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Case Report

Corrected QT Interval Prolongation Complicating Incoercible Vomiting in a Coronavirus Disease 2019 Patient Under Chloroquine and Azithromycin

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Abstract

Administration of chloroquine with azithromycin for the treatment of coronavirus disease 2019 (COVID-19) carries increased risk of corrected QT interval (QTc) prolongation and cardiac arrhythmias. But it is difficult to identify the real cause of QTc prolongation when two or more risk factors are gathered. This was the case of our female patient presenting with QTc prolongation after starting chloroquine and azithromycin.

Introduction

On December 31, 2019, several cases of pneumonia were associated with a novel coronavirus, which was subsequently named 2019 nCoV by the world health organization. As for now, its spreading worldwide as a pandemic. The coronavirus disease (COVID-19) has potential to damage vital organs such as lungs, heart, liver, and kidneys in adults [1]. Among possible therapies, chloroquine and hydroxychloroquine have been advocated as a promising therapy because of its anti-inflammatory and potential antiviral properties. The drugs, known for their immunosuppressive and antimalarial effects, have risen to the top of many

treatment algorithms alone or in combination with azithromycin. All of these drugs are QTc prolonging [2]. We report the case of a patient treated for COVID-19, in which the risk of QTc prolongation increased when other conditions were added.

Patient and Observation

A 37-year-old woman with no medical history, presented for head ache, anosmia, dry cough, arthralgia and fever of 40°c evolving for two days. The patient had previously contacted her husband which tested positive for COVID-19 a day before. She was well appearing, and her blood pressure and hemodynamic constants were normal (blood pressure of 110/70 mmhg, blood oxygen saturation level of 95%, heart rate of 67 pulse per minute, respiratory rate of 21 breath per minute). She had class I obesity with a body mass index of 32. Physical examination noted pharyngitis and rhinitis. There were no further signs suggestive of lower respiratory tract involvement. Also, no gastrointestinal complaints before presenting to the hospital were noted. Throat swab tested positive for SARS-CoV-2 nucleic acid using real-time polymerase chain reaction (RT-PCR). Meanwhile, laboratory workup revealed thrombocytopenia (platelets of 131000/mm3), leucopenia (white blood count of 2930/mm3, lymphocytes of 980/mm3, neutrophils of 1600/mm3), hyperferritinemia of 366 ng/ml, and high CRP of 27 mg/l. Her QTc was 380 ms on electrocardiogram (ECG). The patient was treated according to the Moroccan protocol for the management of adult cases of COVID-19 [3]. Hence, she was given chloroquine (500 mg two times per day for ten days) and azithromycin (500 mg once a day the first day, then 250 mg every day for six days), along with vitamin C (1g two times a day for ten days) and Zinc supplements (90 mg two times a day for ten days). From the first day of treatment, the patient developed incoercible vomiting despite antiemetics (metopimazine 10 mg twice a day per intravenous). By the second day, she reported dizziness. Serum electrolytes testing found hypokalemia of 3.2 mmol/l. ECG found prolonged QTc of 510 ms. Potassium supplementation was started (potassium chloride: 40 mEq per dose, two times a day per oral). Temporary cessation of chloroquine and azithromycin was necessary. After what her vomiting resolved and potassium level normalized (K+ of 3.8 mmol/l). QTc interval was back to normal with 370 ms. Resumption of treatment was possible by the fourth day. In this perspective, chloroquine was withdrawn and replaced with hydroxychloroquine (200 mg three times per day for ten days). Since then, clinical signs improved quickly, daily ECGs proved normal, and no new side effects were noted. Our patient was asymptomatic by the sixth day, while her blood tests revealed no more cytopenia or inflammation, and her potassium level remained normal. Two consecutive throat swabs for SARS-CoV-2 PCR were negative on the ninth and tenth day of admission. The patient was discharged home after a hospital stay of twelve days.

Discussion

Sudden cardiac death is among the most common causes of cardiovascular death in patients with COVID-19 [2]. The majority of sudden cardiac deaths are caused by acute ventricular arrhythmia following repolarization disturbances [2]. There are many factors that predispose to QT prolongation including, e.g. age, female gender, left ventricular hypertrophy, heart failure, myocardial ischemia, hypertension, diabetes mellitus, increased thyroid hormone concentrations, elevated serum cholesterol, high body mass index, slow heart rate and electrolyte abnormalities (including

hypokalemia and hypomagnesaemia) [4]. However, one of the most common causes of acquired QTc prolongation is the use of specific drugs, probably partly explained by gene–drug interactions [5]. As of July 20, 2020, 17236 cases and nearly 273 deaths of COVID-19 have been reported in Morocco [6]. The Moroccan ministry of health approved in early April 2020 a nationwide protocol using the association of chloroquine or hydroxychloroquine with azithromycin in all adults testing positive for COVID-19 [3]. Both drugs are QTc prolonging [7], which poses a risk of sudden cardiac death in certain populations. There are a number of confounding factors in our case that may have led to long QTc syndrome, including hypokalemia, azithromycin use and chloroquine use. Her condition was rapidly resolved after treatment withdrawal, simultaneously with the use of anti-emetics and potassium supplementation. In cases like this, Metopimazine is a safe agent as it is not a QTc prolonging drug. On the other hand, hydroxychloroquine was very well tolerated. In a cohort study including 90 patients, the ones who received hydroxychloroquine for the treatment of pneumonia associated with COVID-19 were at high risk of QTc prolongation, and concurrent treatment with azithromycin was associated with greater changes in QTc [8]. Hypokalemia increases vulnerability to various tachyarrhythmias, and for that specific reason, we should closely monitor electrolytes and QTc in patients with COVID-19 when we start medications like azithromycin and also chloroquine [9]. The current recommendation to assess QTc before starting medication and close monitoring in patients with additional risk factors or patients using other medications that could enhance the QTc prolongation [8].

Conclusion

Clinicians should carefully weigh risks and benefits if considering chloroquine and azithromycin, with close monitoring of QTc. Monitoring of other concomitant QT-prolonging conditions like hypokalemia will likely decrease the frequency of adverse drug events.

Competing Interests

The authors declare no competing interest.

Authors' Contributions

HN: writing the paper, KF, RQ, AB, IS: final approval.

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