A regular feature of the *American Journal of Critical Care*, the **ECG Puzzler** addresses electrocardiogram (ECG) interpretation for clinical practice. We welcome letters regarding this feature.

Noteworthy Electrocardiographic Changes Following Pharmacologic Treatment of COVID-19

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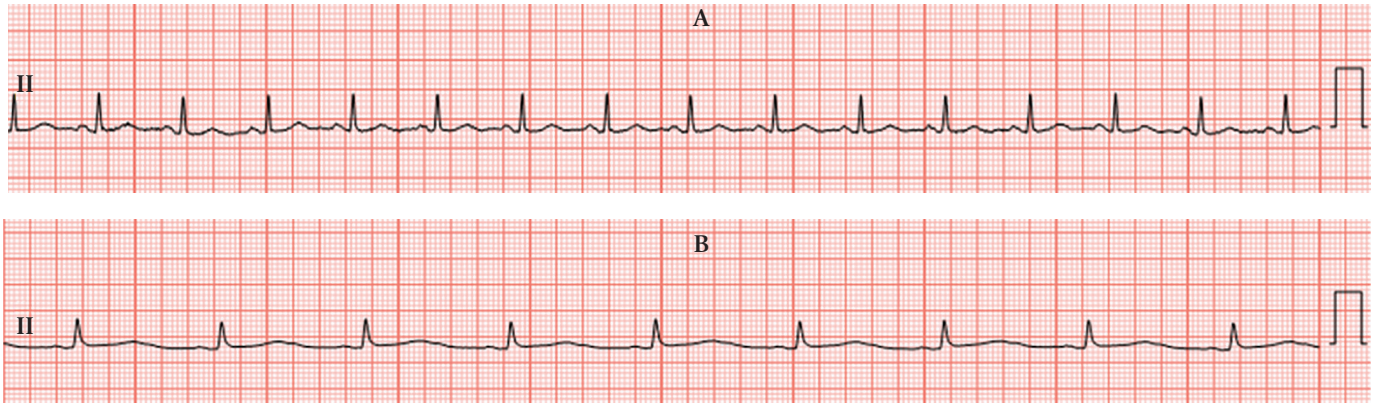
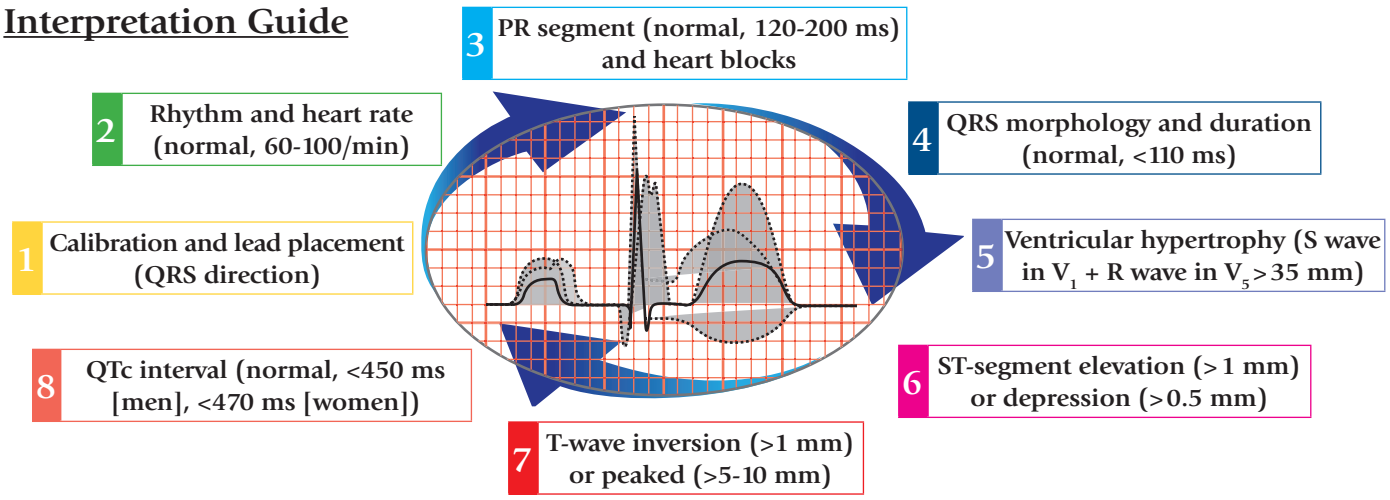
Scenario: A 67-year-old woman arrived in the emergency department with shortness of breath after a 4-day period of dry cough and fever. Significant history included diabetes, hypertension, and asthma, which were all well controlled before admission. Her baseline vital signs were temperature 100.7 °F (38 °C), blood pressure 95/60 mm Hg, and oxygen saturation of 94% on 4 L/min of oxygen per nasal cannula. The patient was subsequently admitted to the intensive care unit (ICU) and ultimately tested positive for coronavirus disease 2019 (COVID-19). Her respiratory status deteriorated quickly, requiring intubation, and it was decided to start treatment with azithromycin and hydroxychloroquine. Two days later, new onset paroxysmal atrial fibrillation developed and the patient was started on amiodarone. Rhythm strip A was obtained on the day of admission to the ICU, and rhythm strip B was obtained 24 hours after initiating amiodarone and 3 days after initiating azithromycin and hydroxychloroquine.





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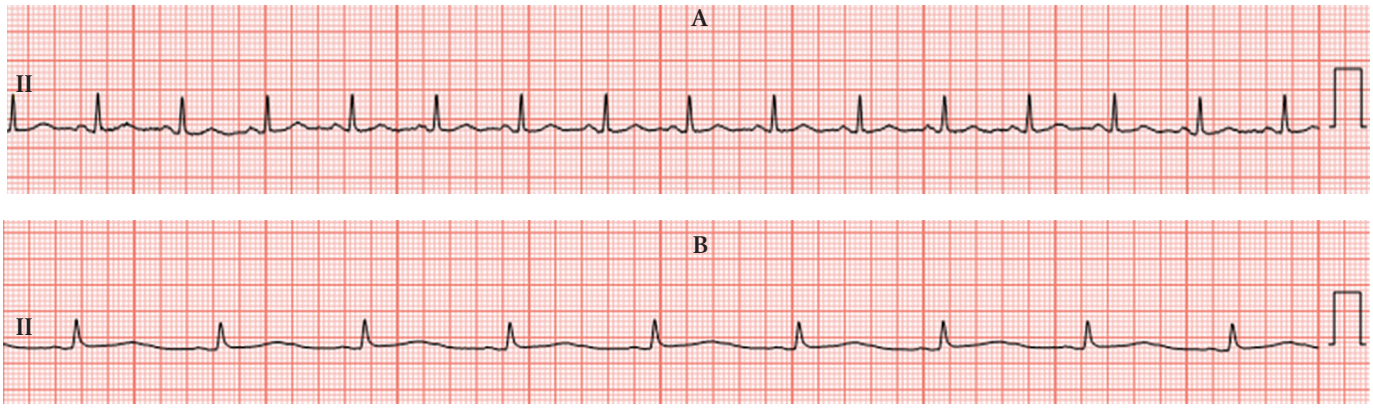

Answers and Rationale

Interpretation Guide

1. Both rhythm strips (A and B) are properly calibrated at 10 mm/mV
2. (A) Sinus rhythm rate 94 beats per minute; (B) sinus bradycardia 55 beats per minute
3. Normal PR interval (0.16 ms) in both rhythm strips with P waves noted before each QRS complex
4. Normal QRS duration and morphology in both rhythm strips
5. Cannot assess ventricular hypertrophy with only lead II
6. No ST-segment deviations in either rhythm strip
7. No inverted or peaked T waves in either rhythm strip
8. QTc interval normal in strip A but extremely prolonged at 651 ms in strip B

ECG Interpretation

(A) Normal sinus rhythm on admission to ICU; (B) Sinus bradycardia with drug-induced long-QT syndrome on day 3.

Clinical Implications

A number of risk factors are known to contribute to drug-induced long-QT syndrome, placing patients at risk for the development of torsades de pointes, a multifocal ventricular tachycardia that can deteriorate to ventricular fibrillation and sudden cardiac death. Some risk factors that place patients at a higher risk of drug-induced QT prolongation include use of more than 1 QT-prolonging agent, heart disease, congestive heart failure, advanced age, female sex, electrolyte disturbances, and impaired hepatic and/or renal function.

Drug-induced QT prolongation is caused by medications that interact with the potassium channel, particularly the hERG channel, leading to an excess of positively charged ions extending the repolarization phase of the ventricular action potential in myocytes in the midmyocardium. Data indicate that hydroxychloroquine and azithromycin interact with the hERG channel and can result in QT prolongation. Although amiodarone markedly prolongs the QT interval, it is rarely associated with torsades de pointes; this is hypothesized to be due to uniform potassium inhibition across the myocardium, which reduces the substrate for the development of arrhythmias. However, with the combination of multiple QT-prolonging drugs, such as in this case, the potentiating effect is known to increase risk of torsades de pointes.

Management

Close monitoring and reducing modifiable risk factors, such as correcting electrolyte abnormalities and adjusting medication dosage, can improve the safe use of QT-prolonging medications.

Electrocardiographic monitoring and discontinuing azithromycin and/or reducing the dose of hydroxychloroquine if the QTc increases by >60 ms from the predrug measurement or if the QTc exceeds 500 ms is recommended. In this particular case, the azithromycin, hydroxychloroquine, and amiodarone were all discontinued because extreme QTc prolongation was noted and the patient had maintained sinus rhythm for several days. Ongoing assessment for recurrence of atrial fibrillation, which may require amiodarone, is indicated. The QTc normalized the following day. Although other aggressive and supportive treatments were maintained, this patient died of respiratory failure related to COVID-19.