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Fever-induced type-1 Brugada pattern: A sign of an unmasked Brugada syndrome or just a Brugada phenocopy?

Short title: Fever and type-1 Brugada pattern

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Brugada syndrome (BrS) is a hereditary channelopathy of the right ventricular outflow tract that might potentially lead to malignant arrhythmogenesis and sudden cardiac death [1, 2]. Currently, the diagnosis of this phenomenon is largely based on the detection of spontaneous or induced type-1 Brugada pattern (manifesting as a coved ST-segment elevation (≥2 mm) in the right precordial leads) on electrocardiogram (ECG) [2]. In their recently published article, Franke et al. [1] have reported a coincidental detection of type-1 Brugada pattern in two little girls in the setting of SARS-CoV-2-related-multisystem inflammatory syndrome (MIS) presenting with high fever. In this context, we would like to highlight potential implications of fever-induced type-1 Brugada pattern.

In clinical practice, hyperthermia might have the potential to convert concealed BrS (with type-2 [saddleback type] or 3 ECG pattern, or rarely normal ECG at baseline) to overt BrS (with type-1 ECG pattern) [1, 2]. Importantly, hyperthermia has also been regarded as an adverse factor that should be strictly avoided in patients with an established diagnosis of BrS (regardless of whether it is overt or concealed) [1, 2]. In this setting, adverse impact of fever might be associated with the

emergence of further disturbances in depolarization and repolarization currents (further inactivation of sodium and/or activation of potassium currents) that all appear to be central to the pathogenesis of BrS [2]. Importantly, asymptomatic subjects with a fever-induced type-1 Brugada pattern (as in the patients reported [1]) were previously suggested to have a worse prognosis due to the higher risk of future arrhythmic events [2]. Accordingly, did the authors plan further risk-stratification of the patients through advanced tests including electrophysiological study?

As a distinct phenomenon, Brugada phenocopy is well known to constitute a variety of diverse and reversible conditions (including myocardial ischemia, myopericarditis, ionic abnormalities, hypothermia, etc.) that present with Brugada-like ECG patterns [2]. Importantly, patients with a Brugada phenocopy usually do not suffer BrS-related symptoms, and have a negative drug challenge (mostly performed with sodium channel blockers including ajmaline) [2–4]. However, a portion of patients with a Brugada phenocopy might also have an ambiguous genetic testing as well as a family history of sudden cardiac death. This may suggest an overdiagnosis of BrS particularly in those with a phenocopy [2].

In contrast to hypothermia [2], hyperthermia has been an underrecognized etiology of Brugada phenocopy in previously healthy subjects. Accordingly, the exact mechanisms of fever-associated Brugada phenocopy are still nebulous. However, this phenomenon might emerge in the presence of substantially higher body temperatures (as compared with unmasked BrS) potentially suggesting alternative mechanisms other than ionic current disturbances. Specifically, febrile conditions including MIS and Kawasaki disease might serve as potential etiologies of Brugada phenocopy largely through mechanisms including right ventricular outflow tract inflammation and cytokine storm, etc. In the literature, fever-induced reversible type-1 and type-2 ECG patterns have been rarely reported, and termed as ‘Brugada-like ECG changes’ [3, 4]. Importantly, absence of BrS-related symptoms and family history, and more importantly negative drug challenge emerged as important characteristics of these patients [3, 4].

Based on the above-mentioned notions, it seems necessary to differentiate between unmasked BrS and Brugada phenocopy in the setting of hyperthermia. In this context, we hold the opinion that fever-induced conversion from a baseline type-2 or type-3 ECG pattern to a type-1 ECG pattern most likely suggests an unmasked BrS. On the other hand, fever-induced conversion from a normal baseline ECG pattern to type-2 or type-3 ECG pattern most likely suggests a Brugada phenocopy. These conditions might not warrant a drug challenge following defervescence and restoration of

the baseline ECG pattern. However, fever-induced conversion from a normal baseline ECG pattern to a type-1 ECG pattern (as in the patients reported [1]) might suggest either a phenocopy or an unmasked BrS. This potentially warrants a drug challenge for the final diagnosis. Therefore, did the authors perform or plan a drug challenge for their patients? Finally, evolution of malignant arrhythmias following a fever-induced type-1 ECG pattern strongly suggests an unmasked BrS.

In conclusion, Franke et al. [1] should be congratulated for their thought-provoking clinical vignette. Hyperthermia has important implications both in the settings of BrS and Brugada phenocopy [1–4]. However, further aspects of Brugada phenocopy associated with hyperthermia still need to be established.

REFERENCES

1. Franke M, Książczyk TM, Pietrzak R, et al. Incidental diagnosis of Brugada syndrome in two girls hospitalized for pediatric inflammatory multisystem syndrome related to COVID-19 (PIMS-TS). Kardiol Pol. 2022 [Epub ahead of print], doi: 10.33963/KP.a2022.0183, indexed in Pubmed: 35924994.
2. Tomé G, Freitas J. Induced Brugada syndrome: Possible sources of arrhythmogenesis. Rev Port Cardiol. 2017; 36(12): 945–956, doi: 10.1016/j.repc.2017.06.015, indexed in Pubmed: 29233646.
3. Unlu M, Bengi F, Amasyali B, et al. Brugada-like electrocardiographic changes induced by fever. Emerg Med J. 2007; 24(1): e4, doi: 10.1136/emj.2006.041202, indexed in Pubmed: 17183028.
4. Mody P, Pandey A, Joglar J. Fever-induced electrocardiographic changes. J Gen Intern Med. 2015; 30(1): 136–137, doi: 10.1007/s11606-014-2992-9, indexed in Pubmed: 25205622.