

Levofloxacin Associated Fatal Oro-Facio-Brachial Dystonia in Cirrhosis

Cyriac Abby Philips¹, Philip Augustine²

ABSTRACT

Fluoroquinolones are rarely associated with severe dystonic syndromes. We present the case of a middle aged cirrhotic who presented with severe fatal oro-facio-brachial dystonia secondary to intravenous levofloxacin use. Levofloxacin has been very rarely shown to be associated with such severe involuntary movement disorders. A commonly used antibiotic as part of anti-tubercular regimen, caution must be maintained for prevention of severe adverse reactions while using levofloxacin.

Key words: Dystonia, Fluoroquinolone, Critical care, Cirrhosis, Portal hypertension.

INTRODUCTION

Dystonias comprise a group of disorders defined by excessive involuntary muscle contractions resulting in abnormal postures and/or repetitive movements with varied clinical manifestations and causes. Identification of syndromic patterns with accurate diagnostic testing can help understand potential-causes leading to specific etiology-based management. In majority of cases, a cause cannot be identified and treatment is symptomatic. Dystonias are characterized by different parameters such as: Age at onset – from infancy to late adulthood; body distribution – from focal (one isolated region), segmental (2 or more contiguous regions), multifocal (2 or more non-contiguous regions), hemidystonia (half the body) to generalized (trunk plus 3 other sites); based on temporal pattern - static or progressive; variations - persistent, action-specific, diurnal or paroxysmal; with associated features – such as isolated (with or without tremor) or combined (with other neurological or systemic features).^[1] Movement disorders in cirrhosis commonly encompass asterixis, intention tremor, bradykinesia, Parkinsonism, abnormal ocular movements and those associated with alcoholism such as choreoathetosis and restless leg syndrome.^[2] Drug induced movement disorders are difficult to diagnose, but can be considered in the event of strong causality. In this report, we present the case of a middle aged cirrhotic who presented with immediate severe fatal oro-facio-brachial dystonia secondary to intravenous levofloxacin use. Levofloxacin has been very rarely shown to be associated with such severe involuntary movement disorders.

CASE REPORT

A 58-year-old, compensated male-cirrhotic with Child Pugh score 7 and model for end stage liver disease score of 9 without uncontrolled sepsis and with normal renal function test and electrolytes and arterial ammonia levels (Table 1) who received 2 doses of intravenous levofloxacin for community acquired pneumonia developed severe contorted spasms of the face, mandible (Figure 1A-B) and upper limbs, 4 hours after drug exposure. The severity increased in frequency and intensity within 60 min, causing multiple tongue lacerations and oro-mucosal bleeding (Figure 1C and Video). These were uncontrolled with 10 mg of lorazepam, 6 mg of midazolam and 50 micrograms of fentanyl 1 hr later. Immediate intubation and mechanical ventilation was performed after discussion with the family members who were reluctant, in view of personal beliefs and financial constraints. Unfortunately, after a prolonged course on mechanical ventilation, complicated by an acute variceal bleed, the patient died due to sepsis and multi organ failure, 6 days later.

DISCUSSION

Cirrhosis is not commonly associated with dystonia except in Wilson's disease patients. The commonest movement disorders seen in cirrhosis patients include asterixis and peripheral tremors and those associated with cirrhotic Parkinsonism that includes bradykinesia and rigidity. Our patient had a compensated liver disease with near normal electrolytes and ammonia in the presence of ongoing infections and hence acute onset severe dystonia was not attributable to liver disease per se. Drug therapy for acute dystonia include anticholinergics, dopaminergics, GABAergics, muscle relaxants and others such

Cyriac Abby Philips¹, Philip Augustine²

¹Hepatology and Liver Transplant Medicine, PVS Institute of Digestive Diseases, PVS Memorial Hospital, Cochin, Kerala, INDIA.

²Gastroenterology, PVS Institute of Digestive Diseases, PVS Memorial Hospital, Cochin, Kerala, INDIA.

Correspondence

Cyriac Abby Philips

Philip Augustine Associates, PVS Memorial Hospital Campus, Kaloor, Cochin 682017, Kerala, INDIA.

Phone: +91 9207745776

Email: abbyphilips@gmail.com

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Table 1: Laboratory values of the patient at admission to intensive care unit

Parameter	Result	Normal Range
Hemoglobin (g/dL)	10.2	12 – 14
Platelet count (x 10 ⁶ / mm ³)	98000	1.5 – 4.5
Total leucocyte count (per mm ³)	15500	4000 – 10000
Total bilirubin (mg/dl)	2.8	0.3 – 1.9
Direct bilirubin (mg/dl)	1.4	0 – 0.3
Aspartate transaminase (IU/L)	76	12 – 40
Alanine aminotransferase (IU/L)	58	12 – 40
Alkaline phosphatase (IU/L)	128	44 - 147
Sodium (mmol/L)	133	135 – 145
Potassium (mmol/L)	4.2	3.5 – 5.0
Magnesium (mEq/L)	2.1	1.5-2.5
Calcium (mg/dL)	8.8	8.5 – 10.2
Arterial ammonia (µmol/L)	78	35-65
Urea (mmol/L)	8.2	2.5 to 7.1
Creatinine (mg/dL)	1.2	0.6 to 1.2

as carbamazepine, cyproheptidine, gabapentin, lithium, tizanidine and zolpidem. In severe cases, complete sedation and mechanical ventilation might be required to prevent airway compromise as seen with our patient. Surgical management and botulinum injections also have been utilized in refractory or chronic cases.^[3] Fluoroquinolones have been found to be associated with a plethora of neuropsychiatric adverse effects, such as seizures, insomnia, confusion, psychosis, paranoia and hallucinations.^[4] Defective inhibition in basal ganglia and cortical pathways lead to dystonia. Commonly used in clinical practice, quinolones have intrinsic γ -amino-butyric acid type-A receptor antagonist properties that could impair inhibition in brain in predisposed individuals, leading to dystonic symptoms.^[5] Levofloxacin induced severe movement disorders are reported rarely and fatality never reported in literature until now.^[6] Future genome wide association studies can potentially identify genetic factors in at risk patients and help in precision pharmacotherapy. The state of the art approach to gene based medical management will in due course allow for abrogation of adverse effects associated with commonly used medications such as fluoroquinolones.^[7]

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Figure 1: Severe spastic contortions of the face, mouth (A), lips and mandible (B) leading to severe tongue bite and oral bleeding (C).

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