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Case Report

A Noteworthy Case of Myasthenic Crisis Induced by Levofloxacin

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ABSTRACT

This case report discusses a patient with a past medical history of Myasthenia gravis who was admitted to the hospital for community-acquired pneumonia and was then sent into a myasthenic crisis secondary to treatment with Levofloxacin. Although Levofloxacin can be effective at resolving community-acquired pneumonia, this antibiotic can precipitate muscular pathologies in certain population subsets. This is an interesting case of an acute myasthenic crisis being induced by Levofloxacin, leading the patient into acute hypoxic respiratory failure. It is critical to thoroughly consider, and if possible, avoid, any class of medications that may affect muscular function in individuals with myasthenia gravis.

Keywords
Myasthenia gravis; Levofloxacin; Fluoroquinolones; Neuromuscular junction; Myasthenic crisis; Myasthenia Gravis Foundation of America (MGFA) clinical classification; Antibiotic-induced exacerbation; Ocular muscle weakness; Respiratory muscle involvement; Treatment strategies; Molecular mechanisms; Adverse drug reactions; The coding symbols for a thesaurus of adverse reaction terms (COSTART) frequency classification.

INTRODUCTION

Levofloxacin is a fluoroquinolone with broad-spectrum activity typically used for community-acquired pneumonia, nosocomial pneumonia, acute bacterial sinusitis, inhalation anthrax, skin infections, chronic bacterial prostatitis, complicated urinary tract infections, pyelonephritis, and the plague. A variety of risks come with taking levofloxacin, including the risk of weakening muscle and tendon structures, inducing tendinitis and tendon rupture, as well as aortic aneurysm.[1]

This case report is about the unique presentation of a patient given levofloxacin for pneumonia, which led to an acute myasthenia gravis crisis.

CASE PRESENTATION

The patient is a 69-year-old Caucasian female with a past medical history significant for Myasthenia Gravis (stable for many years), thymoma status post thymectomy, lung adenocarcinoma, atrial fibrillation, asthma, and chronic obstructive pulmonary disease requiring 2 liters of oxygen. She presented to the emergency department with complaints of severe dyspnea for 5 days, shortness of breath with ambulation, occasional dry non-productive cough, and mild wheezing relieved by inhalers. She was recently treated for an *Escherichia coli* urinary tract infection with ciprofloxacin with no adverse effects. The patient has at least 15 listed allergies, some of which include antibiotics such as Cephalosporins, Vancomycin, Macrolides, and Trimethoprim Sulfa. She denied any fevers, chills, or chest pressure. On admission, the patient was afebrile, had a mildly elevated heart rate of 100, elevated blood pressure of 174/86 mmHg, and was tachypneic at a respiratory rate of 22 saturating 97% on 2 L *via* nasal cannula. Her physical exam was notable for an irregularly irregular rhythm. She denied any wheezing, edema, weakness, difficulty speaking and swallowing, double vision, or fatigue.

Her initial laboratory data revealed a white blood count (WBC) count of 19.6×10^9 per liter (neutrophils=79%, lymphocytes=17%, monocytes=4%), an red blood cell (RBC) count of 2.60×10^9 per liter, a hemoglobin of 8.1 g/dL, and a and a platelet count of 220×10^9 per liter. She had hypokalemia (2.9 mmol/L) and hypomagnesemia (1.4 mg/dL). Her N-terminal pro–B-type natriuretic peptide (NT-ProBNP) was elevated at 485 picograms/milliliter (Table 1). Her urinalysis was turbid, glucose 50 mg/dL, protein 200 mg/dL, with large WBCs/microliter. Her urine culture

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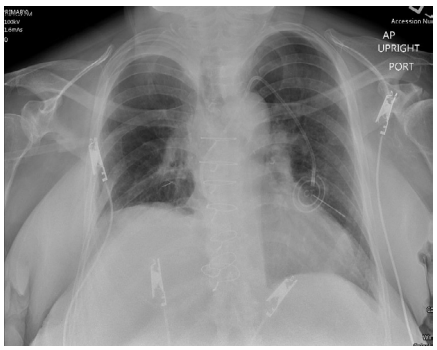
was positive for less than 10,000 mixed flora. Her viral respiratory panel was negative. Her chest X-ray showed a hazy left upper lung infiltrate (Figure 1).

Table 1. *Admission and Arterial Blood Gas Labs*

Admission Labs	
WBC	19.6×10³ /uL
RBC	2.60×10 /L
Hgb	8.1 g/dL
Platelet count	220×10 /L
Potassium	2.9 mm/L
Magnesium	1.4 mg/dL
NT-ProBNP	485 pg/mL
Arterial Blood Gas	
PH	7.54
HCO_3	32.2
Base Excess	9.3

Figure 1. *Chest X-ray Showed a Hazy Left Upper Lung Infiltrate*



She received Levofloxacin and a 30 cc/Kl IV fluid bolus. Levofloxacin was the agent of choice due to the patient's multiple drug allergies, and she had tolerated fluoroquinolones well in the past. Levofloxacin was given for acute bacterial pneumonia suspected to be gram-positive or atypical. The patient did meet sepsis criteria at the time of admission, including an elevated white blood cell count, tachypnea, and the source of infection, pneumonia. Within 1 hour of receiving Levofloxacin, she developed increased tachypnea, tachycardia, hypertension, and hypoxia, requiring 3 liters of oxygen. Over the next few minutes, the patient quickly deteriorated and developed labored breathing, hot flashes, and profuse diaphoresis. The patient also reported that her throat felt like it was closing up. She described a raspy voice and worsening air hunger. A nuclear ventilation and perfusion study performed that day was negative for perfusion deficits. An arterial blood gas revealed respiratory alkalosis with a potential of Hydrogen (pH) of 7.54, a bicarbonate of 32.2, and a base excess of 9.3 (Table 1). Following the course of the described events, there was a suspicion of an allergic reaction to Levofloxacin exacerbating her myasthenia gravis. The Levofloxacin infusion was immediately stopped, and the patient was placed on high-dose glucocorticoids and given supportive therapy with antihistamine and breathing treatments. Considerations were given to non-invasive ventilation, but the patient's respiratory status improved significantly following the course of action as described above. The patient was initially transitioned from Levofloxacin to azithromycin. She was ultimately transitioned from Azithromycin to Amoxicillin-clavulanic acid for concern of patients also developing allergic reactions to Azithromycin, as reports were found of Azithromycin-induced myasthenia gravis crises. She was discharged on day 5, once her respiratory status stabilized on Amoxicillin-clavulanic acid and the general support measures. It is evident based on this patient's hospital course that Levofloxacin triggered a myasthenic crisis, inducing generalized bulbar weakness, diaphoresis, labored breathing, and severe dysphagia in the setting of acute left upper lobe pneumonia. The patient had significant improvement in her clinical status when Levofloxacin was stopped.

DISCUSSION

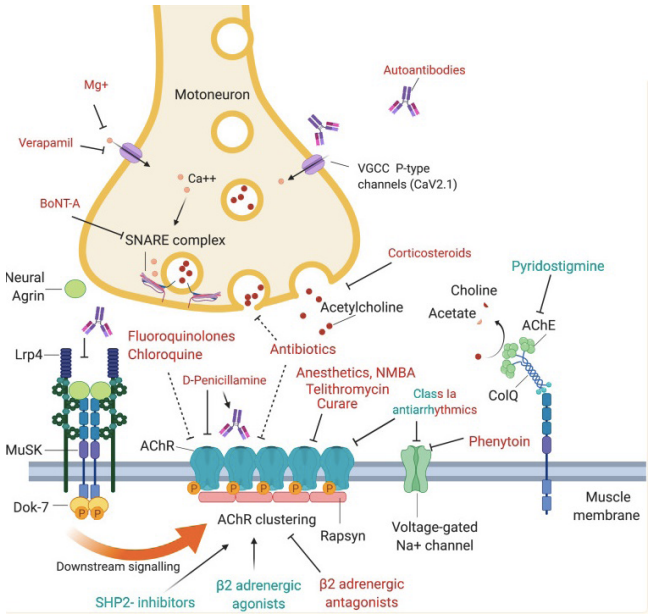
The patient presented in the above case is an example of acute hypoxic respiratory failure due to a myasthenic crisis induced by treatment with Levofloxacin in the setting of community-acquired pneumonia. The change in respiratory status over the first 24 hours of treatment with Levofloxacin in this patient could have quickly become a life-threatening complication.[2] Per the Myasthenia Gravis Foundation of America (MGFA) classification of MG, she had moderate weakness predominantly affecting oropharyngeal and airway muscles, defining her as Class IIIB.

A fairly common cause of myasthenic crises is medication. Levofloxacin is part of a class of antibiotics, namely Fluoroquinolones, that is considered dangerous for this subset of patients. Multiple case reports have noted myasthenia gravis exacerbations developed a median of one day within receiving a Fluoroquinolone.[3] This observation was supported by a discussion with several pharmacists relating to this particular case. The rapid reaction of the patient being discussed makes her an outlier. However, she had a 5-day history of pneumonia with increased shortness of breath, likely making her more prone to entering into myasthenic crises. It has been shown that a number of the older Fluroquinolones dose-dependently decrease the amplitude of endplate potentials.[4] Specifically, they accomplish this by blocking acetylcholine receptors on the post-synaptic nerve (Figure 2).[5]

It is unclear if patients with myasthenia gravis are consistently educated on the list of medications that can exacerbate their condition. Patients such as this, who are stable without any medications regulating the disease at baseline, are still at high-risk of developing myasthenic crises.

Additionally, it's important to note that, typically, in patients who develop myasthenic crises, non-invasive ventilation is an eventuality. Patients often develop severe bulbar muscle weakness manifested by labored breathing, upper airway obstruction, severe dysphagia, and extreme weakness. The patient in this scenario did not have accessory muscle use as she was experiencing general-

Figure 2. *Drugs and Antibodies that Affect the Function of the Neuromuscular Junction*



ized muscle weakness. The two predominant autoantibodies found in myasthenic gravis are against nicotinic acetylcholine receptors (AChR) and muscle-specific kinase (MuSK). Given this patient's past medical history of thymoma status post-thymectomy, it is likely she has AChR antibodies and not MuSK antibodies, which more commonly display severe features of bulbar weakness.[6] The determination of such antibodies was not done during the present hospitalization. Frequently, patients in myasthenic crises end up needing advanced airways in less than 1 hour; however, prompt recognition and intervention, such as in the case above, can mitigate the risk of respiratory failure. Immediate treatment with high-dose glucocorticoids is essential for recovery and a good prognosis. IVIg can also be used in the setting of myasthenic crises; however, this patient recovered well after the Levofloxacin infusion was stopped and after receiving high-dose glucocorticoids. With the limited availability of data, it is stipulated that about 10-20% of patients with myasthenia gravis may experience at least one episode of myasthenic crises.[7] The annual risk of developing myasthenic crises in patients with myasthenia gravis is 2-3%.[8]

Primary care providers should make sure to reconcile medications, educate on pharmaceutical contributors to myasthenia gravis exacerbation, and recommend vaccination to help avoid infectious triggers.[9] All medical team members of this population subset need to be alert to signs of increasing muscle weakness in this patient, as this often precedes a true myasthenic crisis.[10]

If a myasthenic crisis has been induced, no matter the cause, there are two pharmacological therapies available. The patient may either be treated with IVIg or plasma exchange, according to the severity of the crisis. A retrospective multicenter study focused only on patients experiencing myasthenic crises and noted plasma exchange was more effective overall, although not without its complications, including infection and cardiovascular instability.[2]

CONCLUSION

Levofloxacin is typically a very effective treatment for community-acquired pneumonia. However, fluoroquinolones are a class of antibiotics with many known side effects, specifically afflicting muscle and tendon structures in certain patient population subsets. Patients with myasthenia gravis can display extreme and life-threatening symptoms due to these side effects. It is essential to recognize early signs of increased muscle weakness so that triggers may be removed and/or treated with medications that rapidly reverse the weakness.[5] From a primary care physician perspective, the most important part of caring for this group of patients is to emphasize education about exacerbating factors, provide a list of medications known to exacerbate myasthenia gravis, and vaccinate against the most common infectious causes, including pneumonia.[9]

CONSENT

The authors have received written informed consent from the patient.

CONFLICT OF INTEREST

No potential conflict of interest related to this article was reported.

REFERENCES

1. Podder V, Sadiq NM. Levofloxacin. Treasure Island (FL), USA: StatPearls Publishing; 2023. Website. https://www.ncbi.nlm.nih.gov/books/NBK545180/. Updated September 23, 2022. Ac-

cessed February 1, 2024.

2. Wendell LC, Levine JM. Myasthenic crisis. *Neurohospitalist*. 2011; 1(1): 16-22. doi: 10.1177/1941875210382918

3. Jones SC, Sorbello A, Boucher RM. Fluoroquinolone-associated myasthenia gravis exacerbation: Evaluation of postmarketing reports from the US FDA adverse event reporting system and a literature review. *Drug Saf*. 2011; 34(10): 839-847. doi: 10.2165/11593110-000000000-00000

4. Sieb JP. Fluoroquinolone antibiotics block neuromuscular transmission. *Neurology*. 1998; 50(3): 804-807. doi: 10.1212/wnl.50.3.804

5. Krenn M, Grisold A, Wohlfarth P, et al. Pathomechanisms and clinical implications of myasthenic syndromes exacerbated and induced by medical treatments. *Front Mol Neurosci*. 2020; 13: 156. doi: 10.3389/fnmol.2020.00156

6. Koneczny I, Herbst R. Myasthenia gravis: Pathogenic effects of autoantibodies on neuromuscular architecture. *Cells*. 2019; 8(7): 671. doi: 10.3390/cells8070671

7. Claytor B, Cho SM, Li Y. Myasthenic crisis. *Muscle Nerve*. 2023; 68(1): 8-19. doi: 10.1002/mus.27832

8. Berrouschot J, Baumann I, Kalischewski P, Sterker M, Schneider D. Therapy of myasthenic crisis. *Crit Care Med*. 1997; 25(7): 1228-1235. doi: 10.1097/00003246-199707000-00027

9. Gummi RR, Kukulka NA, Deroche CB, Govindarajan R. Factors associated with acute exacerbations of myasthenia gravis. *Muscle Nerve*. 2019; 60(6): 693-699. doi: 10.1002/mus.26689

10. Bedlack RS, Sanders DB. On the concept of myasthenic crisis. *J Clin Neuromuscul Dis*. 2002; 4(1): 40-42. doi: 10.1097/00131402-200209000-00009