COVID-19 and QT interval prolongation: more than just drug toxicity?

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A 70-year-old Caucasian man with a history of hypercholesterolaemia, no relevant family or other medical history and normal electrocardiogram (ECG) presented at the emergency room with a 6-day history of cough, fever, and dyspnoea. Blood oxygen saturation was 95% and chest X-ray showed patchy interstitial bilateral opacities suggestive of COVID-19 pneumonitis. Blood tests revealed lymphopenia (600/µL) and elevated fibrinogen (639 g/L), lactate dehydrogenase (405 U/L), and C-reactive protein (185 mg/L). The polymerase chain reaction for SARS-CoV2 was positive and he received 400 mg of hydroxychloroquine b.i.d. on hospital admission followed by 200 mg b.i.d. for four additional days. This treatment was complemented with 500 mg of azithromycin during these 5 days. The patient had progressive deterioration and was placed under mechanical ventilation (Day 6 from admission). He remained stable for the following 5 days when he developed sinus bradycardia which was reverted with isoproterenol infusion during 2 days. Two days later, bradycardia (42 b.p.m.) reappeared together with deep negative T waves on ECG monitoring. The following day (Day 14) a 12-lead ECG (Figure 1A) showed diffuse T-wave inversion and severe QT (620 ms) and QTc (532 ms and 560 ms by Bazett and Fridericia methods, respectively) interval prolongation. Isoproterenol infusion quickly restored normal heart rate (70 b.p.m.) and new ECGs (Days 16 and 22) showed normal QTc interval with flat and inverted T waves in most ECG leads (Figure 1B). Electrolyte balance and renal function indicators were within normal values during the whole hospital stay. High-sensitive troponin I was 12, 447, 221, 109, and 56 ng/L on days 6, 14, 15, 16, and 17, respectively (50 ng/L reference value). A transthoracic echocardiogram (Day 22) showed moderate global left ventricular hypertrophy (15 mm of interventricular septum), normal systolic function, and no ventricular segmental defects. This together with clinical improvement led to commencing the patient on intermittent mechanical ventilation (Day 22).

Figure 1 12 lead ECG recorded on days 14 (panel A) and 22 (panel B) from hospital admission. Panel A shows sinus rhythm at 42 bpm, diffuse T wave inversion and 620 ms QT interval (QTc of 532 ms and 560 ms by Bazett and Fridericia methods respectively). Panel B shows sinus rhythm at 103 bpm, diffuse T wave inversion and 360 ms QT interval (QTc of 473 ms and 432 ms by Bazett and Fridericia methods respectively).
The use of antiviral drugs during the COVID-19 pandemic has raised concerns about QT interval prolongation.\(^1\) However, QT interval prolongation may result from mechanisms other than drug toxicity such as electrolyte imbalances, ischaemia, or myocardial inflammation. Hydroxychloroquine and azithromycin half-lives are 32 ± 9 days and 68 h, respectively. However, the late onset of bradycardia and QT prolongation together with the quick recovery of these alterations and persistence of diffuse T-wave inversion make drug toxicity unlikely as the main mechanism for them. Repolarization abnormalities due to myocardial ischaemia have recently been reported in COVID-19 patients\(^2\) but the mild change in troponin levels and diffuse T-wave inversion make unlikely that they were the only mechanism for QT prolongation in this patient. Finally, inflammation can prolong ventricular action potential duration by modulating the expression and/or function of several cardiomyocyte ion channels, specifically K\(^+\) and Ca\(^{++}\) channels (inflammatory cardiac channelopathies).\(^3\) Diffuse T-wave inversion and transient troponin elevation supports a significant role of myocardial inflammation on QT prolongation in this patient. This case emphasizes that QT prolongation may result from mechanisms other than or concurrent with drug toxicity in COVID patients.

Data availability: The data that support the findings of this case report are available from the corresponding author, JLM, upon reasonable request.

Conflict of interest: none declared.

References

