Monotherapy with erythromycin results in severe rhabdomyolysis

Lukas Birkner, Dimitri Zolotov, Mario Iasevoli

ABSTRACT

Introduction: Rhabdomyolysis is a potentially life-threatening condition caused by muscle necrosis and extravasation of intracellular muscle contents into the blood circulation. An elevation in serum creatine kinase is most confirmatory laboratory test. Erythromycin is an inhibitor of the CYP3A4 enzyme system which is responsible for the metabolism of several drugs, particularly some statins. Although rhabdomyolysis associated with macrolid-statin interaction has been previously described, we report the first case of erythromycin-induced rhabdomyolysis.

Case Report: In our case, a 38-year-old male admitted with pneumonia developed rhabdomyolysis associated with erythromycin administration.

Conclusion: Clinicians need to be aware of the risks this potential adverse drug reaction poses.
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Keywords: Erythromycin, Penicillin intolerance, Pneumonia, Rhabdomyolysis

INTRODUCTION

Rhabdomyolysis is a potentially life-threatening condition characterized by the leaking of creatine kinase and other intracellular proteins and electrolytes into the blood circulation [1]. The most common symptoms of rhabdomyolysis include muscle weakness, brown urine, electrolyte imbalances, acute renal failure and disseminated intravascular coagulation. An elevation in serum creatine kinase (CK) and myoglobin is the most confirmatory laboratory test for rhabdomyolysis since all cases are associated with it [2, 3].

Although there are multiple physical and nonphysical causes of rhabdomyolysis the most common cause is medication [4]. Especially, rhabdomyolysis related to macrolide-statin interaction, such as clarithromycin or ketoconazole interacting with simvastatin, has been previously described in literature [5].

CASE REPORT

We report a case of 38-year-old male presented with a clinical diagnosis of common acquired pneumonia.
He was treated with erythromycin (500 mg two times a day) for one and a half days due to a known penicillin intolerance. The patient subsequently developed joint and muscle pain after the first day of administration and an anuria with growing nausea after the second day without a documented source of infection. Consequently, the patient was admitted to our inpatient hospital complaining of an anuria. An extremely elevated creatine kinase concentration of 40205 U/L (normal <200) was discovered after the first day of hospitalization and reached 228456 U/L the following day. The estimated glomerular filtration rate (GFR) was reduced to <10 ml/min (normal 120 ml/min per 1.73 m²). Other parameters indicating rhabdomyolysis were serum aspartate aminotransferase (AST) 5789 U/l (normal 5–34), serum alanine aminotransferase (ALT) 1093 U/l (normal < 55) and serum lactate dehydrogenase (LDH) increased to a maximum of 10,100 U/l (normal 125–243). Rhabdomyolysis associated with acute renal failure and hepatopathy was diagnosed. Erythromycin was immediately stopped and the patient received dialysis treatment as required over the course of two and a half weeks. The serum CK gradually decreased. Two weeks later creatine kinase returned to 2927 U/L. During the course of the dialysis treatment the micturition gradually increased and muscle pain subsided. No further laboratory tests were ordered.

Erythromycin was thought to be the precipitating factor for rhabdomyolysis because the patient was neither taking other medication nor had a conspicuous anamnesis or relevant pre-existing conditions. Additionally, using the Naranjo adverse drug reactions probability scale a score of 6 was determined. Thus erythromycin can be considered a probable cause of rhabdomyolysis [6].

**DISCUSSION**

Rhabdomyolysis associated with macrolid-statin interaction has been previously described, however, rhabdomyolysis related to erythromycin has not been reported until now [7]. Erythromycin is an inhibitor of the CYP3A4 enzyme system, which is responsible for the metabolism of several drugs, particularly some statins as simvastatin or atorvastatin. Any documented cases of erythromycin induced rhabdomyolysis involved drug interactions with statins through inhibition of CYP3A4 enzyme system. It has a similar spectrum of activity as clarithromycin [8].

Of interest, clarithromycin induced rhabdomyolysis has been previously reported in a few cases. A five-year-old Asian-American girl was admitted with 102°F fever and a five-day history of productive cough. The patient was prescribed clarithromycin 125 mg twice a day. After five days a creatine kinase concentration of 9.49 U/L (normal <177) was discovered. Clarithromycin was immediately stopped and the child recovered [9, 10]. Undoubtedly, both cases show parallels, such as the elevation of serum CK associated with the respective drug and the course of recovery, although differences in the severity must be noted.

In our case, there was a definite connection between erythromycin exposure-withdrawal and the gradual recovery of the patient. Considering the sequence of events we ruled out infection as the possible cause of rhabdomyolysis. As a matter of fact the patients symptoms were inconspicuous, while serum CK drastically increased one day after the start of treatment with erythromycin. Thus, the chronological relationship between the appearance of myalgia and the start of erythromycin suggest the conclusion that erythromycin is the responsible agent in our case.

**CONCLUSION**

We reported a probable case of erythromycin-induced rhabdomyolysis. The mechanism behind this adverse drug reaction is not understood, although there have been a few cases of rhabdomyolysis associated with macrolides. Clinicians need to be aware of the risks this potential adverse drug reaction poses, especially concerning patients at risk for rhabdomyolysis.

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**Author Contributions**

Lukas Birkner – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Dimitri Zolotov – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Mario Iasevoli – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

**Guarantor**

The corresponding author is the guarantor of submission.

**Conflict of Interest**

Authors declare no conflict of interest.

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