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CASE REPORT

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Wolff-Parkinson-White, Brugada phenocopy, and flecainide toxicity: All in one patient

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Key Clinical Message

Accessory pathway Wolff-Parkinson-white is sometimes not manifested till later in life, as the conduction properties of AV node become slower, other mechanisms are also possible. Brugada pattern on EKG can be associated with various underlying clinical conditions, such as mechanical compression of RVOT by tumors. It is essential to have high index of suspicion for flecainide toxicity when encountering arrhythmias in patients taking the drug.

KEYWORDS

Brugada, flecainide, phenocopy, toxicity, Wolff-Parkinson-white

1 | INTRODUCTION

We herein report a case that encompasses three uncommon, yet important electrophysiological entities, Wolff-Parkinson-white (WPW), Brugada phenocopy, and Flecainide toxicity in a patient with acute myeloid leukemia. A brief review of the literature is discussed.

2 | CASE PRESENTATION

A 54-year-old male with history of hypertension, diabetes, and acute myeloid leukemia (AML) underwent matched unrelated donor stem cell transplant in May 2015; as his disease recurred, he underwent stimulated donor lymphocyte infusion in January 2016 complicated by graft versus host disease manifesting with oral, skin, ocular, liver, and pericardium involvement; subsequently, the patient underwent pericardial window in April 2017.

He continued to be on chemotherapy with Decitabine, his disease course was also complicated by recurrent deep venous thrombosis and pulmonary embolism in April 2018 and a left femur fracture in May 2018.

In July 2017, he presented with multiple episodes of supraventricular tachycardia (SVT), Figure 1, and he was diagnosed with WPW syndrome with intermittent pre-excitation (right posteroseptal accessory pathway as evident by negative delta wave in V1, QRS complex transition at V1-V2, and negative delta wave in inferior leads, I, II AVF, Figures 2 and 3. EKG several years ago was reported as normal with no evidence of pre-excitation (image not provided). Patient preferred to try medical treatment and to avoid electrophysiological study with ablation, he responded well to flecainide and metoprolol.

In July 2018, the patient was admitted to the bone marrow service after an episode of unresponsiveness concerning for seizure along with shortness of breath in the setting of recently diagnosed pneumonia, heart failure exacerbation, and progression of cardiac leukemia.

Physical examination was remarkable for scattered lung rales bilaterally and traces pedal edema. Patient was afebrile.

A laboratory panel on admission found the following abnormal results: hemoglobin 10.1 g/dL; platelet count: 107 000; BUN: 37; creatinine: 2.35; aspartate transaminase (AST): 94; alanine transaminase (ALT): 29; albumin: 2.1 g/dL; lactate dehydrogenase: 901 IU/L; lactic acid: 2.5 mm/L; and troponin I levels: 0.0-0.09 ng/mL.

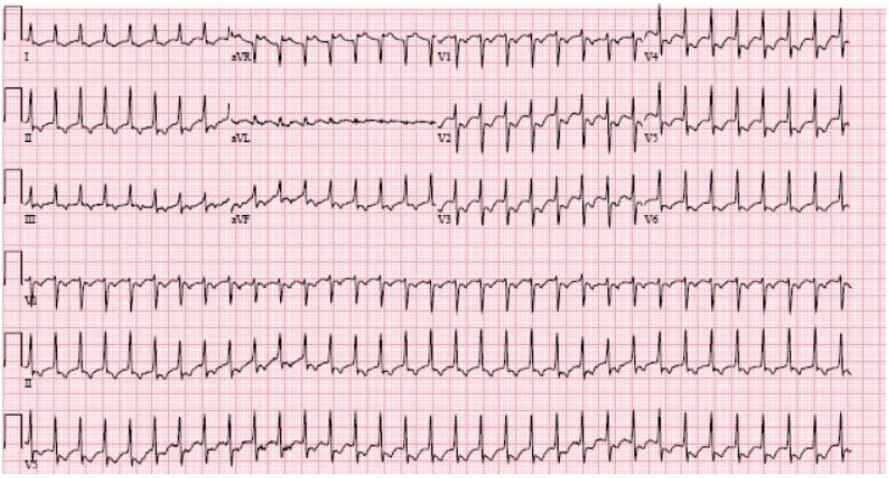

FIGURE 1 Twelve leads EKG showing an episode of SVT (July 2017)

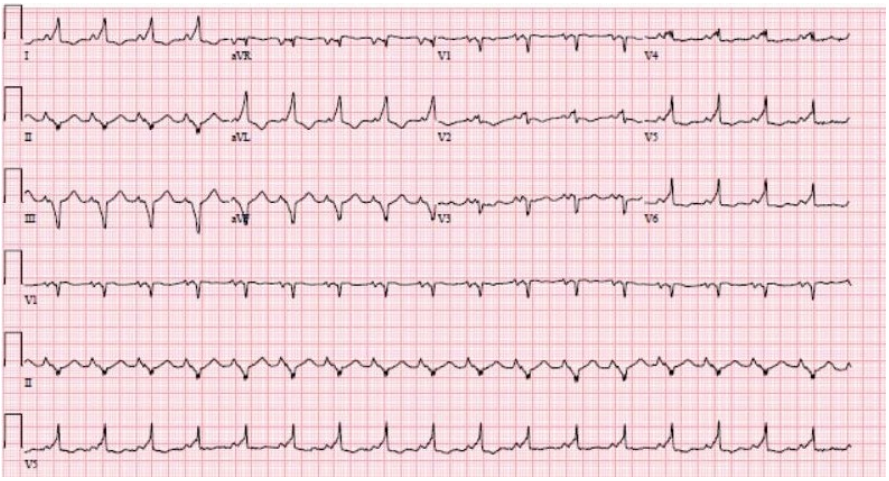

FIGURE 2 Twelve leads EKG showing right posteroseptal accessory pathway (July 2017)

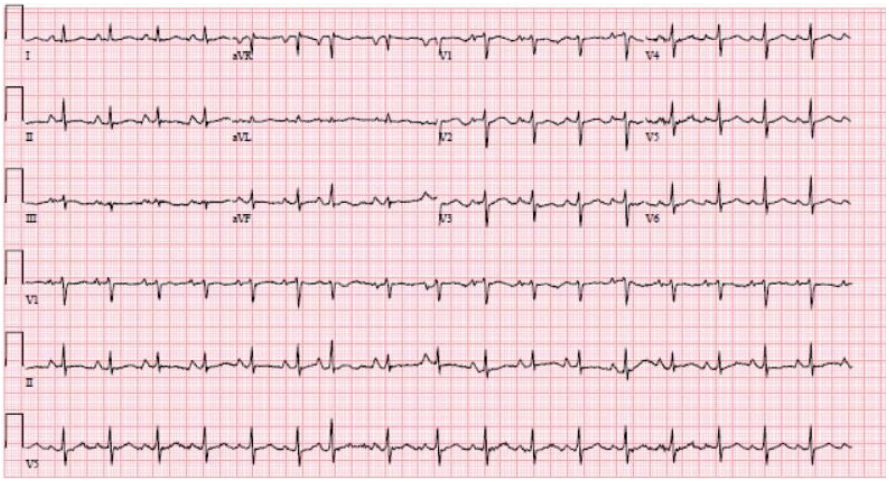

FIGURE 3 Twelve leads EKG showing sinus tachycardia without evidence of accessory pathway (July 2017)

All electrolytes including potassium were within normal ranges.

Home medications were as follows: flecainide 100 mg twice daily; amlodipine; dabigatran; doxycycline; duloxetine; Lasix; metoprolol XL; pantoprazole; and albuterol inhaler.

He was noted to have intermittent polymorphic ventricular tachycardia (PMVT) and pauses on telemetry, along with progressive widening of the QRS complex on EKGs.

On his second day of admission, he developed cardiopulmonary arrest and asystole.

In view of worsening kidney and liver functions, he was suspected to have flecainide toxicity, amiodarone, which was started during resuscitation, was discontinued, he was started on IVF and sodium bicarbonate ($NaHCO_3$), epinephrine and atropine were given, and he regained his pulse with no further pauses or PMVT. His pauses and PMVT did not recur

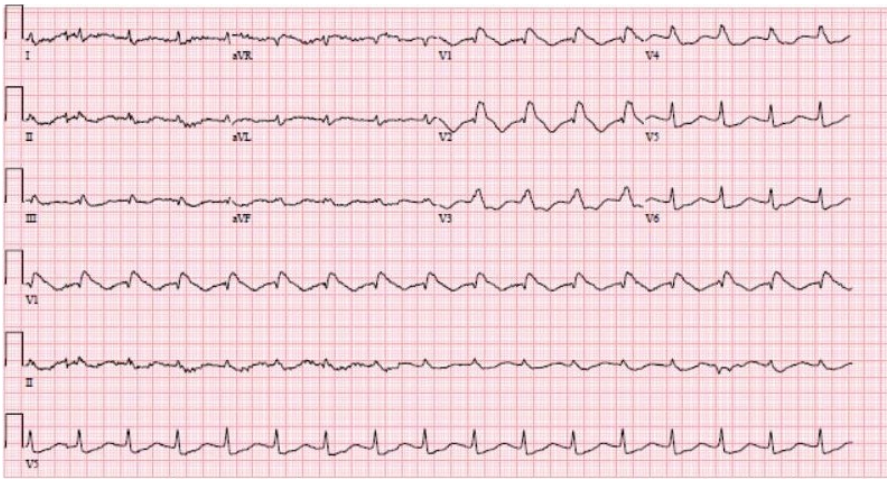

FIGURE 4 Twelve leads EKG showing persistent Brugada pattern (July 2018)

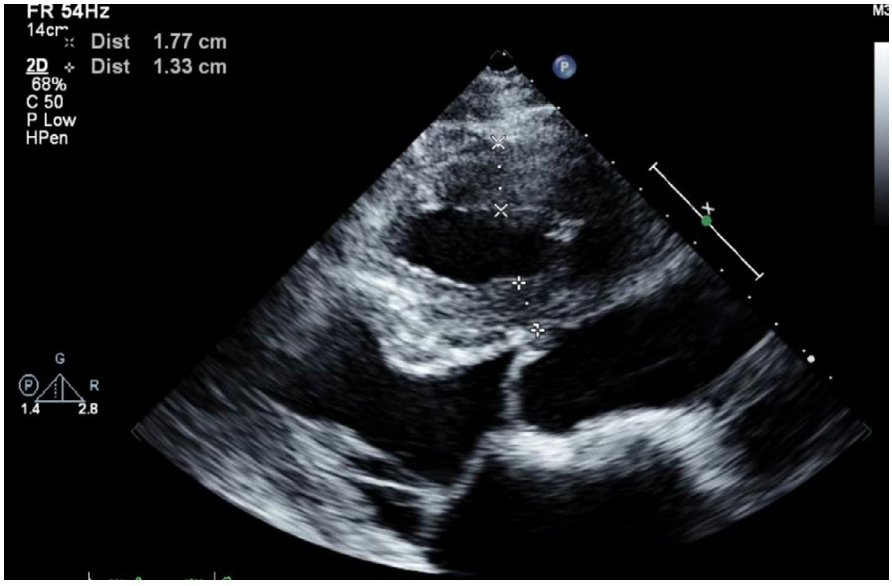

FIGURE 5 Parasternal view of 2-D echocardiogram showing remarkable thickening of the right ventricle and right ventricle outflow tract from the infiltrative tumor involvement (July 2018)

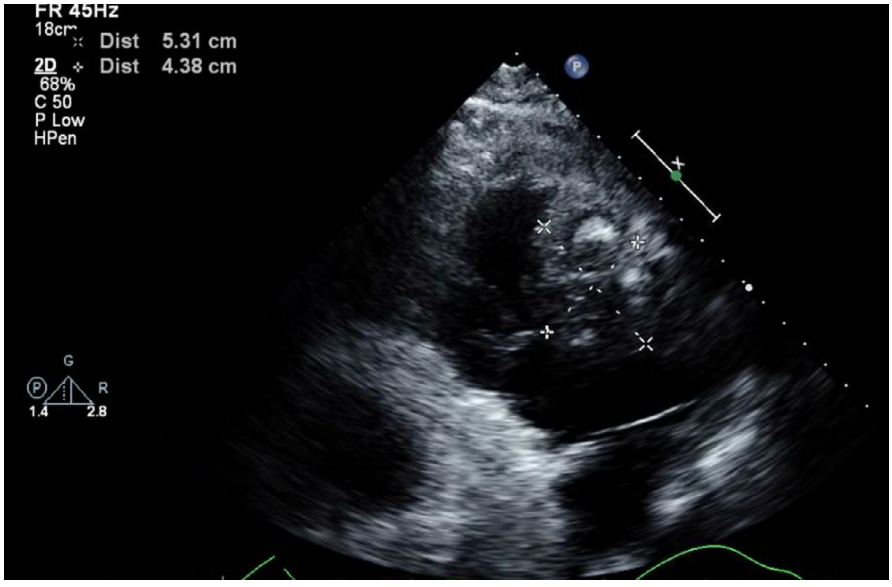

FIGURE 6 Modified parasternal view of 2-D echocardiogram showing a tumor mass involving the juncture of right ventricle and right ventricle outflow tract (July 2018)

and he remained in sinus rhythm, his QRS became narrower, Figure 4, with persistent Brugada pattern, and his flecainide level was supratherapeutic at 1.32 μg/mL (normal range 0.2-0.99 μg/mL).

A transthoracic echocardiogram revealed evidence of infiltrative tumor in his RA, RV, RVOT, and septum concerning for progression of disease, Figures 5 and 6.

During the course of his admission his respiratory status decompensated and he was started on mechanical ventilation. Patient then developed mixed shock in the setting of infiltrative tumor, heart failure, and sepsis which did not respond to broad-spectrum antibiotics with meropenem and vancomycin, in addition to vasopressors including norepinephrine and vasopressin.

In the setting of worsening shock and progression of disease, family meeting was held and decision was made to transition to comfort care. For the few days before he expired, he remained free of pauses or other arrhythmias, including PMVT.

3 | DISCUSSION

This case encompasses three uncommon, yet important electrophysiological entities, the first is WPW. No electrocardiogram prior to the diagnosis of AML showed any evidence of pre-excitation, a routine EKG later showed the WPW pattern, and this was followed by episodes of SVT.

It is possible that the accessory pathway in our patient became manifest or intermittent as the conduction properties of his AV node became slower with aging; however, another possible mechanism is that there is a growth of tissue in the form of infiltrative leukemia involving the RA and RV where the cancerous tissues were clearly identified. While this was not reported before in the literature to our knowledge, we think that it can be a possible mechanism.

Acquired accessory pathway has been described rarely, especially after Fontan procedure,[1-3] The mechanism of which has been assumed to be due to the presence of previously unapparent congenital AP and that changes in the conduction properties in the atrial myocardium after surgical intervention and surgical injury to the AV node could slow conduction, allowing a previously unapparent AP to become manifest.[2,3] However, surgically created accessory connections at the atrioinfundibular anastomosis are another cause of WPW syndrome after the Fontan procedure. The growth of myocardial cells or excitable tissues across the suture line, or the presence of electronic transmission through this line, is the main explanation for this finding.[1]

Another interesting feature of this case is that it represents a form of Brugada phenocopy, in which the mechanical compression of the RVOT by infiltrative tumor may have led to an EKG identical appearance to Brugada pattern which persisted after flecainide was discontinued.

Brugada phenocopy as a new EKG phenomenon that has recently been described as a cause of identical EKG appearance but etiologically distinct clinical entity.[4-6]

Flecainide at supratherapeutic level in our patient is thought to have caused the conduction abnormalities manifesting as pauses, broad QRS, and PMVT. It is essential to have high index of suspicion for flecainide toxicity when encountering these arrhythmias in patients taking the drug.[7]

Sodium bicarbonate ($NaHCO_3$) is commonly used to reverse drug-induced sodium channel blockade caused by different agents including flecainide.[8] While there are no definitive guidelines for management of severe flecainide intoxication, intravenous fat emulsion (IFE) and extracorporeal membrane oxygenation (ECMO) have been successfully used.[9-11]

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

EKA: data collection, writing the paper. MB: data collection, writing the paper. SCV: writing the paper. PAS: writing the paper.

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REFERENCES

1. Peinado R, Gnoatto M, Merino JL, Oliver JM. Catheter ablation of multiple, surgically created, atrioventricular connections following Fontan-Björk procedure. *Europace*. 2007;9(9):848-850.
2. Razzouk AJ, Gow R, Finley J, Murphy D, Williams WG. Surgically created Wolff-Parkinson-White syndrome after Fontan operation. *Ann Thorac Surg*. 1992;54(5):974-977.
3. Rosenthal E, Bostock J, Gill J. Iatrogenic atrioventricular bypass tract following a Fontan operation for tricuspid atresia. *Heart*. 1997;77(3):283-285.
4. Tomé G, Freitas J. Induced Brugada syndrome: possible sources of arrhythmogenesis. *Rev Port Cardiol*. 2017;36(12):945-956.
5. Gottschalk BH, Anselm DD, Brugada J, et al. Expert cardiologists cannot distinguish between Brugada phenocopy and Brugada syndrome electrocardiogram patterns. *Europace*. 2016;18:1095-1100.
6. Anselm DD, Evans JM, Baranchuk A. Brugada phenocopy: a new electrocardiogram phenomenon. *World J Cardiol*. 2014;6:81-86.
7. Valentino MA, Panakos A, Ragupathi L, Williams J, Pavri BB. Flecainide toxicity: a case report and systematic review of its

electrocardiographic patterns and management. *Cardiovasc Toxicol*. 2017;17(3):260-266.
8. Bruccoleri RE, Burns MM. A literature review of the use of sodium bicarbonate for the treatment of QRS widening. *J Med Toxicol*. 2016;12(1):121-129.
9. Rothschild L, Bern S, Oswald S, Weinberg G. Intravenous lipid emulsion in clinical toxicology. *Scand J Trauma Resusc Emerg Med*. 2010;18:51.
10. Sivalingam SK, Gadiraju VT, Hariharan MV, Atreya AR, Flack JE, Aziz H. Flecainide toxicity—treatment with intravenous fat emulsion and extra corporeal life support. *Acute Card Care*. 2013;15(4):90-92.
11. Brumfield E, Bernard KR, Kabrhel C. Life-threatening flecainide overdose treated with intralipid and extracorporeal membrane oxygenation. *Am J Emerg Med*. 2015;33(12):1840.e3-5.

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