CASE REPORT

Wide complex tachycardia in a patient with COVID-19 treated with chloroquine/azithromycin

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Abstract

Azithromycin and chloroquine/hydroxychloroquine are being used internationally off-label to treat patients with coronavirus disease 2019 (COVID-19) based on in vitro and weak studies involving humans. However, the evidence about the benefit of these drugs is very uncertain and on the other hand, information regarding possible harms is on the rise. There are increasing reports associating chloroquine/hydroxychloroquine with/without azithromycin with prolonged QT and ventricular arrhythmias (monomorphic or polymorphic ventricular tachycardia) in COVID-19 patients. We present the case of a severe acute respiratory syndrome coronavirus 2-infected kidney transplant patient for which he received treatment with chloroquine plus azithromycin and on Day 4 of therapy, the patient suddenly developed a wide complex tachycardia. Because of the increasing reports of adverse effects related to these drugs, their use should be avoided until further evidence of clinical benefit is available.

INTRODUCTION

The pandemic of coronavirus disease 2019 (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) presents an unprecedented challenge to identify effective drugs for prevention and treatment. The aminoguanidine drugs chloroquine and hydroxychloroquine have received worldwide attention as potential therapies. Optimism for repurposing these drugs stems from two lines of evidence: inhibition of coronaviridae (including SARS and SARS-CoV-2) in vitro and an open-label non-randomized study that involved treatment using hydroxychloroquine (combined in some patients with azithromycin, an azalide antibiotic with putative antiviral properties) that reported improved virologic clearance in the intervention group [1]. Regimens employed vary but are generally equivalent to 400–1200 mg hydroxychloroquine (250–1000 mg chloroquine) per day for ~5 days [2]. However, both agents can cause rare and serious adverse effects (<10%), including corrected QT (QTc) prolongation, hypoglycemia, neuropsychiatric effects and retinopathy. The potential risk of arrhythmias must be monitored, especially in critically ill patients and in those taking concomitant QT interval prolonging medications such as azithromycin and fluoroquinolones [1]. The safety profile of these drugs in the context of COVID-19 patients is still unknown, although there are increasing reports of adverse effects with this treatment. In this regard, we present the case of a patient with COVID-19 treated with chloroquine plus azithromycin who developed a sudden episode of wide complex tachycardia (WCT).

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WCT in a patient with COVID-19 treated with chloroquine/azithromycin

Figure 1: Wide complex tachycardia presented in the patient.

Figure 2: The rhythm following pharmacologic cardioversion.

CASE

A 43-year-old man was admitted to the emergency department due to intermittent fever, dry cough and progressive dyspnea started a week ago. He had a 24-year history of hypertension and chronic renal disease due to non-specific glomerulonephritis, receiving a kidney transplant from a cadaveric donor 6 months ago and surgical parathyroidectomy due to tertiary hyperparathyroidism. His medications were nifedipine 30 mg twice daily, metoprolol 100 mg twice daily, mycophenolic acid 500 mg twice daily, tacrolimus 1 mg twice daily, prednisone 25 mg/day, calcium carbonate 4 g/day and calcitriol 0.25 mcg/day. Physical examination revealed tachycardia, shortness of breath and a peripheral capillary oxygen saturation level of 83% (room air). Relevant laboratory findings were leucopenia (1980 mm3, normal range [NR] 4000–10 000 mm3), lymphopenia (0.200 mm3, NR 0.600–3400 mm3) and lactate dehydrogenase 981 U/L (NR 240–480 U/L); Serum electrolytes were normal: sodium 136 mmol/L (NR 136–145 mmol/L), potassium 4.1 mmol/L (NR 3.5–5.1 mmol/L), magnesium 1.8 mg/dl (NR 1.6–2.5 mg/dl), calcium 8.8 mg/dl (8.6–10.2 mg/dl), phosphorus 3.91 mg/dl (NR 2.7–4.5 mg/dl). Electrocardiogram (ECG) showed sinus tachycardia. Chest radiograph showed bilateral ground glass image. The SARS-CoV-2 polymerase chain reaction with nasopharyngeal swab was positive.

The patient was classified as COVID-19 severe disease according to World Health Organization classification [3] and was transferred to the department of Internal Medicine where he was evaluated to select the management as follows: the QTc of the baseline ECG was calculated manually using the Bazett formula, being 410 ms (NR 350–480 ms), and a validated risk score to predict QT interval prolongation in hospitalized patients was performed, by which he was classified as 'low risk' (6 points) [4]. Therefore, a standard regimen with chloroquine plus azithromycin was started (chloroquine 500 mg twice on day 1, then 500 mg daily on Days 2–5 plus azithromycin 500 mg daily on Day 1, then 250 mg daily on Days 2–5). An informed consent for the treatment was obtained according to the institutional standards. However, on Day 4 of therapy, the patient suddenly developed a fast-WCT at 180 beats/min, managed as ventricular tachycardia (VT) with amiodarone 300 mg IV. Unfortunately, it was not possible to record the complete 12 lead ECG, only a DII rhythm strip. A close inspection showed possible atrio-ventricular dissociation (Fig. 1, red dots) that suggests the diagnosis of VT. The rhythm following cardioversion 5 min after starting amiodarone infusion was visualized with a DII rhythm strip, which showed an irregular rhythm, QRS 110 ms at 100 beats/min on average with biphasic T waves with ST-segment depression, without organized atrial activity, suggesting atrial fibrillation. There was no evidence of prolonged QT (Fig. 2). A measurement of troponin I was obtained during the arrhythmia episode, which was 0.2 ng/dl (NR 0.0–0.6 ng/dl). Laboratory tests obtained on the same day (prior to the arrhythmia episode) were not relevant to explain the event (leucocytes 2050 mm3, neutrophils 1790 mm3, lymphocytes 0.110 mm3, sodium 139 mmol/L, potassium 4.26 mmol/L, magnesium 1.7 mg/dl, calcium 9.1 mg/dl, phosphorus 4.1 mg/dl).

A Cardiology Service consultation was requested; unfortunately, the patient presented a cardiac arrest (50 min after pharmacological cardioversion) without response to cardiopulmonary resuscitation and died.

DISCUSSION

The use of either chloroquine or hydroxychloroquine and azithromycin for treatment of SARS-CoV-2 infection is currently supported primarily by in vitro and weak studies involving humans [1]. Nevertheless, azithromycin and chloroquine/hydroxychloroquine are being used internationally off-label to treat patients with COVID-19 [5]. While multiple studies are
planned or underway, the current evidence about the benefit is very uncertain and on the other hand, information regarding possible harms is on the rise. In fact, both drugs are listed as definite causes of torsade de pointes at crediblemeds.org, thereby increasing the risk of drug-induced torsade de pointes and drug-induced-sudden cardiac death. In a retrospective study that included 251 hospitalized patients with COVID-19, the treatment with hydroxychloroquine (400 mg twice on Day 1, then 400 mg daily on Days 2–5) along with azithromycin (500 mg daily for 5 days) was associated with a prolonged QTc of ≥500 ms (a known marker of high-risk malignant arrhythmia and sudden cardiac death) in 23% of cases and with a torsade de pointes in one patient (estimated incidence at 0.4%) [6]. In perspective, this is 4 times the estimated incidence of single infusion of IV sotalol induced torsade de pointes (0.1%) [7].

In the present case, although we were unable to get a 12 lead ECG, we considered that the WTC was very likely a monomorphic VT based on the analysis of the DII rhythm strip. We hypothesize that such condition was possibly related to the combined chloroquine/azithromycin therapy along with the previously described associated medical conditions. The appearance of VT (without torsade de pointes) has been described in patients who received high doses of chloroquine (600 mg twice daily for 10 days) [8]. Although the dose of chloroquine was lower in the case presented, it is possible that the simultaneous use of azithromycin and tacrolimus (another medication with known capacity to increase QTc) had had a synergistic cardiotoxic effect. Another factor to consider is a possible myocarditis. Myocardial injury with elevated troponin levels occurs in 20–30% of hospitalized patients with COVID-19, with higher rates (55%) among those with pre-existing cardiovascular disease [9]. Myocarditis is a potential mechanism that could result in arrhythmogenesis among COVID-19 patients [10]. In the present case, the patient did not present with elevated troponins suggesting myocarditis. However, in autopsy cases, myocardial viral activity in the absence of evidence of myocarditis has been reported [11]. Therefore, we speculate that the presence of SARS-CoV-2 in the cardiomyocyte could result in alteration of signaling pathways that, together with proarrhythmogenic drugs, generated the arrhythmia in this patient.

In conclusion, due to the absence of clinical benefit on morbidity and mortality with the use of antimalarials or azithromycin or the combination of both drugs in patients with COVID-19, and given the increase in reports of adverse effects related to these drugs, their use should be avoided until further evidence regarding their safety and efficacy is available.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Informed consent for publication has been obtained from the authorized representative of the patient, in line with the COPE best practice guidelines.

CONFLICTS OF INTEREST STATEMENT

The authors declared no conflicts of interest.

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