Title

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CLINICAL VIGNETTE

Transient Brugada Pattern in a Patient on Flecainide

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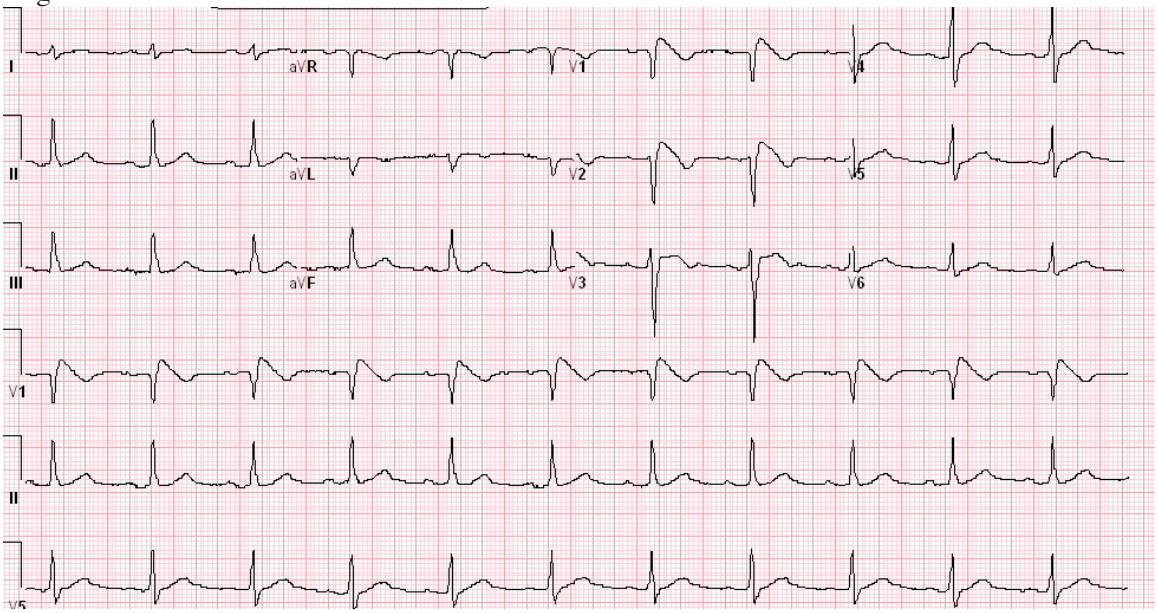
A 65-year-old female tourist was evaluated in the emergency room after a witnessed syncopal episode. This was her first episode and she woke up to full consciousness, without bystander cardiopulmonary resuscitation (CPR) or defibrillation and was stable upon transport to the emergency room. She admitted to recent onset of nausea and abdominal discomfort about 24 hours prior to her episode.

Her past medical history was significant for paroxysmal atrial tachyarrhythmia, which was well controlled on flecainide 100 mg bid for the past 7 years. Two of her siblings were also being treated for atrial tachycardia.

Her vital signs in the emergency room were notable for a low grade fever of 100.7, heart rate 88, blood pressure 127/88, and oxygen saturation of 97% on room air. Physical exam was unremarkable.

Presenting EKG revealed precordial coved ST elevation in her right precordial leads.

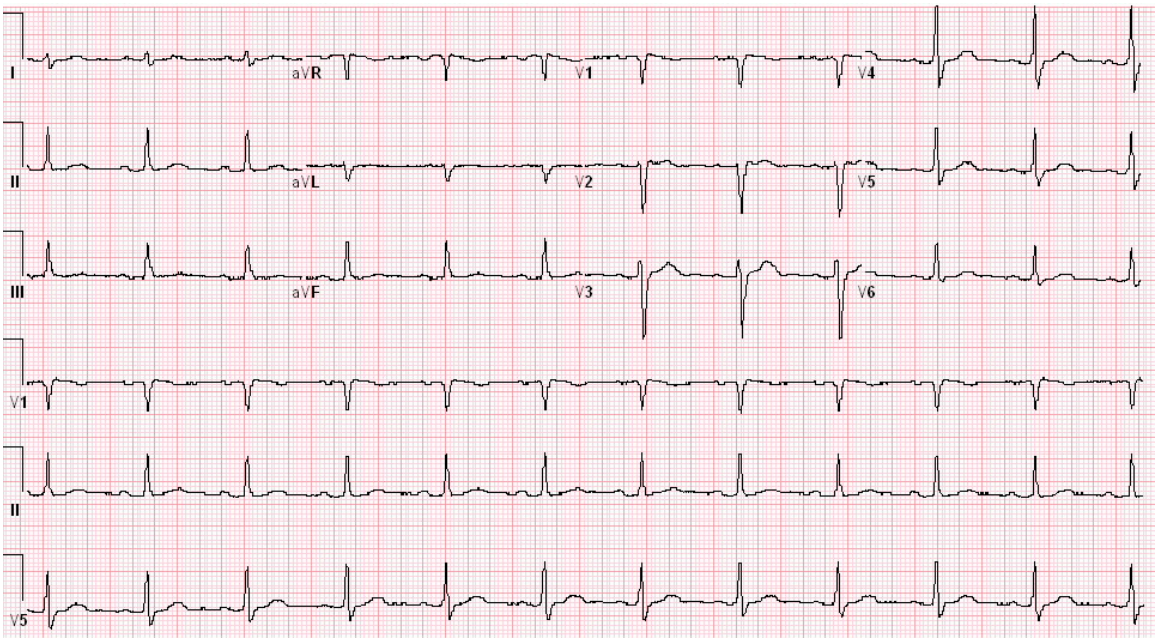
Ekg 1



Laboratory data was unremarkable.
Flecainide was discontinued and patient was monitored on telemetry.

After 24 hours, there was transition to type 3 Brugada pattern with no arrhythmias on monitoring.

EKG 2:



Concerning was her presentation of syncope (which could represent a nonsustained malignant arrhythmia or an episode of vasovagal syncope
precipitated by recent viral infection with a characteristic prodrome).

The controversies in management of the brugada pattern were reviewed with the patient. Work up of sodium channelopathy and the role of implantable defibrillators were discussed. The patient chose to follow up with her cardiologist in her country and left against medical advice.

Discussion

Brugada syndrome:

Brugada's syndrome is characterized by an electrocardiographic (ECG) pattern of right bundle branch block and ST-segment elevations in the right precordial leads (brugada pattern) and ventricular fibrillation.

The cellular defect involves a mutation of a cardiac sodium channel gene causing an outward shift in the ionic current[1]. Mutations of the SCN5A gene encoding for the alpha subunit of the cardiac sodium channel (INa) have been reported as the genetic basis of the disease[2, 3].

Three types of repolarization patterns in the right precordial leads have been recognized.

Characteristic	Type 1	Type 2	Type 3
J wave amplitude	≥2 mm	≥2 mm	≥2 mm
T wave	Negative	Positive or biphasic	Positive
ST-T configuration	Coved-type	Saddleback	Saddleback
ST segment, terminal portion	Gradually descending	Elevated by ≥1 mm	Elevated by <1 mm

Type 1 is diagnostic of Brugada syndrome and is characterized by coved ST-segment elevation, while types 2 and 3 are characterized by a saddleback ST-segment configuration[1,2].

The ECG abnormality may be intermittent and accentuated just before and after episodes of ventricular fibrillation. The true incidence is not known due to reporting biases. Although there is a strong population dependence, an estimated 4% of all sudden deaths and at least 20% of sudden deaths in patients with structurally normal hearts are due to the syndrome[1].

Proactive Testing

Concealed forms may be unmasked or modulated by sodium channel blockers (flecainide, ajmaline, procainamide). Fever has been described as a trigger for the Brugada syndrome (temperature-sensitive channel)[4,5].

Atrial Fibrillation and Brugada

The data regarding flecainide-induced Brugada-type ECG pattern in patients with AF is limited. Beldner et al reported only three cases with ECG changes consistent with Brugada syndrome among 87 (2.3%) patients treated with flecainide (average daily dose 198 ± 61 mg) for AF. No ventricular arrhythmias occurred in any of these patients during follow-up[3]. Patients with Brugada syndrome do exhibit a high incidence (20%) of atrial arrhythmias, mainly AF[6].

Pharmacotherapy

No pharmacologic therapy has been proven to reduce the occurrence of ventricular arrhythmias or sudden death[7,8,9]. Theoretically, drugs that counteract the ionic current imbalance in Brugada syndrome may be used in clinical cases of electrical storms. For example, quinidine and tedisamil, which blocks Ito, have been shown to normalize the ECG pattern in patients with Brugada syndrome[10]. Isoproterenol, which boosts the L-type calcium current, can also counteract the ionic current imbalance[11].

The website www.BrugadaDrugs.org has been established to educate patients and professionals about potentially dangerous medications.

Genetic Testing

Patients with high likelihood of the disease may be genetically tested for a mutation in SCN5A, which codes for the alpha subunit Na_v 1.5 of the cardiac sodium channel. The results of this test support the clinical diagnosis and are important for the early identification of family members at potential risk. The yield of genetic testing remains relatively low at this time, with mutations in SCN5A found in only 11-28% of index cases[12].

Sudden Death Risk Stratification

Role of EP Study
The predictive value of this approach is controversial and debated[13,14,15]. In a large registry of Brugada syndrome patients from Europe, only symptoms and a spontaneous type 1 Brugada ECG pattern, but not EPS, were predictive of arrhythmic events[16].

Implantable Defibrillators

At present, implantation of an automatic implantable cardiac defibrillator is the only treatment proven effective in treating ventricular tachycardia and fibrillation and preventing sudden death in patients with Brugada syndrome.

Indications for ICD implantation were published in the report of the Second Consensus Conference on Brugada syndrome[1].

Conclusion

The clinical significance of the Brugada type ECG pattern among patients treated with flecainide for atrial fibrillation (AF) remains unknown. The present report suggests that patients with AF may represent a population with an increased incidence of flecainide-induced Brugada-type ECG changes.

A possible genetic link between AF and Brugada syndrome may exist. Over 100 mutations of the SCN5A gene have been identified in BS up to now[2]. SCN5A mutations and polymorphisms have also been detected in subjects with lone AF and may increase the susceptibility to INa blockade-induced proarrhythmia[4,17].

It has recently been reported that nearly 6% of AF probands carry heterozygous mutations or rare variants in the SCN5A gene[8]. These mutations and/or polymorphisms may be clinically silent and manifest under certain conditions, including the Ina blocking test.

Although our patient had no family history of Brugada syndrome or sudden cardiac death, she could belong to the above group (silent carriers of Brugada syndrome), and therefore be at high risk of developing a ventricular arrhythmic event under flecainide treatment. Fever may have also potentiated the brugada pattern (temperature sensitive channel).

It is also possible that she may have a minor mutation in an ion channel gene that does not have severe functional consequences with respect to ventricular arrhythmias, even in the presence of a type Ic drug (our patient was on flecainide for 8 years without clinical sequelae), but results in typical precordial ECG changes during sinus rhythm.

Further studies, including screenings for SCN5A gene mutations and/or polymorphisms, are required to evaluate the clinical significance of flecainide-induced Brugada type ECG pattern.

REFERENCES

1. **Antzelevitch C, Brugada P, Borggrefe M, Brugada J, Brugada R, Corrado D, Gussak I, LeMarec H, Nademanee K, Perez Riera AR, Shimizu W, Schulze-Bahr E, Tan H, Wilde A**. Brugada syndrome: report of the second consensus conference: endorsed by the Heart Rhythm Society and the European Heart Rhythm Association. *Circulation*. 2005 Feb 8;111(5):659-70. Epub 2005 Jan 17. Review. Erratum in: Circulation. 2005 Jul 26;112(4):e74. PubMed PMID: 15655131.
2. **Rossenbacker T, Priori SG**. The Brugada syndrome. *Curr Opin Cardiol*. 2007 May;22(3):163-70. Review. PubMed PMID: 17413271.
3. **Beldner S, Lin D, Marchlinski FE**. Flecainide and propafenone induced ST-segment elevation in patients with atrial fibrillation: clue to specificity of Brugada-type electrocardiographic changes. *Am J Cardiol*. 2004 Nov 1;94(9):1184-5. PubMed PMID: 15518618.
4. **Darbar D, Kannankeril PJ, Donahue BS, Kucera G, Stubblefield T, Haines JL, George AL Jr, Roden DM**. Cardiac sodium channel (SCN5A) variants associated with atrial fibrillation. *Circulation*.

2008 Apr 15;117(15):1927-35. Epub 2008 Mar 31. PubMed PMID: 18378609; PubMed Central PMCID: PMC2365761.

5. **Antzelevitch C, Brugada R**. Fever and Brugada syndrome. Pacing Clin Electrophysiol. 2002 Nov;25(11):1537-9. *Review*. PubMed PMID: 12494608.
6. **Letsas KP, Sideris A, Efremidis M, Pappas LK, Gavrielatos G, Filippatos GS, Kardaras F**. Prevalence of paroxysmal atrial fibrillation in Brugada syndrome: a case series and a review of the literature. *J Cardiovasc Med (Hagerstown)*. 2007 Oct;8(10):803-6. Review. PubMed PMID: 17885518.
7. **Márquez MF, Salica G, Hermosillo AG, Pastelín G, Gómez-Flores J, Nava S, Cárdenas M**. Ionic basis of pharmacological therapy in Brugada syndrome. *J Cardiovasc Electrophysiol*. 2007 Feb;18(2):234-40. Review. PubMed PMID: 17338775.
8. **Márquez MF, Salica G, Hermosillo AG, Pastelín G, Cárdenas M**. Drug therapy in Brugada syndrome. *Curr Drug Targets Cardiovasc Haematol Disord*. 2005 Oct;5(5):409-17. Review. PubMed PMID: 16248833.
9. **Yang F, Hanon S, Lam P, Schweitzer P**. Quinidine revisited. *Am J Med*. 2009 Apr;122(4):317-21. Epub 2009 Feb 25. Review. PubMed PMID: 19249010.
10. **Antzelevitch C, Brugada P, Brugada J, Brugada R, Nademanee K, Towbin J**. The Brugada syndrome. In: Clinical approaches to tachyarrhythmias. Armonk NY: Futura Publishing Company; 1999.
11. **Antzelevitch C**. The Brugada syndrome: ionic basis and arrhythmia mechanisms. *J Cardiovasc Electrophysiol*. 2001 Feb;12(2):268-72. Review. PubMed PMID: 11232628.
12. **Kapplinger JD, Tester DJ, Alders M, Benito B, Berthet M, Brugada J, Brugada P, Fressart V, Guerchicoff A, Harris-Kerr C, Kamakura S, Kyndt F, Koopmann TT, Miyamoto Y, Pfeiffer R, Pollevick GD, Probst V, Zumhagen S, Vatta M, Towbin JA, Shimizu W, Schulze-Bahr E, Antzelevitch C, Salisbury BA, Guicheney P, Wilde AA, Brugada R, Schott JJ, Ackerman MJ**. An international compendium of mutations in the SCN5A-encoded cardiac sodium channel in patients referred for Brugada syndrome genetic testing. *Heart Rhythm*. 2010 Jan;7(1):33-46. Epub 2009 Oct 8. PubMed PMID: 20129283; PubMed Central PMCID: PMC2822446.
13. **Brugada P, Geelen P, Brugada R, Mont L, Brugada J**. Prognostic value of electrophysiologic investigations in Brugada syndrome. *J Cardiovasc Electrophysiol*. 2001 Sep;12(9):1004-7. PubMed PMID: 11573688.
14. **Priori SG, Napolitano C, Gasparini M, Pappone C, Della Bella P, Giordano U, Bloise R, Giustetto C, De Nardis R, Grillo M, Ronchetti E, Faggiano G, Nastoli J**. Natural history of Brugada syndrome: insights for risk stratification and management. *Circulation*. 2002 Mar 19;105(11):1342-7. PubMed PMID: 11901046.
15. **Gehi AK, Duong TD, Metz LD, Gomes JA, Mehta D**. Risk stratification of individuals with the Brugada electrocardiogram: a meta-analysis. *J Cardiovasc Electrophysiol*. 2006 Jun;17(6):577-83. PubMed PMID: 16836701.
16. **Probst V, Veltmann C, Eckardt L, Meregalli PG, Gaita F, Tan HL, Babuty D, Sacher F, Giustetto C, Schulze-Bahr E, Borggrefe M, Haissaguerre M, Mabo P, Le Marec H, Wolpert C, Wilde AA**. Long-term prognosis of patients diagnosed with Brugada syndrome: Results from the FINGER Brugada Syndrome Registry. *Circulation* 2010 Feb 9;121(5):635-43. Epub 2010 Jan 25. PubMed PMID: 20100972.
17. **Chen LY, Ballew JD, Herron KJ, Rodeheffer RJ, Olson TM**. A common polymorphism in SCN5A is associated with lone atrial fibrillation. *Clin Pharmacol Ther*. 2007 Jan;81(1):35-41. PubMed PMID: 17185997; PubMed Central PMCID: PMC1933493.

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