Brugada Syndrome Case: Difficult Differentiation Between a Concealed Form and Tricyclic Antidepressant-induced Brugada Sign


Abstract

We describe a case of Brugada syndrome, in which recurrent syncope with convulsive seizures was induced after antidepressant treatment. The patient had been treated with five kinds of psychotropic drugs. The twelve-lead ECG after the syncope exhibited an RSR'-pattern in the precordial leads, however, a coved type ST-segment elevation was induced by a pilsicainide test. Although ventricular fibrillation was not induced in the electrophysiologic study, an ICD implantation was considered as the recommended therapy since Brugada syndrome unmasked by antidepressants could not be ruled out. The possible contribution of antidepressants to Brugada type ST-segment changes is discussed.

Key words: Brugada syndrome, antidepressant

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Introduction

It has been shown that psychotropic drugs may cause a Brugada-type electrocardiogram (ECG) (1-9). Among them, recently much attention has been focused on tricyclic antidepressants and a Brugada ECG pattern since ventricular fibrillation (VF) sometimes accompanies such drug overdoses (3). In the cellular electrophysiologic field, some tricyclic antidepressant drugs have been shown to block sodium channels and the transient outward currents, which is compatible with the actions underlying the Brugada type ECG changes (10-14). On the other hand, in the clinical setting it may not be easy to differentiate between Brugada syndrome unmasked by psychotropic drugs and a drug-induced Brugada sign. Indeed, an SCN5A polymorphism of His 558Arg was reported in a patient with a tricyclic antidepressant overdose who presented with VF (5). In addition, antidepressants may cause syncope or convulsive seizures as a manifestation of its own adverse effects. In that sense, it is occasionally very tough for cardiologists to determine a therapeutic plan, including an indication for an implantable cardioverter defibrillator (ICD), in patients with a Brugada-type ECG pattern induced by antidepressants. We encountered a case of Brugada syndrome, in which recurrent syncope with convulsive seizures occurred after antidepressant treatment. Here, we discuss the possible contribution and mechanisms of the effects of the antidepressants on the Brugada type ST-segment changes.

Case Report

A 40-year-old man was admitted to the Asahikawa Medical College Hospital for close examination of recurrent syncope with convulsions. He had no family history of sudden cardiac death. From 3 years prior, he had suffered from depression, and hence, he had been treated with five different kinds of psychotropic drugs; nortriptyline hydrochloride (tri-
Figure 1. (a) An ECG obtained in the emergency room. (b) ECGs obtained on admission. ECGs recorded from the third and second intercostal spaces are also shown.

cyclic antidepressants), mianserin hydrochloride (tricyclic antidepressant), sertraline hydrochloride (selective serotonin reuptake inhibitors), brotizolam (benzodiazepine hypnotics) and amantadine hydrochloride (dopamine agonists). In mid-February 2007, he suddenly presented with syncope accompanied by convulsive seizures while working at his desk and was referred to our Department of Emergency Medicine. On arrival at our hospital, his consciousness level was alert, and no abnormalities were found in the blood sampling, neurological findings, Brain CT or Brain MRI, and hence, he was followed up without any medications. Two years later, he again suddenly fell down; he fell into a swimming pool after standing up, and was referred to our Department of Emergency Medicine after cardiopulmonary resuscitation had been performed on him. The twelve-lead ECG on arrival in the emergency room revealed an RSR’-pattern in lead V1 and saddle-back type ST-segment elevation in lead V2 (Fig. 1-a). Although his consciousness recovered and no neurological deficits were observed in the emergency room, he was admitted to the Department of Neurosurgery for close examination. After admission, no abnormal findings on the brain CT, brain MRI or electroencephalogram were detected and hence, he was discharged. Two weeks later, in early March, he again presented with syncope while walking outside and was referred to the emergency room at the nearest hospital, and was finally admitting to our department for close examination for any ECG abnormalities or syncope. The twelve-lead ECG on admission revealed slight ST-segment elevation in leads in V1 and V2 in the 4th intercostal leads, however, an RSR’-pattern in leads V1 and V2 was noted in the 3rd and 4th intercostal space recordings (Fig. 1-b). In the pilsicainide provocation test, coved-type ST-segment changes in leads V1 and V2 were induced by a 50 mg administration of the drug (Fig. 2). Interestingly, after the pilsicainide, the PQ interval and QRS duration were markedly prolonged from 200 msec to 300 msec and 80 msec to 120 msec, respectively. Furthermore, a treadmill exercise test revealed a coved type ST-segment elevation associated with a T wave alternance-like phenomenon after exercise (Fig. 3). On the other hand, the head up tilt test was negative. The echocardiographic study was normal and late potentials were found to be negative on the signal-averaged ECG. In the coronary angiogram, no stenosis was detected. In the electrophysiologic study, ventricular fibrillation could not be induced by two consecutive extrastimuli or burst stimulation from the right ventricular apex or right ventricular outflow tract. From the results described above, this patient was diagnosed with Brugada syndrome. However, it was very difficult to differentiate between Brugada syndrome unmasked by antidepressants, that is, a concealed form of Brugada syndrome versus an acquired form of Brugada syndrome, since nortriptyline has been reported to cause Brugada type ST-segment changes and ventricular fibrillation. Although no ventricular fibrillation was induced in the electrophysiologic study and he had no familial history of sudden death, an ICD implantation was considered as one of the safe therapeutic choices to avoid the risk of sudden cardiac death. After consulting with a psychiatrist, and obtaining informed consent regarding the indication for an ICD implantation and the risk for the sudden cardiac death, nortriptyline was discontinued and careful observation of any symptoms and ECG changes was continued. Although
Figure 2. ECG changes induced by 50 mg pilsicainide administration. A coved-type ST-segment elevation in leads V1 and V2 was induced by the pilsicainide provocation. An ECG recorded from the third intercostal space is also shown.

Figure 3. ECG changes before and after a treadmill exercise test. Note that there was coved-type ST-segment elevation in leads V1 and V2 after the exercise.

the patient has been asymptomatic after 1 month of follow-up, an ICD implantation is still under consideration as a therapeutic choice.
In the present case, we encountered difficulty in determining the therapeutic plan because we could not clarify the cause of the syncope, which should be differentiated between that caused by arrhythmias due to Brugada syndrome and that caused by a drug’s adverse effect such as convulsive seizures. Furthermore, although the pilsicainide provocative test and response to the exercise test were considered to be typical of Brugada syndrome, the fact that no VF was induced in the electrophysiologic study and no familial history of sudden death was noted in this case made our recommendation for an ICD implantation difficult.

In the present case, among the drugs prescribed for the patient’s depression, only nortryptiline has been reported to cause drug-induced Brugada syndrome (3, 7-9). Furthermore, it has been demonstrated that nortryptiline could induce not only Brugada-type ECG changes but also VF by an overdose ingestion (3). Recently, Bebarta et al reported the incidence of a Brugada ECG pattern and serious complications in those patients in a large series of intentional tricyclic antidepressant ingestions (9). According to their report, 2.3% of tricyclic antidepressant ingestions [9 of 402] were associated with the development of a Brugada ECG pattern, and the patients with a Brugada ECG pattern had an increased risk of seizures, although no death or dysrhythmias were found in that group (9).

In the cellular electrophysiological field, it has been reported that some kinds of antidepressants, such as imipramine and amitryptiline block the cardiac Na channels in a manner similar to that of the class I antiarrhythmic agents (10-13). Other experimental findings have also suggested that imipramine affects the transient outward current (14). Moreover, some selective serotonin reuptake inhibitors have been reported to block neuronal Na channels, which may suggest the effects of those psychotropic drugs on cardiac Na channels (15). Accordingly, it is considered that the Brugada type ECG pattern in the present case could be explained by the psychotropic drug’s actions as described above. On the other hand, it has been reported that the provocative tests with Na’ channel blockers such as flecainide or ajmaline possess a high sensitivity and specificity to identify SCN5A-related Brugada syndrome patients (16, 17). Furthermore, an SCN5A polymorphism of His 558Arg has also been documented in a patient with a tricyclic antidepressant overdose (5). In the present case, a coved-type ST-segment elevation concomitant with prominent increases in the PQ and QRS intervals was provoked after infusing pilsicainide, suggesting that this case was an SCN5A-related Brugada syndrome patient (16, 18). Thus, we could not rule out the possibility that the Brugada type ECG changes could have been induced or unmasked due to the genetic background since we did not perform a genetic analysis.

In the present case, five different kinds of psychotropic drugs were used, and hence, it also might not be possible to rule out the additive effects of those drugs on the ECG. However, his depressive state was tough to treat, so we initially intended to stop the nortryptyline which is considered to be the most probable causative drug for a Brugada sign. As for the indication for an ICD, we basically recommended an ICD implantation in order to avoid any sudden cardiac death in this case. After obtaining his informed consent regarding the risk of sudden death, the merits and demerits of the ICD therapy, and the possibility of adverse effects from the antidepressant, an ICD therapy was considered if a continuous psychotropic drug therapy, including tricyclic antidepressants, would become required. Generally speaking, in cases with a Brugada ECG pattern and syncope after receiving antidepressants, it is considered very difficult to decide whether an ICD therapy should be performed or not since the adverse effects of the drug primarily need to be ruled out. In addition, some antidepressants may have sodium channel blocking effects, in other words, it might be similar to a state in which patients are exposed to a sodium channel blocker provocation test every day, and in that sense, it might be said that ICD therapy should be recommended for patients who need permanent antidepressant therapy. Further studies from the cellular electrophysiologic and genetic points of view are necessary to resolve these problems in patients with a Brugada sign while under antidepressant therapy.

References

outcomes of these patients after intentional tricyclic antidepressant ingestion. Am J Cardiol 100: 656-660, 2007.


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