Gatifloxacin-induced rhabdomyolysis

George P, Das J, Pawar B[1], Badyal D[2]

Departments of Internal Medicine, [1]Nephrology and [2]Pharmacology, Christian Medical College and Hospital, Ludhiana - 141 008, India

Correspondence:
Pratish George
E-mail: pratishgeorge@gmail.com

Received : 19-12-06
Review completed : 31-10-07
Accepted : 01-11-07
PubMed ID : 18626179
J Postgrad Med 2008;54:233-4

Flouroquinolone antibiotics cause musculoskeletal adverse effects like myalgia, arthralgia, tendon disorders and rhabdomyolysis.[1] Ofloxacin and levofloxacin rarely cause rhabdomyolysis,[2] but gatifloxacin has not yet been reported to cause rhabdomyolysis.

A 50-year-old male was admitted with intermittent fever and lower urinary tract symptoms for two days. No oliguria or dark urine was noticed. No alcohol abuse, illicit drugs, unprescribed medication use, unaccustomed exercise or trauma was present. A routine health evaluation two months prior was normal. Clinical examination at admission was unremarkable.

Renal failure (blood urea 52 mg/dl, serum creatinine 3.2 mg/dl, serum potassium 5.8 meq/dL, metabolic acidosis) with leucopenia (total leucocyte count 3200/mm^3) was observed. Bacteriuria was present on urine microscopy (urine white blood cells 60/HPF). Leptospira antibodies were negative. Ultrasonography of the kidneys was normal. He was treated with intravenous gatifloxacin 200 mg once daily.

The renal failure worsened over the next three days (blood urea 100 mg/dl, serum creatinine 5.5 mg/dl, worsening metabolic acidosis) and he complained of severe muscular pain and weakness. Grade 4 muscle power with generalized muscle tenderness and an inability to sit up, stand or walk unsupported was noticed. The serum muscle enzymes were elevated [creatinine phosphokinase (CPK) 5915 U/L, lactate dehydrogenase (LDH) 1466 U/L, serum glutamic oxaloacetic transaminase (SGOT) 364 U/L.] Urine and serum myoglobin were not significantly raised. Hypocalcemia (serum calcium 6.6 mg/dl), hypophosphatemia (2 mg/ dL), hyperuricemia (serum uric acid 10.4 mg/dL) and thrombocytopenia (platelet count 96000/cu mm) developed. Creatinine phosphokinase peaked at 7314 U/L. Electromyography did not show evidence of myopathy.

Gatifloxacin-induced rhabdomyolysis was considered and intravenous cefoperazone/sulbactam 1 g twice daily was used instead, along with rehydration and furosemide-alkaline diuresis. Twenty-four hours after stopping gatifloxacin, his renal functions improved and a downward trend of muscle enzymes was noticed. Five days later his renal function normalized and the muscle enzymes declined significantly (CPK 304 U/L, LDH 751 U/L, SGOT 145 U/L) with resolution of all muscle symptoms. He was discharged with a word of caution on future use of quinolones. He did not come for review subsequently.

Discussion

The distinctive clinical presentation and temporal association of gatifloxacin with symptoms, biochemistry values and subsequent improvement after withdrawal suggested that rhabdomyolysis in this patient was gatifloxacin-induced. An objective assessment by the use of Naranjo probability scale two days after stopping gatifloxacin revealed a score of six, indicating drug-related rhabdomyolysis.[3] Drugs directly or indirectly impairing the production and use of adenosine triphosphate (ATP) by skeletal muscle or increasing energy requirements exceeding the rate of ATP production, can cause rhabdomyolysis.[4] The clinical profile and investigations did not suggest attributable infective causes for rhabdomyolysis (sepsis, pyomyositis, dengue fever and infection with Legionella, Salmonella, Falciparum malaria, Influenza or HIV).[5] The early onset of rhabdomyolysis in this patient suggested a direct effect on muscles and collagen fibers by gatifloxacin. Adverse effects of fluoroquinolones appear to be class-mediated or due to structural modification. Structure-side-effect relationships of substitution in quinolones show phototoxicity at positions R_5 and X_8, genetic toxicity at R_1, R_5, R_7 and X_8 and theophylline interaction at R_1 and R_7.[6] A review of the literature showed no previous association of rhabdomyolysis with gatifloxacin.

Presentation in rhabdomyolysis may vary from an asymptomatic illness (with only elevation in CPK) to a life-threatening condition associated with extreme elevations in CPK (levels more than 5000 U/L indicate serious muscle injury), acute renal failure and disseminated intravascular coagulation.[7] Other important biochemical findings include hyperkalemia, hypocalcemia, hyperphosphatemia, hyperuricemia, metabolic acidosis and raised levels of other muscle enzymes including lactate dehydrogenase, aldolase, aminotransferases, and carbonic anhydrase III.[1,7]

The patient responded well to conservative management

of acute renal failure and rhabdomyolysis after stopping gatifloxacin.

References

1. Poels PJ, Gabreels FJ. Rhabdomyolysis: A review of the literature. Clin Neurol Neurosurg 1993;95:175-92.
2. Hsiao SH, Chang CM, Tsao CJ, Lee YY, Hsu MY, Wu TJ. Acute rhabdomyolysis associated with ofloxacin-levofloxacin therapy. Ann Pharmacother 2005;39:146-9.
3. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, *et al*. A method of estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30:239-45.
4. Knochel JP. Mechanisms of rhabdomyolysis. Curr Opin Rheumatol 1993;5:725-31.
5. Lee VWS, Harris D, Anderson RJ, Schrier RW. Acute renal failure. In: Schrier RW, editor. In diseases of the kidney and urinary tract. Vol 2. 8th ed. Philadelphia: Lippincott, Williams and Wilkins; 2007. p. 1001.
6. Lipsky BA, Baker CA. Fluoroquinolone toxicity profiles: A review focusing on newer agents. Clin Infect Dis 1999;28:352-64.
7. Huerta-Alardin AL, Varon J, Marik PE. Bench-to-bedside review: Rhabdomyolysis-an overview for clinicians. Crit Care 2005;9: 158-69.

Source of Support: Nil, **Conflict of Interest:** Not declared.