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Case Report

Levofloxacin induced psychosis: a rare case report

Daleep Singh[1]*, Akhil Kapoor[1], Mukesh Kumar Singhal[1], Vikram Singh[2], Harvindra Singh Kumar[1]

[1]Department of Radiation Oncology, Acharya Tulsi Regional Cancer Treatment & Research Institute, Bikaner, Rajasthan, India,
[2]Department of Psychiatry, Sardar Patel Medical College & Associated Group of Hospitals, Bikaner, Rajasthan, India

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***Correspondence to:**
Dr. Daleep Singh,
Email: drsihag123@gmail.com

ABSTRACT

Levofloxacin is a commonly prescribed antibiotic for treating bacterial infections in routine clinical practice. A wide range of side-effects have been ascribed to the quinolone group of drugs, the most common being gastrointestinal. Central nervous system is rarely involved; neuropsychiartic complications are among the least reported adverse reactions. We report a rare case of levofloxacin induced acute psychosis in a young male presenting in out-patient department with signs of urinary tract infection along with pneumonitis.

Keywords: Levofloxacin, Acute psychosis, Quinolone

INTRODUCTION

Various drugs are implicated as a cause of mental status changes as a side-effect. Fluoroquinolones constitute an under-recognized cause of the same. The central nervous system (CNS) side-effects of levofloxacin are rare and include headache, dizziness, convulsion, hyperkinesia, hypertonia, paraesthesia, insomnia, abnormal dreaming, agitation, anxiety, and confusion.[1] There have been only isolated reports of paranoia, delirium, depression, hallucination, manic reaction, toxic psychoses, withdrawal syndrome, suicide attempt or ideation. These adverse reactions usually occur only at high doses or when predisposing factors are present. Risk factors for neurotoxicity included renal insufficiency, elderly age, underlying CNS disease and increased CNS penetration of drug.[2] We report a rare case of levofloxacin induced acute psychosis in a young male presenting in outpatient department (OPD) with signs of urinary tract infection along with pneumonitis.

CASE REPORT

A 28-year-old male with no medical and psychiatric comorbidities presented to us in OPD with complaints of low grade fever, burning micturition and generalized body ache from 2 days. On examination, 100.4°F temperature was recorded. No focus of infection could be ascertained by physical examination. Patient was advised complete blood count, urine examination and chest X-ray posterior-

anterior (PA) views. His hemoglobin was 10.5 g/dl, total leucocyte count (TLC) 12,500 cells/cmm with neutrophils 79%, lymphocytes 16%, monocytes 4% and basophils 1%. Urine analysis revealed 1-3 red blood cells/high power field (hpf) with 16-17 pus cells/hpf. Chest X-ray PA view showed evidence of right lower lobe pneumonitis.

A provisional diagnosis of pneumonitis with urinary tract infection was made. As the general condition of the patient was good, oral antibiotics with supportive care was planned. On first day, urine and sputum sample was sent for culture and sensitivity and oral levofloxacin 500 mg/day as a single dose was prescribed. Both urine and sputum culture was sensitive to levofloxacin. Hence, we continued oral levofloxacin. Three days after starting of levofloxacin, patient developed acute onset of restlessness, irritation and purposeless wandering. By this time, TLC had returned to normal and fever subsided. Thus, response to the drug was good. However, patient's psychological symptoms rapidly worsened to irrelevant and incoherent speech, insomnia, violent behavior, auditory hallucinations, derangement of personality and loss of contact with reality causing deterioration of normal social functioning. Plasma glucose, serum electrolytes and cerebrospinal fluid study were within normal limits.

Patient was referred to psychiatrist where diagnosis of drug induced acute psychosis was made. This diagnosis could not be ascribed to his clinical diagnosis of pneumonia as the patient developed symptoms following 3 days of levofloxacin therapy. Other causes of delirium such as drug abuse, hypoglycemia, dyselectrolytemia, diabetic ketoacidosis, and meningitis were excluded. Other drugs the patient was receiving were paracetamol and sodium citrate, which are not known to cause such side-effects. The treating psychiatrist stopped levofloxacin and prescribed lorazepam. After 2 days of stopping levofloxacin, the patient was alert and well oriented with no hallucinations. His speech was normal in flow and content, and his concentration and recall were also normal.

DISCUSSION

Levofloxacin is a third-generation fluorinated quinolone broad-spectrum antibiotic that is active against both gram positive and gram negative bacteria. It inhibits two essential bacterial enzymes, DNA gyrase and topoisomerase IV.[3]

Most adverse reactions are mild to moderate; however, sometimes serious adverse effects occur. In pooled results from 7537 patients exposed to levofloxacin in 29 clinical trials, 4.3% discontinued treatment due to adverse drug reactions.[4] The most common adverse reactions leading to discontinuation were gastrointestinal, including nausea, vomiting, and constipation. Other uncommon, but serious adverse events include irreversible peripheral neuropathy, anaphylaxis, hepatotoxicity, CNS effects, prolongation of the Q-wave and the end of the T-wave (QT) interval, blood glucose disturbances, and photosensitivity, among others. According to the European dossier data, from 5388 patients treated with levofloxacin, 12% of patients developed an adverse effect, possibly related to the drug; but only 1% of these were classified as serious. Psychosis occurred in only 1/6 million prescriptions;[1] however, it is an important problem that has to be considered with this group of antibiotics.

The common CNS side-effects (incidence ranging from 1% to 10%) include headache and dizziness. Uncommon adverse effects (0.1-1%) include convulsions, hyperkinesias, hypertonia, paresthesia, somnolence, tremor, vertigo, abnormal gait, and syncope. Axonal polyneuropathy is a rare (<0.1%) reaction. The side-effects for which frequency is not reported include abnormal coordination, coma, hypoesthesia, involuntary muscle contractions, hyperesthesia, paralysis, speech disorder, stupor, encephalopathy, leg cramps, ataxia, migraine, seizures, and pseudotumorcerebri. There have been post-marketing reports of abnormal electroencephalogram, exacerbation of myasthenia gravis, anosmia, ageusia, parosmia, dysgeusia, encephalopathy, dysphonia, hypoacusis, and tinnitus.[5] The WHO reported 82 cases of anti-biomania (antimicrobial induced mania).[6] Of these, clarithromycin was implicated in 23 (27.6%) cases, ciprofloxacin in 12 (14.4%) cases, and ofloxacin in 10 (12%) cases. Rest cases stemmed from cotrimoxazole, metronidazole, and erythromycin.

The development of these effects seems to be related to the degree to which the fluoroquinolones bind to gamma aminobutyric acid (GABA) receptor and their differing potential to act as GABA antagonist and bind to the N-methyl-D-aspartate receptor, leading to CNS excitation.[7,8]

The authors would like to conclude with the message that since fluoroquinolones are widely used in the treatment of various infections; hence it is important to be aware of adverse effects of these drugs. Mental state changes are rare, but may occur after levofloxacin administration as depicted in the present case. Thus, it is advisable to administer this drug under close clinical monitoring and to take urgent psychiatric consultation at the earliest discernable changes in the mental state.

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