

Levofloxacin-induced visual hallucinations: A case report and review of the literature

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Abstract

A 52-year-old female, nonalcoholic, with no significant past medical history, was empirically treated with intravenous administration of levofloxacin (LVFX, 750 mg/day) for bronchopneumonia. On day 2, she reported seeing people who are not there (visual hallucinations). She had no history of psychiatric disorders or any family history of mental illness. The patient underwent EEG and brain magnetic resonance imaging (MRI), which resulted normal. Hence, psychiatric and neurological examinations excluded delirium, encephalitis, meningitis, structural neurological lesions. Any endocrine dysfunction (e.g., hypoglycemia, dyselectrolytemia, diabetic ketoacidosis) or toxic ingestion were also excluded. However, the possibility of levofloxacin-induced acute psychosis was considered and, on day 3, levofloxacin was discontinued with a complete resolution of the patient's visual hallucinations by her sixth day of hospitalization. The Naranjo Probability Scale (NPS) for determining the likelihood of whether an adverse drug reaction (ADR) is actually due to the drug rather than the result of other factors was calculated as + 6 ('probable'). In literature, the association between psychiatric adverse events and assumption of fluoroquinolones is known, but only a few cases after assumption of levofloxacin have been reported. However, the true prevalence of levofloxacin-induced neuropsychiatric adverse effects could be underestimated. Therefore, physicians and psychiatrists should consider neuropsychiatric adverse effects when prescribing levofloxacin or other fluoroquinolones.

KEY WORDS: Drug-related side effects and adverse reactions; fluoroquinolones; levofloxacin; hallucinations, visual.

Riassunto

Una donna di 52 anni, non etilista e con anamnesi negativa per patologie, venne sottoposta a terapia antibiotica empirica con levofloxacin 750 mg/die somministrata per via endovenosa per una broncopolmonite. Il secondo giorno la paziente riferiva di vedere persone che non erano presenti (allucinazioni visive). La paziente che riferiva un'anamnesi familiare e personale negativa per patologie psichiatriche venne sottoposta ad EEG e a risonanza magnetica dell'encefalo. Quindi, una visita specialistica neurologica e psichiatrica esclusero il delirio, l'encefalite, la meningite e lesioni neurologiche organiche. Altri disturbi endocrinologici (per es. ipoglicemia, diseletrrolitemia, chetoacidosi diabetica) o l'ingestione di sostanze tossiche vennero anche escluse. Tuttavia, la possibilità di una psicosi causata dall'assunzione di levofloxacin venne considerata, ed al terzo giorno la levofloxacin venne interrotta con una completa risoluzione delle allucinazioni visive della paziente entro il sesto giorno di ricovero. Il Questionario Naranjo Probability Scale (NPS) usato per determinare se la reazione avversa al farmaco fosse dovuta al farmaco o ad altre cause diede un risultato pari a + 6 ('probabile'). In letteratura l'associazione tra eventi avversi di tipo psichiatrico e l'assunzione di fluorochinoloni è conosciuta, ma sono stati descritti solo pochi casi dovuti all'assunzione di levofloxacin. Tuttavia, la loro reale prevalenza può essere sottostimata. Pertanto, i clinici e gli psichiatri dovrebbero considerare questo tipo di complicanze quando prescrivono la levofloxacin o altri fluorochinoloni.

TAKE-HOME MESSAGE

Physicians and psychiatrists should consider possible neuropsychiatric adverse effects when prescribing levofloxacin or other fluoroquinolones.

Competing interests - none declared.

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INTRODUCTION

Levofloxacin is a third-generation fluoroquinolone, which has a good tolerability and efficacy against a wide range of bacterial pathogens [1]. Its most frequently reported adverse events are nausea and diarrhea [2]. Indeed, the most common adverse reactions of fluoroquinolones affect the gastro-enteric system. However, several studies reported neuropsychiatric symptoms as well [3]. In literature, some cases of levofloxacin-induced neurological adverse effect, such as anxiety and insomnia, were also described [4]. Indeed, levofloxacin has an adverse event profile similar to that of other fluoroquinolones. However, levofloxacin-induced hallucinations and psychosis have been rarely described. We report one case of a 52-year-old female who suffered visual hallucinations after the intake of levofloxacin.

CASE REPORT

A 52-year-old female, nonalcoholic, with no significant past medical history, presented to our emergency department with a five days history of fever up to 39°C, productive cough and dyspnea. On initial examination, she was tachycardic (110 beats/minute) with a blood pressure of 130/85 mm and a respiratory rate of 26 breaths per minute. Her arterial blood O₂ saturation (98%) and partial O₂ pressure (92.1 Torr) in room air were normal. She had taken no medications. Laboratory tests showed that white blood cell (WBC) count was elevated (19,400/mm³, neutrophils 72%, lymphocyte 11.4%, and bands 7.3%) as well as C-reactive protein (CRP) (135.01 mg/dL). Her biochemical parameters were within physiological limits. A chest radiographic revealed right lower lobe infiltrate. He was initially diagnosed with bronchopneumonia. Intravenous administration of levofloxacin (LVFX, 750 mg/day) was empirically started. On day 2, she reported seeing people who are not there (visual hallucinations). However, she was not agitated and was orientated to place, person and time; she presented no alterations of sense-perception with no neurological deficits. She did not report auditory

hallucinations. She had no history of psychiatric disorders or any family history of mental illness. Due to suspicion of psychiatric or neurological disease, however, the patient underwent EEG and brain magnetic resonance imaging (MRI), which resulted normal. Moreover, psychiatric and neurological examinations excluded delirium, encephalitis, meningitis, structural neurological lesions (e.g., stroke). Any endocrine dysfunction (e.g., hypoglycemia, dyselectrolytemia, diabetic ketoacidosis) or toxic ingestion were also excluded. Therefore, the possibility of levofloxacin-induced acute psychosis was considered and, on day 3, levofloxacin was discontinued, and patient was switched to an intravenous broad-spectrum antibiotherapy with piperacillin/tazobactam (4.5 g x 3). Finally, visual hallucinations resolved by her sixth day of hospitalization. A further psychiatric evaluation showed her to be oriented with no further hallucinations, and she did not require any antipsychotic medications. Evidence of a causal relationship between the drug and visual hallucinations was assessed through the Naranjo Probability Scale (NPS). The Naranjo algorithm is a questionnaire designed by Naranjo et al. for determining the likelihood of whether an adverse drug reaction (ADR) is actually due to the drug rather than the result of other factors. Total scores range from - 4 to + 13; the reaction is considered 'definite' if the score is 9 or higher, 'probable' if 5 to 8, 'possible' if 1 to 4, and 'doubtful' if 0 or less. Our patient's NPS score was calculated to be as + 6.

DISCUSSION

In literature, the association between psychiatric adverse events and assumption of fluoroquinolones is known. The most frequently reported psychiatric adverse events were mania, acute psychosis, delirium and insomnia [5]. In a study showing results from the French pharmacovigilance system (from 1985 to 2002), five hundred ninety cases were reported (273 males and 316 females), where the most frequently reported psychiatric adverse effects were confusion (51%), hallucinations (27%), agitation (13%), delusion (12%), in-

somnia (8%), somnolence (4%) [3]. However, in literature delirium and hallucinations related to fluoro-quinolones have been reported particularly with ciprofloxacin [6–9], moxifloxacin [10], ofloxacin [11], and pefloxacin [12]. The side adverse effects exercised on central nervous system by quinolones could be due to preventing normal binding of γ -amino butyric acid (GABA) with their receptors, especially among patients using multiple medications such as theophylline or nonsteroidal anti-inflammatory drugs [12]. This mechanism was also taken into account to explain the pathogenesis of the acute anxiety and insomnia due to levofloxacin therapy [4]. However, stopping the drug in time in three young people (1 female and 2 males) cases reported by Kandasamy and Srinath, probably prevented the progress of anxiety and insomnia to major psychiatric disorders like psychosis [4]. Indeed, the central nervous system (CNS)-related side effects of fluoroquinolones including levofloxacin are headache, dizziness, restlessness, tremor, insomnia, hallucinations, convulsions, anxiety, and depression [13, 14]. Some of the CNS-related side effects of levofloxacin have been clarified by Erden et al. in rats and mice [13]. They confirmed that levofloxacin is less effective than ofloxacin in inhibition of GABA response, in agreement with past clinical studies revealing less frequent CNS side effects with levofloxacin compared to ofloxacin [15].

In literature a few cases of levofloxacin-induced psychiatric adverse effects have been described.

In 2008, it was reported a case of levofloxacin-induced acute psychosis during treatment with oral levofloxacin (500 mg/day) in a 50-year-old man affected by diabetic and hypertension with multiple infections and a persisting foot ulcer [16].

Another case was described in a 38-year-old Caucasian man diagnosed with schizoaffective disorder and multiple sclerosis who developed delirium and visual hallucinations after initiating levofloxacin therapy [17].

In 2009, Slobodin et al. showed the case of an 83-year-old man who was admitted for lobe

pneumonia and, after empiric treatment with levofloxacin, on the third day of hospitalization, developed delirium. In this case, when treatment was stopped there was a complete resolution of the patient's symptomatology 2 days later [18].

Another paper reported two cases of levofloxacin-induced neurological adverse effects such as convulsion, involuntary movement (tremor, myoclonus and chorea like) and visual hallucination in elderly patients. The first of two cases was a 67-year-old man with minor alcoholism and a past-history of gastrectomy and cholecystectomy whose was given 300 mg/day of oral levofloxacin and fulfenamic acid for an upper respiratory infection, with onset of hallucinations and first neurological adverse effects after four days. The second case was a 85-year-old man with chronic bronchitis and slight renal impairment, who showed neurological adverse effects after receiving long term administration of 200 mg/day of levofloxacin. In this case, age-related renal and brain impairment might have contributed to onset of neurological adverse effects [19].

We have reported a case of young and healthy female who was treated with intravenous levofloxacin for her bronchopneumonia. Our case was characterized by acute onset of isolated visual hallucinations without any other neuropsychiatric disorders, and by resolution of the symptomatology occurred after discontinuing therapy.

In conclusion, as stated by Kandasamy and Srinath [4], physicians and psychiatrists should be aware of neuropsychiatric adverse effects of levofloxacin, not only in elderly but also in younger patients. Indeed, the few cases reported in literature could underestimate the true prevalence of levofloxacin-induced neuropsychiatric adverse effects.

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