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Brugada phenocopy associated with multiple psychotic drugs

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ABSTRACT

Brugada phenocopy (BrP) is a clinical condition characterized by transient ECG changes of Brugada syndrome (BrS), which can be due to various clinical conditions. We describe a case report of BrP due to psychotic drugs.

Case # 1

A 17-year-old female with no previous history of cardiac arrhythmia as well as syncope was brought to the emergency department due to suicide attempt. She took 10 tablets of Fluvoxamine 100 mg, 5 tablets of Risperidone 2 mg, 10 tablets of Sertraline 100 mg, 8 tablets of Fluoxetine 20 mg, and 40 tablets of metformin 1000 mg. She was lethargic on admission and venous blood gas sample showed severe metabolic and lactic acidosis. Immediate gastric lavage was performed. However, she was still in critical condition.

Twelve-lead ECG revealed sinus rhythm @ 65 bpm with coved-type ST-T changes in V1 and V2 (Fig. 1A). Since there were no antidots to drugs that patient taken and persistent lactic acidosis, decision was made in favor of hemodialysis. She underwent urgent hemodialysis and follow-up 12-lead ECG revealed sinus rhythm @ 74 bpm and incomplete RBBB with QRS duration of 115 msec. No obvious ST elevation mimicking Brugada pattern was observed after hemodialysis (Fig. 1B). Patient was transferred to the intensive care unit and unfortunately died after few hours due to persistent metabolic and lactic acidosis.

Discussion

BrP is a clinical entity where patients present with Brugada ECG patterns (ST elevation in leads V1 and V2) due to secondary reasons and once the patient's underlying condition resolves, there is a prompt resolution of the ST elevation in leads V1-V2 [1,2]. Multiple cardiac and non-cardiac conditions mimicking Brugada ECG changes have been reported and detailed list of these condition can be found at the BrP International Registry and Online Educational Portal (www.brugadaphenocopy.com) [3–7].

Several antipsychotic and antidepressant drugs are known to increase the risk of ventricular arrhythmias and sudden cardiac death. Some of these drugs can induce the Brugada pattern in the 12-lead ECG and type 1 ST changes (coved type) was the most common one [8].

In our case, patient was exposed to SSRIs and oral antidiabetic (metformin). List of drugs along with mechanism depicted in the Table 1. Although tricyclic antidepressants are more prone to induce Brugada pattern, SSRIs can also trigger ST changes in V1–2 [8]. Fluoxetine is a widely used antidepressant compound and its action is primarily attributed to inhibition of the reuptake of serotonin (SSRI) in the central nervous system. Rouleau and colleagues [9] described a patient with a mixed fluoxetine and ethanol intoxication who presented with a transient type-1 Brugada ECG pattern. Fluvoxamine can also trigger Brugada pattern by inhibiting Na currents [10]. In the present case, neither ajmaline challenge test or genetic analysis was performed due to very rapid clinical deterioration and death. Therefore, it would not be possible to rule out Brugada syndrome which could be unmasked by SSRIs.

The mechanism of ST changes was explained by reduction in the inward sodium current and a prominent outward current (Ito), which can lead to a shortened action potential in the right ventricular epicardial tissue. Spatial heterogeneity of action potential duration (APD) between the epicardium and the endocardium contributes to ST segment elevation in the right precordial leads [8]. SSRIs, particularly, fluoxetine, depressed sodium and calcium channels activation and induced significant shortening of APD in guinea pig, rabbit, and canine ventricular myocytes [11]. It has also been shown that fluoxetine blocks Nav1.5 Channels via a Mechanism Similar to that of Class 1 Antiarrhythmics [12]. Another SSRI, sertraline also inhibits sodium channels and can induce Brugada ECG changes [13].

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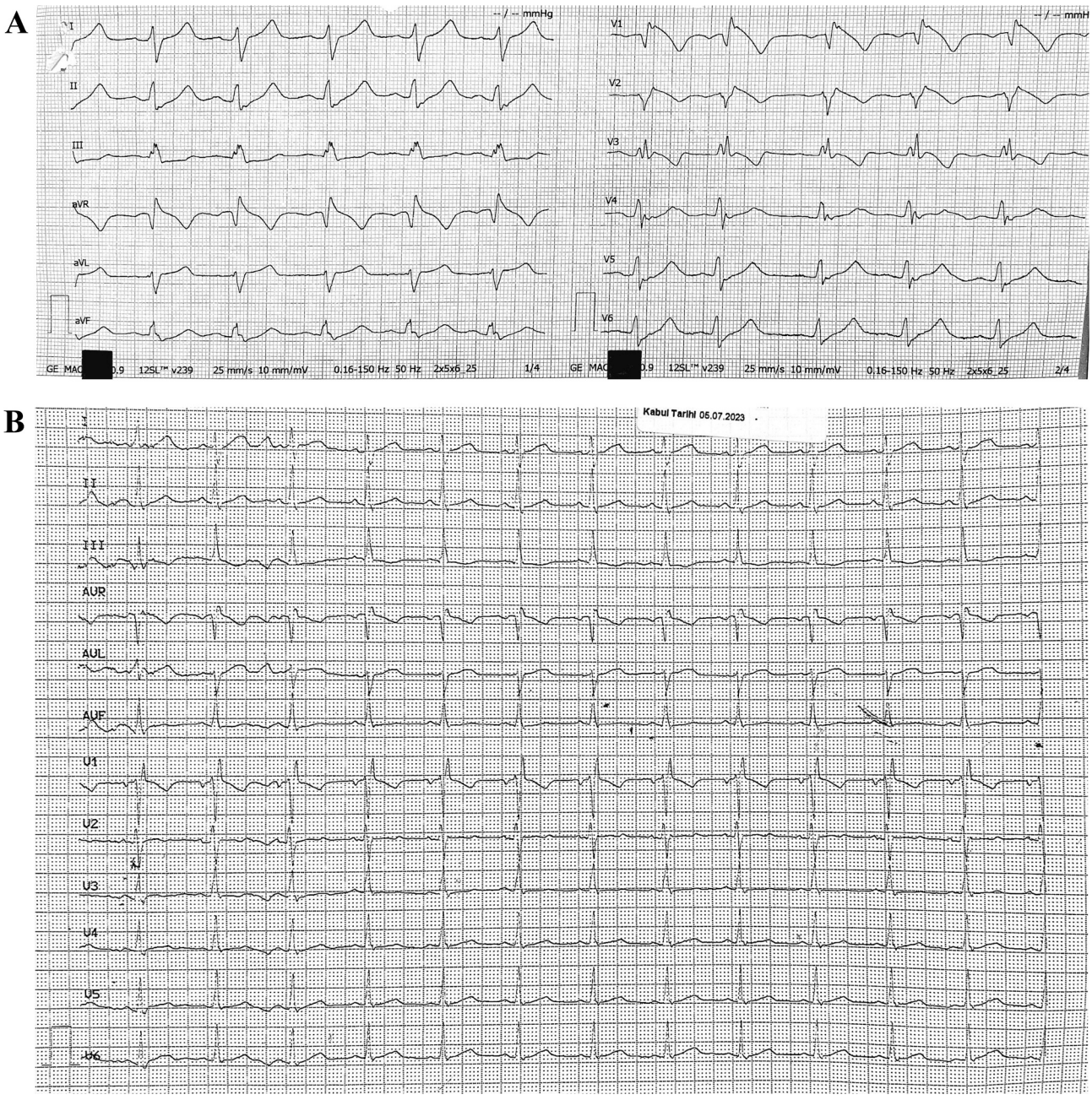

Fig. 1. A: Admission 12-lead ECG showing sinus rhythm with coved-type ST elevation in leads V1 and V2; **B:** Post hemodialysis 12-lead ECG showing incomplete RBBB with resolution of coved-type ST elevation.

Table 1
Exposed agents and mechanism of arrhythmia.

Agent	Class	Clinical indication	Mechanism	Antidote	Reference
Fluvoxamine	SSRI	OCD, Depression	⇓ Na current	None	10
Fluoxetine	SSRI	OCD, Depression	Blocks Na and Ca channels	None	9, 11
Risperidone	Antipsychotic	Schizophrenia and bipolar disorder	NA	None	NA
Sertraline	SSRI	Depression	Blocks K channels, ⇓ Na current	None	13
Metformin	OAD	DM	⇓ Na current	None	14

OAD, oral anti-diabetic; OCD, obsessive compulsive disorder; DM, diabetes mellitus; SSRI, selective serotonin receptor inhibitor.

In addition to SSRIs, patient took excessive dose of metformin, which caused severe metabolic and lactic acidosis. Along with metabolic effects metformin can also affect ionic currents. Metformin increases L-type Ca-current ($I_{Ca,L}$), decreases connexin-43 (Cx43) expression, and reduces sodium currents [14].

In conclusion, although SSRIs have fewer pro-arrhythmic side effects, excessive usage of these drugs can trigger Brugada pattern ECG.

CRediT authorship contribution statement

Enes Elvin Gul: Conceptualization, Methodology, Software, Data curation, Writing – original draft, Writing – review & editing. **Gokhan Bektasoglu:** Software, Validation, Writing – review & editing. **Zeki Dogan:** Visualization, Investigation, Supervision.

Declaration of Competing Interest

All authors declare that the manuscript, as submitted or its essence in another version, is not under consideration for publication elsewhere, and it will not be submitted elsewhere until a final decision is made by the editors of the Journal of Electrocardiology. The authors have no commercial associations or sources of support that might pose a conflict of interest. All authors have made substantive contributions to the study, and all authors endorse the data and conclusions.

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