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CASE REPORT

Brugada Syndrome Unmasked by a Mosquito

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Two weeks after returning from missionary work in Haiti, a 53-year-old woman with no significant past medical history presented with 5 days of worsening fevers, chills, diaphoresis, myalgias, and severe nausea. Notably, she did not take malaria prophylaxis while in Haiti.

Her temperature was 40.1°C, her blood pressure was 100/58 mm Hg, and her heart rate was 102 beats per minute. Physical examination was remarkable only for her ill appearance. Initial lab work revealed anemia (hemoglobin, 10.4 g/dL; hematocrit, 29.4%), thrombocytopenia (23,000/mm),[3] and evidence of acute renal failure (blood urea nitrogen, 58 mg/dL; creatinine, 4.2 mg/dL). Other labs were within normal limits.

Malaria was considered high on the differential diagnosis. A parasite smear was therefore obtained, and the findings were consistent with *Plasmodium falciparum* infection (5.5% parasitemia).

She was admitted to the intensive care unit for hydration and initiation of antimalarial therapy. Her severe nausea prevented administration of oral medications; therefore, the infectious disease consultant recommended treatment with intravenous quinidine.

Prior to initiation of quinidine, an electrocardiogram (ECG) was obtained (Figure 1). No prior ECGs were available for comparison. Prominent ST segment elevation was noted, prompting reassessment of the patient. She denied chest pain. Cardiac enzymes were normal, and an urgent echocardiogram demonstrated normal ventricular function with mild mitral regurgitation. Given that suspicion for acute coronary syndrome was low, the ECG findings were managed conservatively.

Overnight, she defervesced and appeared to improve clinically. Cardiac enzymes remained negative. A repeat ECG obtained several hours after admission revealed complete resolution of the ST elevation (Figure 2). Repeat ECGs remained normal through the time of discharge, and no ventricular arrhythmias were noted on telemetry.

On the basis of the characteristic ECG appearance, a presumptive diagnosis of Brugada syndrome was made. The patient did not have a history of presyncope, syncope, or agonal night-time breathing or a family history of sudden death. Two weeks following discharge, she was seen in the outpatient electrophysiology clinic to discuss further risk stratification. A procainamide challenge, followed by programmed ventricular stimulation (electrophysiology study), was recommended. The procainamide challenge revealed ST segment changes consistent with Brugada syndrome. She was not inducible for ventricular arrhythmias during the electrophysiology study. On the basis of these findings as well as her lack of symptoms, there was no indication for an implantable cardioverter defibrillator.

Discussion

The finding of ST segment elevation in a critically ill patient raises concern for a variety of processes, including myocardial infarction, coronary vasospasm, myocarditis, pericarditis, and electrolyte abnormalities. Our patient's presentation was not consistent with any of these diagnoses, and the ST segment changes had the highly characteristic coved appearance seen in patients with Brugada syndrome.

Brugada syndrome, which was first described in 1992,[1] is an inherited cardiac channelopathy. It is most commonly associated with loss-of-function mutations in SCN5A, the gene that encodes the α subunit of the cardiac sodium channel. The syndrome displays autosomal dominant inheritance with variable penetrance, and affected individuals are at increased risk of sudden death due to ventricular fibrillation.

The classic ECG manifestations of Brugada syndrome consist of an RSR′ pattern (pseudo-RBBB) with a ≥2-mm convex (coved) ST segment elevation and T wave inversion in leads V1 to V3 (Figure 1). There are also 2 less common patterns that display a saddle-back ST-T configuration with lesser ST segment elevation and upright or biphasic T waves. All 3 patterns can be transient, and their expression can be modulated by a number of factors, including autonomic tone, electrolyte abnormalities, ischemia, drugs, and body temperature.

The ECG appearance of Brugada syndrome is the result of the decreased function of the cardiac sodium channel. The inward flow of sodium through this channel is what depolarizes the cell. When this flow is blunted, the repolarizing effect of the transient outward potassium current is left relatively unopposed, and the action potential duration (APD) is shortened. This effect is prominent in the right ventricular outflow tract epicardium (which is why the ECG changes are noted in the precordial leads overlying this territory). Because the APD determines the refractory period of a cell (ie, how soon the cell can be re-excited), the shortening of the APD allows epicardial cells to return to an

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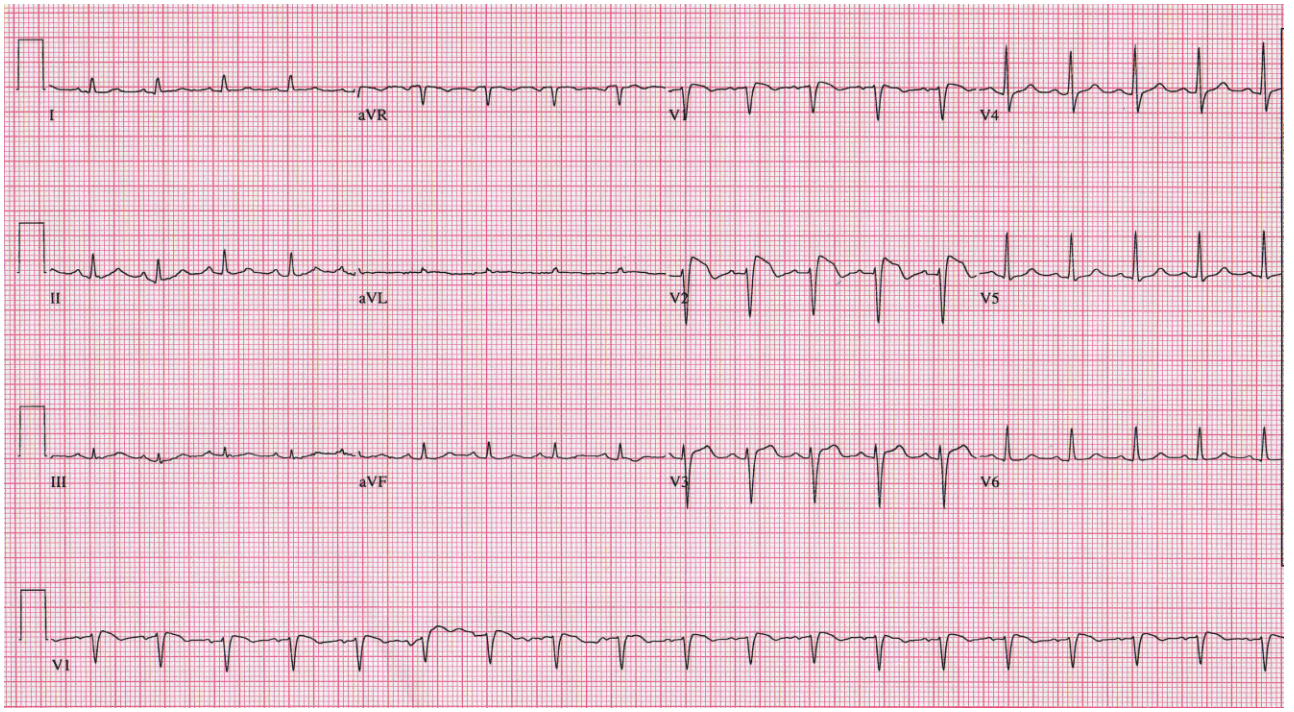

FIGURE 1. Initial ECG. Note the pseudo-RBBB pattern with prominent convex ST segment elevation in leads VI-V3. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

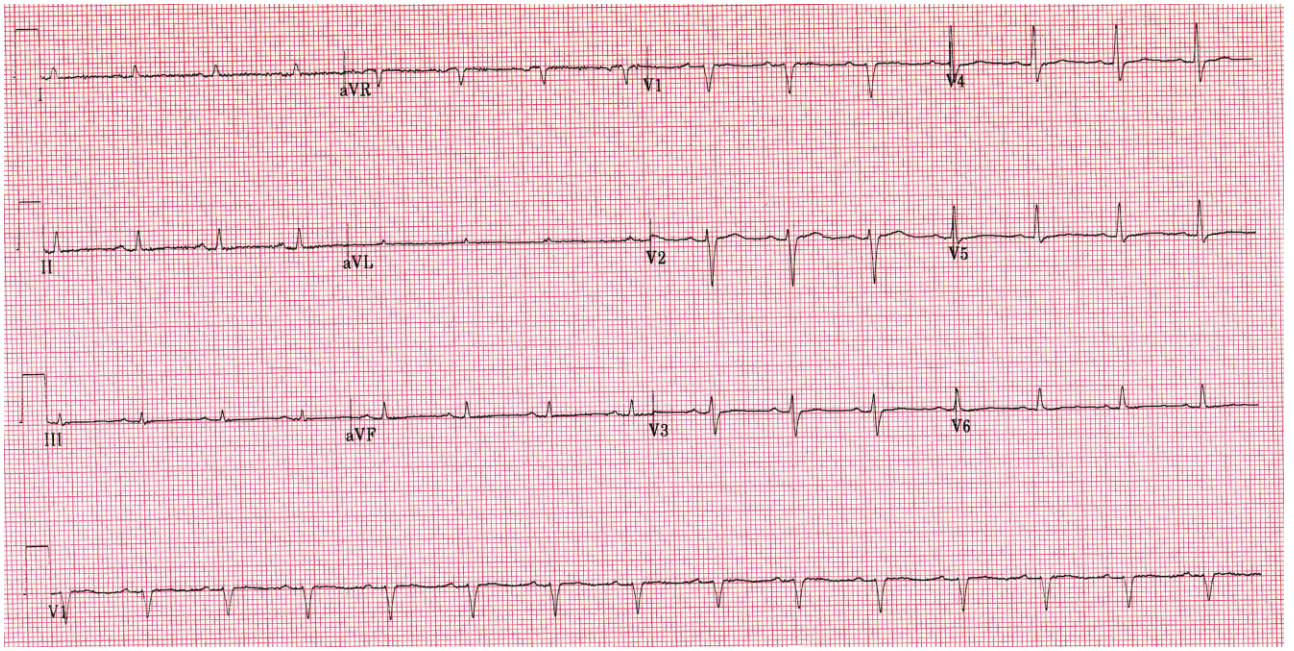

FIGURE 2. ECG after initiation of quinidine and defeverescence. All abnormalities have resolved. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

excitable state while neighboring cells in the other myocardial layers are still refractory. This phenomenon, which is known as transmural dispersion of refractoriness, creates a voltage gradient between cellular layers and provides an ideal substrate for the precipitation of sustained reentrant ventricular arrhythmias.[2]

Two issues related to our case bear further explanation. First, on the basis of quinidine's sodium channel blocking properties (it is a class I antiarrhythmic), one would predict that it would exacerbate Brugada syndrome. Although this is true of other class I drugs, quinidine also is a potent blocker of transient outward potassium current, and this effect can

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actually lead to normalization of the ECG.[2] Second, febrile illness can cause premature inactivation of the sodium channel in patients with Brugada syndrome,[3] and fever can unmask the ECG changes and even promote arrhythmias in susceptible patients.[4] We postulate that our patient had her underlying Brugada syndrome unmasked by her febrile illness and that the initiation of quinidine (blockade of transient outward potassium current) and defervescence (improved sodium current) contributed to the normalization of her ECG.

Although the details of our patient's presentation are somewhat unusual, we hope that this case highlights the dilemma created by the incidental discovery of a Brugada-pattern ECG. Clinicians need to be aware that the cornerstone of the evaluation centers on determining whether the patient has any risk factors for sudden death: ventricular arrhythmias, a family history of sudden death, or symptoms suggestive of aborted sudden death (syncope, seizures, or nocturnal agonal respiration). In the absence of any of these risk factors, asymptomatic individuals are likely at low risk and can be followed clinically. If the diagnosis is in question, the typical ECG pattern can be elicited by challenge with a sodium channel blocking agent (most commonly procainamide). Although many patients will often undergo further invasive risk stratification, the utility of this approach is the subject of controversy. Finally, screening of family members should be considered.

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