided and thus only ciprofloxacin can be incriminated as the causative agent. Although there are some pointers that establish the association of manic syndrome with the use of quinolones in the form of (1) Occurrence of mania following quinolone use, (2) negative family history, (3) no independent manic reactions premorbidly (if the previous two episodes are also attributed to the use of quinolones); however, there is no definitive test

to establish the specificity and strength of association which is a major limitation. Another limiting factor in this report is the lack of documented evidence of prior quinolone use and our reliance on the arbitrament of the caregiver.

Antibiotics are one of the commonly used drugs at each level of healthcare including the primary care. It is prudent to be aware of such rare side effects of antibiotics, which might need the attention of a specialist mental health professional. Hence, it is recommended that a close watch to be kept for serious psychiatric manifestation in patients receiving quinolone antibiotics.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

### References

1. Oliphant CM, Green GM. Quinolones: A comprehensive review. *Am Fam Physician* 2002;65:455-64.
2. Chauhan U, Shanbag P, Kashid P. Ofloxacin-induced hallucinations. *Indian J Pharmacol* 2013;45:189-90.
3. Tomé AM, Filipe A. Quinolones: Review of psychiatric and neurological adverse reactions. *Drug Saf* 2011;34:465-88.
4. Abouesh A, Stone C, Hobbs WR. Antimicrobial-induced mania (antibiomania): A review of spontaneous reports. *J Clin Psychopharmacol* 2002;22:71-81.
5. Das A, Alexander PJ, Bonanthaya V. Mania following typhoid: A case report. *Indian J Psychiatry* 1995;37:143-4.
6. Santangelo CG, Goldstein D, Green S. A case of bipolar disorder and typhoid fever. *Int J Psychiatry Med* 2004;34:267-9.
7. Srivastava S, Bhatia MS, Jhanjee A. Organic mania in dengue. *J Clin Diagn Res* 2013;7:566-7.
8. Hafeiz HB. Psychiatric manifestations of enteric fever. *Acta Psychiatr Scand* 1987;75:69-73.
9. Ali G, Rashid S, Kamli MA, Shah PA, Allaqaband GQ. Spectrum of neuropsychiatric complications in 791 cases of typhoid fever. *Trop Med Int Health* 1997;2:314-8.
10. Aghanwa HS, Morakinyo O. Correlates of psychiatric morbidity in typhoid fever in a Nigerian general hospital setting. *Gen Hosp Psychiatry* 2001;23:158-62.
11. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 5<sup>th</sup> Edition. (DSM-5)*. Washington, DC: American Psychiatric Association; 2013. p. 124-54.
12. Krauthammer C, Klerman GL. Secondary mania: Manic syndromes associated with antecedent physical illness or drugs. *Arch Gen Psychiatry* 1978;35:1333-9.
13. Osuntokun BO, Bademosi O, Ogunremi K, Wright SG. Neuropsychiatric manifestations of typhoid fever in 959 patients. *Arch Neurol* 1972;27:7-13.