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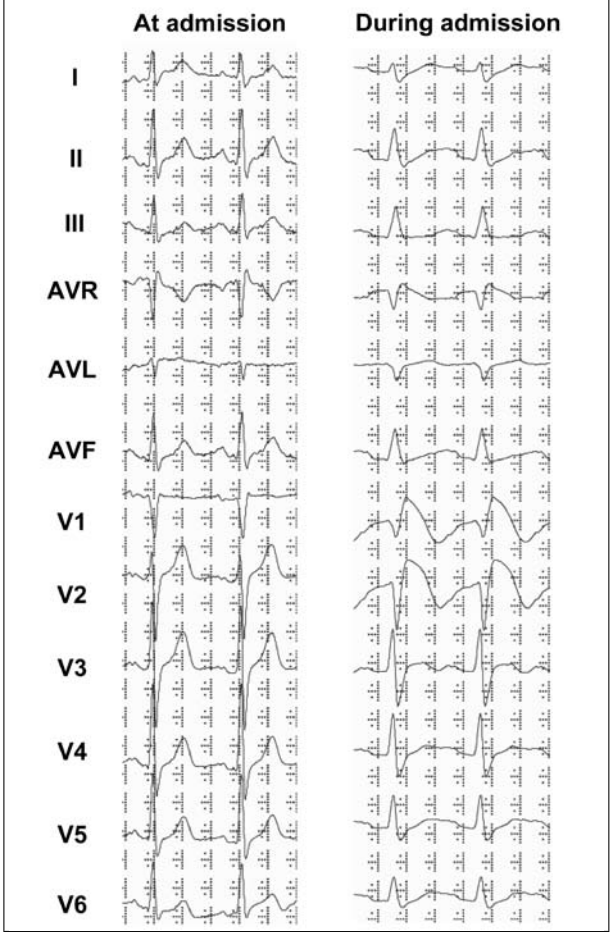
Brugada syndrome induced by amitriptyline toxicity

Dear Editor,

A 52-year-old woman was found comatose with an empty box labelled olanzapine by her side. She was taking olanzapine for psychotic depression, but had no cardiac history or family history of sudden death. Her other vital signs, physical examination, and routine laboratory tests were normal. The ECG showed sinus tachycardia and intraventricular conduction delay with right bundle branch block-like configuration (QRS width 128 ms, *figure 1*; left panel). Such ECG abnormalities had not been previously documented. She was admitted for observation for suspected olanzapine overdose. Several hours later, she sustained pulseless ventricular tachycardia. After resuscitation, the ECG showed that QRS complexes had widened further and merged with typical ST elevations in V_1 and V_2 (*figure 1*, right panel). Such ST elevations in right precordial leads (>2 mm J-point elevation smoothly descending into a negative T wave),[1] with ventricular tachyarrhythmias unrelated to myocardial infarction or structural heart disease, were consistent with Brugada syndrome. It was found that amitriptyline had been prescribed previously. Serum analysis revealed amitriptyline overdose (serum level 2.3 µM, therapeutic level 0.18 to 0.72 µM, toxic level >1.8 µM). She recovered without arrhythmia recurrence, but declined cardiological analysis or follow-up.

Figure 1. *ECG of abnormalities*



Brugada syndrome is an autosomal-dominant disease associated with sudden death following ventricular tachyarrhythmias. Mutations in *SCN5A*, the gene which encodes the cardiac sodium channel that initiates cardiac excitation, are found in ~30%. Other disease-causing genes await discovery. Brugada syndrome may revolve around impaired depolarisation (excitation), abnormal repolarisation, and/or additional derangements.[3] Mutant sodium channels conduct reduced current,[3] explaining conduction slowing. Cardiac sodium channel blockers, e.g., class I antiarrhythmic drugs, evoke lethal arrhythmias through excessive conduction slowing, and are used diagnostically to unmask silent disease carriers.[4] Various drugs prescribed for noncardiac disease also block cardiac sodium channels, e.g., cyclic antidepressants (amitriptyline), lithium, and some anticonvulsants. Accordingly, these drugs may provoke life-threatening arrhythmias in Brugada syndrome patients, or unmask silent carriers. Some patients may have variants in depolarisation-controlling genes that render them vulnerable to proarrhythmia induced by cardiac sodium channel blockers. Brugada syndrome ECGs were reported in 15 of 98 patients with tricyclic antidepressant intoxication.[5] These ECGs normalised when serum levels dropped to <1 µM. On admission, our patient did not have a Brugada syndrome ECG. Possibly, plasma amitriptyline levels were still rising from continued resorption from the gastrointestinal tract. Clearly, repeated ECG recording and rhythm monitoring are required if intoxication with cardiac sodium channel

blockers is suspected. Sodium bicarbonate is the drug of choice for ventricular dysrhythmias following tricyclic antidepressant poisoning.[6] How it unblocks cardiac sodium channels is unresolved.

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