Fever-induced type-1 Brugada pattern: A sign of revealed Brugada syndrome or just a Brugada phenocopy? Author's reply

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We would like to sincerely thank Yalta et al. [1] for their letter to the editor regarding our recent publication on the incidental diagnosis of Brugada syndrome in two young girls in the setting of pediatric inflammatory multisystem syndrome (PIMS-TS). The interest in our article underscores the importance of the presented subject.

Brugada syndrome (BrS), a rare but potentially fatal channelopathy, has recently become one of the most widely discussed cardiac disorders due to its still incompletely understood pathophysiology and clinical course. BrS is usually diagnosed upon finding type-1 Brugada changes on the echocardiogram (ECG), presenting spontaneously, during fever or induced by drugs. However, uncertainties concerning the final diagnosis and its prognosis remain (partly because of the phenomenon of Brugada phenocopies [BrP]), which has led to the development of more complex diagnostic criteria such as the Shanghai Score System [2].

In their recently published letter to the editor, Yalta et al. [1] emphasized the importance of scrupulous exclusion of all possible reasons for Brugada pattern phenocopy, such as metabolic conditions, mechanical compression, myocardial ischemia, pulmonary embolism, or even poor ECG filter [3], which could lead to a false and premature diagnosis of BrS. They also raise a very interesting, yet still not fully answered, question: what is the mechanism and prognostic value of hyperthermia revealing the concealed Brugada pattern? Some experts see it as equal to spontaneous appearance of the type-1 pattern, while others (including the authors of the Shanghai Score System) take a more cautious approach. Whether hyperthermia alone, especially in the context of a multisystem inflammatory condition (PIMS-TS), could be a cause of Brugada pattern phenocopy is a valid question; however, there are currently insufficient data to provide an answer. Also, there are still not enough data to distinguish between the BrS and BrP, based on the ECG obtained after resolution of the type-1 pattern although we agree that the appearance of Brugada pattern 2 or 3 makes a diagnosis of BrS more likely.

In both cases presented in our clinical vignette, we have searched for the possible reasons for Brugada phenocopies and evaluated the patients using the criteria proposed by Anselm et al. [3] to exclude BrP. It is worth mentioning that laboratory abnormalities typical for PIMS-TS, such as hyponatremia or elevated concentrations of cardiac biomarkers, were present. However, in both patients, the ECG normalized only after defervescence, while the other results, including laboratory tests and echocardiogram, remained abnormal.

As we stated in our article, a cascade family screening for BrS led to a diagnosis of ajmaline challenge in Patient 1's father. The patient's genetic testing revealed a variant of unknown significance in the SCN5A gene, and there was a history of sudden cardiac death in the paternal grandfather; therefore, in this family, we believe the diagnosis of BrS is well established. The family screening of Patient 2 was negative, and genetic testing remains in progress. In this case, a differential diagnosis of BrP caused by fever and PIMS could be considered; however, a diagnosis of BrS is equally probable. Since the patient is young and so far asymptomatic, we have advised only lifestyle modifications and planned for regular follow-up in our

department. The provocative test with ajmaline would be useful here, but its value in prepubertal children is limited. Our strategy is to postpone the test until after 16 years of age. Similarly, we would not perform an electrophysiological study at this stage in a young, asymptomatic, and incidentally diagnosed patient. In both cases, we have recommended lifestyle modifications (as routinely given to BrS patients) and regular follow-up while more invasive tests will be considered later in life if symptoms occur [4].

Managing asymptomatic patients with features of BrS is challenging, mainly due to gaps in current medical knowledge. It seems even more difficult to guide asymptomatic pediatric patients although there are attempts to risk stratify children with a diagnosis of BrS [5]. Sinus node dysfunction, atrial arrhythmias, and conduction disorders have been shown to be markers of a high risk of life-threatening events, which is also why we decided to keep both patients in follow-up and monitor for the occurrence of any of the above. Nevertheless, at our center when we communicate with the families, we try to emphasize the low risk of life-threatening arrhythmias in incidentally diagnosed individuals.

Once again, we would like to thank Yalta et al. [1] for their important contribution to the discussion about controversies in diagnosing patients with BrS, especially in the pediatric population.

Article information

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