

Levofloxacin-Related Delirium: Uncommon Psychiatric Manifestations in Throat Infection Treatment

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ABSTRACT

We report a case of a 55-year-old man who had a history of ischemic stroke 6 years back and was on follow-up medications. He got a throat infection for which he took levofloxacin 250mg BD as prescribed by the doctor. After taking levofloxacin, the patient developed delirium and symptoms of acute psychosis such as social withdrawal and suspiciousness within 12-24 hours. The symptoms subsided 1 day after the discontinuation of levofloxacin. It can therefore be suspected that Levofloxacin directly contributed to the episode of delirium and acute psychosis witnessed in the patient. This is one of the rare cases of levofloxacin-induced delirium and acute psychosis symptoms seen up till now since the use of levofloxacin by patients. We, therefore, recommend that levofloxacin should be carefully used in patients with underlying psychiatric disorders and patients on levofloxacin should be regularly followed up to notice any such case of levofloxacin-induced delirium and acute psychosis.

Keywords: Levofloxacin, Delirium, Psychotic disorders.

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INTRODUCTION

Levofloxacin is a third-generation fluoroquinolone antibiotic that is absorbed almost completely after oral administration. Levofloxacin use is associated with some less severe and severe side effects. The most common less severe adverse effects associated with fluoroquinolones are gastrointestinal disturbances (such as nausea, vomiting, and diarrhea) and CNS side effects (headache, dizziness, and insomnia). In addition to this, tendon rupture, arthralgias, prolongation of QT interval, cardiac arrhythmias, and anaphylaxis are other less common and

severe side effects¹. Delirium and acute psychosis are extremely rare and under-recognized adverse effects of levofloxacin.

CASE PRESENTATION

A 55-year-old male patient presented with a history of acute onset of a sense of disorientation in time, place, and person. It was confirmed by the patient's family that there was no past medical or family history of any psychiatric illness. However, the patient had a medical history of ischemic stroke 6 years back and had been taking aspirin 150 mg once

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daily, amlodipine 10 mg once daily, mirtazapine 15 mg once daily, and escitalopram 10 mg once daily since then.

Recently the patient was prescribed Levofloxacin 250mg BD for a throat infection. The symptoms of delirium developed within 12-24 hours of taking Levofloxacin. On the first day of taking levofloxacin, the patient became restless and agitated. He was extremely energetic and talkative with little or no sleep. His speech was incoherent and there were delusions of grandeur and paranoia. On the second day, the symptoms worsened. Auditory hallucinations, self-isolation, catatonic and violent behavior were reported. The psychotic symptoms were evaluated by a consultant psychiatrist at Benazir Bhutto Hospital, Rawalpindi. The consultant confirmed it to be a case of acute psychosis using ICD-10 criteria. The patient was not a user of alcohol, tobacco, or any other illicit drugs.

The temporal association between the use of levofloxacin and the presentation of symptoms suggested that levofloxacin was the most likely cause of the symptoms. Levofloxacin and Mirtazapine were discontinued immediately and the symptoms of delirium and acute psychosis were resolved completely within 48 hours of discontinuing mirtazapine and levofloxacin. Levofloxacin was replaced with cefixime to treat the infection. The patient was kept under follow-up and remained asymptomatic thereafter.

DISCUSSION

Levofloxacin works by inhibiting the bacterial enzyme, DNA gyrase. This enzyme is involved in bacterial DNA synthesis and replication. Hence, these antibiotics are bactericidal². To date, there have been reported only a few cases of levofloxacin-induced delirium in the medical literature which makes this case a bit interesting.

Worldwide only a few cases of levofloxacin-induced delirium and acute psychosis have been seen and reported. levofloxacin-induced delirium and acute psychosis is thus a rare occurrence and warrants reporting when such an incident is seen. Out of the few cases of Levofloxacin-induced delirium and acute psychosis that have been seen worldwide, levofloxacin has been implicated in causing delirium and acute psychotic symptoms in elderly patients^{3,4,5}. Patients with renal dysfunction, patients with a past medical history of psychiatric and neurological illnesses, and other comorbidities^{6,7,8}. Levofloxacin has been reported to cause delirium with acute psychotic symptoms in young and healthy patients⁹. Thus, cases of levofloxacin-induced delirium and acute psychosis are rare but some have been reported. We therefore intend to report another rare case of levofloxacin-induced delirium and

acute psychosis seen in a male with a history of ischemic stroke.

The exact mechanism by which fluoroquinolones cause delirium and psychosis has not been found. However, it has been proposed that fluoroquinolones can bind and inhibit GABA receptors which results in CNS stimulation. Inhibition of GABA receptors leads to CNS overactivation because GABA is an inhibitory system present in the CNS. Individuals who are deficient in inhibitory GABA-dependent cortical networks are at increased risk of developing psychotic symptoms after levofloxacin administration¹⁰.

Another hypothesis suggests that Mirtazapine can be the direct cause of the symptoms observed in this patient. Levofloxacin has an indirect effect in causing delirium by inhibiting CYP1A2 which in turn leads to high levels of Mirtazapine¹¹. Mirtazapine inhibits central alpha-2-adrenergic receptors which results in increased levels of serotonin and norepinephrine in the brain. A rise in norepinephrine release in locus coeruleus has been associated with hyperactive delirium. To support this hypothesis, there have been studies that show that agonism of alpha-2-adrenergic receptors decreases the risk of hyperactive delirium in rats and humans¹². Thus, in this case, delirium and acute psychosis can be explained by the combined use of mirtazapine and levofloxacin. However, because withdrawal of levofloxacin in this patient relieved the symptoms of delirium and acute psychosis and the patient was taking mirtazapine for the last 6 years continuously but had never reported such occurrence before.

CONCLUSION

The CNS side effects of fluoroquinolones are highly unrecognized but they can be extremely severe particularly if the patients are on anti-depressant drugs. Hence, physicians should be aware of these possible neurotoxic adverse effects of the fluoroquinolones while prescribing these antibiotics to patients with a past medical history of any known psychiatric or neurological illness, elderly patients with impaired renal function, Levofloxacin and should be immediately discontinued in case of manifestation of any of the neurotoxic symptoms.

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CONFLICT OF INTEREST

No conflict of interest exists.

PATIENT CONSENT

An informed consent was taken from the patient before obtaining the data from the patient and writing this case report.

AUTHORS CONTRIBUTIONS

All authors contributed equally.

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