Myasthenia gravis exacerbation and diarrhea associated with erythromycin treatment

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1. Introduction

Myasthenia gravis (MG) is an important neurological disorder that can be seen in any countries around the world [1]. MG is classified as a neuromuscular disorder that the abnormal weakness of certain muscles is the main clinical manifestation. This problem can be seen worldwide and is an important problem in clinical neurology. MG is a disorder presenting with the weakness of muscle and it can be problematic for normal life of the patient. In the most severe case, the patient might have respiratory failure and there is a need for intubation. Mechanical ventilation may be required. The aggressiveness of management depends on the severity of the clinical problem and this has to be considered case by case.

Long-term medication by suppressive drug is usually used for controlling MG. The drugs used for controlling MG include anticholinesterase inhibitors, immunomodulating agents and intravenous immune globulin. To control the weakness, symptom is the goal for management of the patient with MG. An important problem in management of the case with MG is the control of exacerbation[2]. There are several possible causes of exacerbation of MG including the use of drug. In general practice, there are many common drugs including antibiotics. In tropical world, the use of antibiotic to manage the infection is common and this can be the problem for the patients with MG. The good example of drugs that can cause exacerbation of MG is fluoroquinolones[3]. Here, the authors report a case of MG exacerbation and diarrhea associated with erythromycin treatment.

2. Case report

This was a consulted case. The patient was a male patient presenting with the main complaint of acute diarrhea after intake of erythromycin for his acute pharyngitis. The physician in charge observed that the patient developed left eye ptosis and consulted the case. On history taking, this patient has underlying MG and been controlled by oral mestinon. The patient noted that he visited the physician in charge and got erythromycin for management of acute pharyngitis but he felt gastrointestinal upset and had several diarrhea within 2 h after drug intake. He noted that he had never got erythromycin. He also noted that he did not notify to the physician that he had underlying MG. This case was diagnosed to have a possible gastrointestinal side effect due to erythromycin and the MG exacerbation associated with erythromycin. In this case, pyridostigmine therapy was given and the patient was dramatically improved. Of interest, the present case got early observation of the exacerbation and the good treatment outcome could be noted. To confirm the case, the oral provocative test was also done and the positive test could be seen.

3. Discussion

MG is an important medical disorder. It is classified as a kind of neuromuscular problem due to the autoimmune disorder. The
antibodies formed by acetylcholine nicotinic post synaptic receptors at the neuromuscular junction of skeletal muscles can be seen in MG and this pathological process is the main pathogenesis of the clinical disease[1]. In general, the patients with MG usually have the complaint when there are symptoms. The main symptoms include specific muscle weakness rather than generalized weakness and the weakness is usually the chief complaint that is notified to the physicians. In most cases, extraocular muscle weakness or ptosis is the main muscle weakness. The problem can be seen in most patient and almost all MG patients experience this clinical problem. In some cases, the limb weakness can be seen but this is considered uncommon clinical manifestation. The specific medication is required for control of the problem. In some severe cases, the more complex management such as plasmapheresis and thymectomy might be required.

The control of clinical symptoms is the main target of medical management of the patient with MG. Most patients with MG can be successfully managed and controlled. Nevertheless, the exacerbation of the clinical problem can be seen in some cases and this is considered a big problem that needs urgent management. There are many possible causes of exacerbation of MG. The factors that might induce exacerbation or trigger the MG clinical problems include sunlight, surgical operation, immunization and vaccination, emotional insult and psychological stress, menstruation or hormonal usage, viral infection and drug. Drug-induced exacerbation of MG is an important problem to be watched in clinical practice. The problem can be severe and urgent management is needed[4]. Several drugs are confirmed as triggering agent for exacerbation of MG. The examples are ciprofloxacin, aminoglycosides, chloroquine, procaine, lithium, phenytoin, beta-blockers and statins. In severe case, respiratory difficulty can be seen and this can be a fatal condition in acute medicine. Several drugs are listed and reported as cause of exacerbation of MG. Those common drugs are antiinflammatory drug, steroid and antibiotic[5,6]. Antibiotic is a group of common drugs used at present. The use of antibiotic in the patient with MG has to be carefully monitored. Bhattacharyya et al. noted that close observation of MG is an important antibiotic-induced neurotoxicity[7]. The condition can be serious and fatal if there is a delayed diagnosis[2]. The aggressiveness of therapy might be needed in cases with exacerbation of MG and the success of management is usually linked to early diagnosis of the disorder.

In fact, several antibiotics including erythromycin can induce MG exacerbation[7-9]. Historically, the problem usually occurs within 2–4 h after getting problematic antibiotic[7,9]. This can also be observed in the present case. The erythromycin- and new erythromycin derivative-induced exacerbation of MG, especially for telithromycin[10-13] and azithromycin[14] have to be closely observed in any MG patient receiving the drug. Additionally, the present case also shows concomitant antibiotic side effect as diarrhea[15]. This is the first report on this concomitant problem. Of interest, the use of antibiotic to manage tropical infection is common and this can be the problem for the patients with underlying MG[16]. To ask whether the patient has underlying disease that might be problematic for common antibiotic therapy must be generally done in routine practice[17,18]. For any cases with exacerbation of MG, urgent management of the crisis is needed[4]. The hospitalization should be considered. At the same time, finding of the aggravating factors, which might be a drug, has to be done[4]. In any case with the unexplained exacerbation of MG, the differential diagnosis should include the condition of drug-induced exacerbation of MG and erythromycin has to be included into the list.

4. Conclusion
Here, the authors report a case of MG exacerbation and diarrhea associated with erythromycin treatment. This condition due to common antibiotic used for management of simple disease can be seen and should not be forgotten by practitioner.

Conflict of Interest Statement
The authors report no conflict of interest.

References
[1] Gilhus NE, Verschuuren JJ. Myasthenia gravis: subgroup classification and therapeutic strategies. Lancet Neurol 2015; 14(10): 1023-36.
[2] Eymard B. [Myasthenia, from the internist’s point of view]. Rev Med Interne 2014; 35(7): 421-9. French.
[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): 839-47.
[4] Hetherington KA, Losek JD. Myasthenia gravis: myasthenia vs. cholinergic crisis. Pediatr Emerg Care 2005; 21(8): 546-8.
[5] Cartwright MS, Jeffery DR, Nuss GR, Donofrio PD. Statin-associated exacerbation of myasthenia gravis. Neurology 2004; 63(11): 2188.
[6] Bae JS, Go SM, Kim BJ. Clinical predictors of steroid-induced exacerbation in myasthenia gravis. J Clin Neurosci 2006; 13(10): 1006-10.
[7] Bhattacharyya S, Darby R, Berkowitz AL. Antibiotic-induced neurotoxicity. Curr Infect Dis Rep 2014; 16(12): 448.
[8] Absher JR, Bale JF Jr. Aggravation of myasthenia gravis by erythromycin. J Pediatr 1991; 119(1 Pt 1): 155-6.
[9] May EF, Calvert PC. Aggravation of myasthenia gravis by erythromycin. Ann Neurol 1990; 28(4): 577-9.
[10] Telithromycin: review of adverse effects. Prescrire Int 2014; 23(154): 264-6.
[11] Bertrand D, Bertrand S, Neveu E, Fernandes P. Molecular characterization of off-target activities of telithromycin: a potential role for nicotinic acetylcholine receptors. Antimicrob Agents Chemother 2010; 54(12): 5399-402.
[12] Liu CN, Somps CJ. Telithromycin blocks neuromuscular transmission and inhibits nACHR currents in vitro. Toxicol Lett 2010; 194(3): 66-9.
[13] Perrot X, Bernard N, Vial C, Antoine JC, Laurent H, Vial T, et al. Myasthenia gravis exacerbation or unmasking associated with telithromycin treatment. Neurology 2006; 67(12): 2256-8.
[14] Cadisch R, Streit E, Hartmann K. [Exacerbation of pseudoparalytic myasthenia gravis following azithromycin (Zithromax)]. Schweiz Med Wochenschr 1996; 126(8): 308-10. German.
[15] Griffith RS, Black HR. Erythromycin. Med Clin North Am 1970; 54(5): 1199-215.
[16] Van Berkel MA, Twilla JD, Englund BS. Emergency department management of a myasthenia gravis patient with community-acquired pneumonia: does initial antibiotic choice lead to cure or crisis? J Emerg Med 2016; 50(2): 281-5.
[17] Brown SD. Benefit-risk assessment of telithromycin in the treatment of community-acquired pneumonia. Drug Saf 2008; 31(7): 561-75.
[18] Bol P. [Myasthenia gravis]. Ned Tijdschr Tandheelkd 2001; 108(10): 416-7. Dutch.