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CASE REPORT

INTERMEDIATE

CLINICAL CASE

Multisystem Inflammatory Syndrome in Children Unmasking Brugada Type 1 Pattern

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ABSTRACT

We describe the case of a 14-year-old boy hospitalized for multisystem inflammatory syndrome in children who developed atrial fibrillation during the acute phase and a transient Brugada type 1 pattern in the subacute phase. Eight months later, a provocative test with ajmaline confirmed the suspicion of Brugada syndrome. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2022;4:205–210) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 14-year-old Caucasian boy was admitted to our intensive care unit because of multisystem inflammatory syndrome in children (MIS-C) in December 2020, during the coronavirus disease 2019 pandemic.

Five days prior to the admission, he had developed fever, nausea, vomiting, and diarrhea. On the day of admission, skin rash and conjunctivitis appeared.

LEARNING OBJECTIVES

- To perform a provocative test with ajmaline when Brugada type 1 pattern is elicited in MIS-C to distinguish BP from BrS.
- To carefully monitor on electrocardiography not only in the acute inflammatory phase of MIS-C but also in the subacute phase and during follow-up to detect Brugada type 1 pattern.

MEDICAL HISTORY

The patient had no history of medical illness and had a negative family history for cardiovascular diseases.

He practiced competitive sports; previous electrocardiographic (ECG) and stress test results were normal.

DIFFERENTIAL DIAGNOSIS

A Brugada phenocopy (BP) was suspected, given the underlying inflammatory status during hospitalization and the negative family and medical histories.

To discriminate between Brugada syndrome (BrS) and BP, the patient was referred to an electrophysiology center. Electrocardiography showed sinus rhythm, QRS fragmentation in D3, and "saddleback" ST-segment elevation in modified precordial leads (MPLs) (**Figures 1 and 2**). Electrocardiograms with standard leads and MPLs of his parents and sister

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ABBREVIATIONS AND ACRONYMS

BP = Brugada phenocopy

BrS = Brugada syndrome

ECG = electrocardiographic

MIS-C = multisystem inflammatory syndrome in children

MPL = modified precordial lead

SARS-CoV-2 = severe acute respiratory syndrome-coronavirus-2

were obtained and did not show any abnormal findings.

An ajmaline provocation test was proposed and accepted by the patient and his parents. Five minutes after intravenous infusion of ajmaline 1 mg/kg, a Brugada pattern appeared (Figure 3).

INVESTIGATIONS

On admission to the intensive care unit, the patient was hypotensive and tachycardic; the body temperature was 38.3°C, the heart rate 112 beats/min, and the oxygen saturation 96% in ambient air. Electrocardiography showed sinus rhythm, normal ventricular conduction, and diffuse alterations of ventricular repolarization; transthoracic echocardiography highlighted biventricular dilatation and global hypokinesia with severe reduction of left ventricular ejection fraction (30%).

Blood tests showed altered N-terminal pro-brain natriuretic peptide (17,290 ng/L; normal range: <125 ng/L), troponin (1,556 ng/L; normal range: <15 ng/L), C-reactive protein (27 mg/dL; normal range: <0.5 mg/dL), procalcitonin (35 ng/mL; normal range: <0.05 ng/mL), D-dimer (2,713 μg/L; normal range: <500 μg/L), fibrinogen (850 mg/dL; normal range: 170-419 mg/dL), and sodium (129 mEq/L; normal range: 135-145 mEq/L). Nasopharyngeal swab for severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) was negative, as we expected given that the epidemiologic link was within the previous 5 weeks, but the results of an anti-SARS-CoV-2 immunoglobulin G antibody chemiluminescent immunoassay were positive.

MANAGEMENT

At admission, noninvasive ventilation in nasal continuous positive airway pressure was started, and intravenous immunoglobulin, low-dose adrenaline, and high-dose steroid were administered. The patient experienced early onset of atrial fibrillation at 140 beats/min and underwent cardioversion because of hemodynamic instability.

During the following 24 hours, the patient's clinical condition improved, and ECG findings were normal (Figure 4). Soon after immunoglobulins were administered, a Brugada type 1 pattern appeared in the apyretic patient and persisted for 2 days (Figure 5).

On hospital day 12, the Brugada pattern transiently reappeared despite complete normalization of transthoracic echocardiographic parameters and apyrexia. On hospital day 15 day, the patient was discharged with normal findings on electrocardiography and 12-lead Holter electrocardiography. Results of cardiac magnetic resonance imaging 1 month after hospitalization were normal.

FIGURE 1 Basal Electrocardiogram With Conventional Precordial Leads

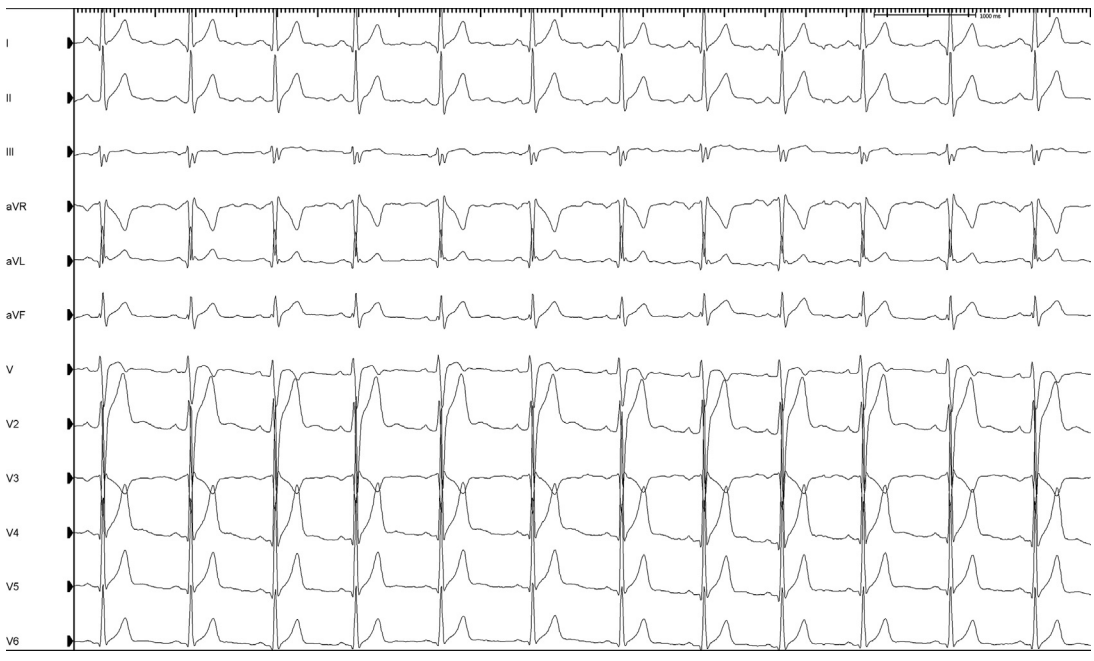


FIGURE 2 Basal Electrocardiogram With Modified Precordial Leads

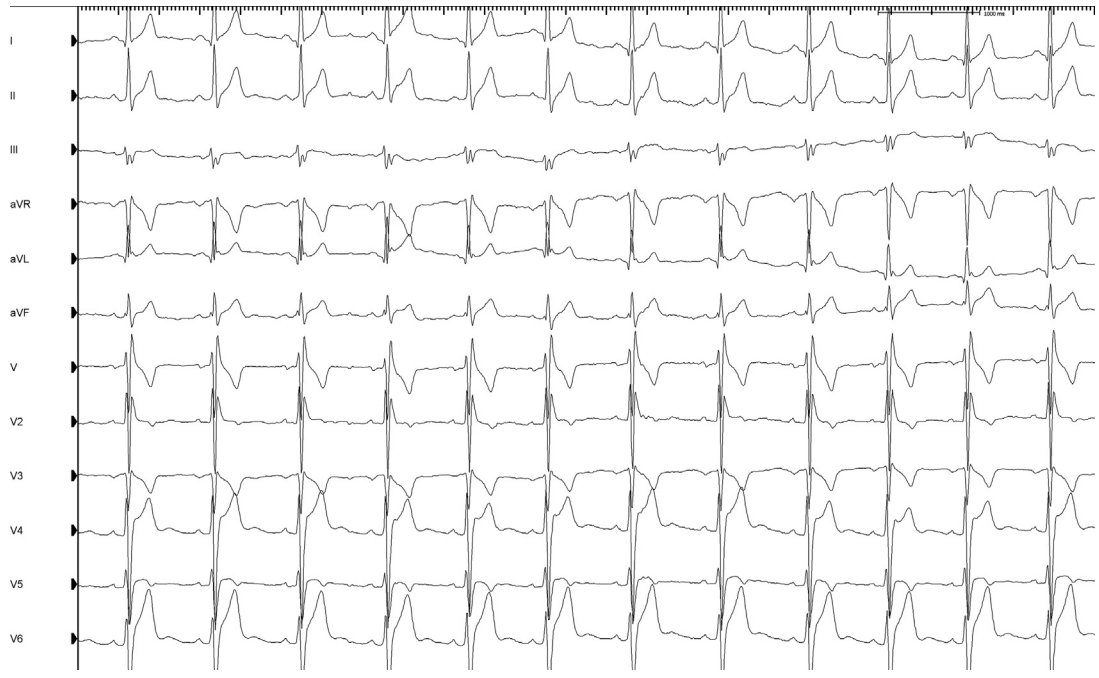


FIGURE 3 Electrocardiogram With Modified Precordial Leads After Infusion of Ajmaline 1 mg/kg

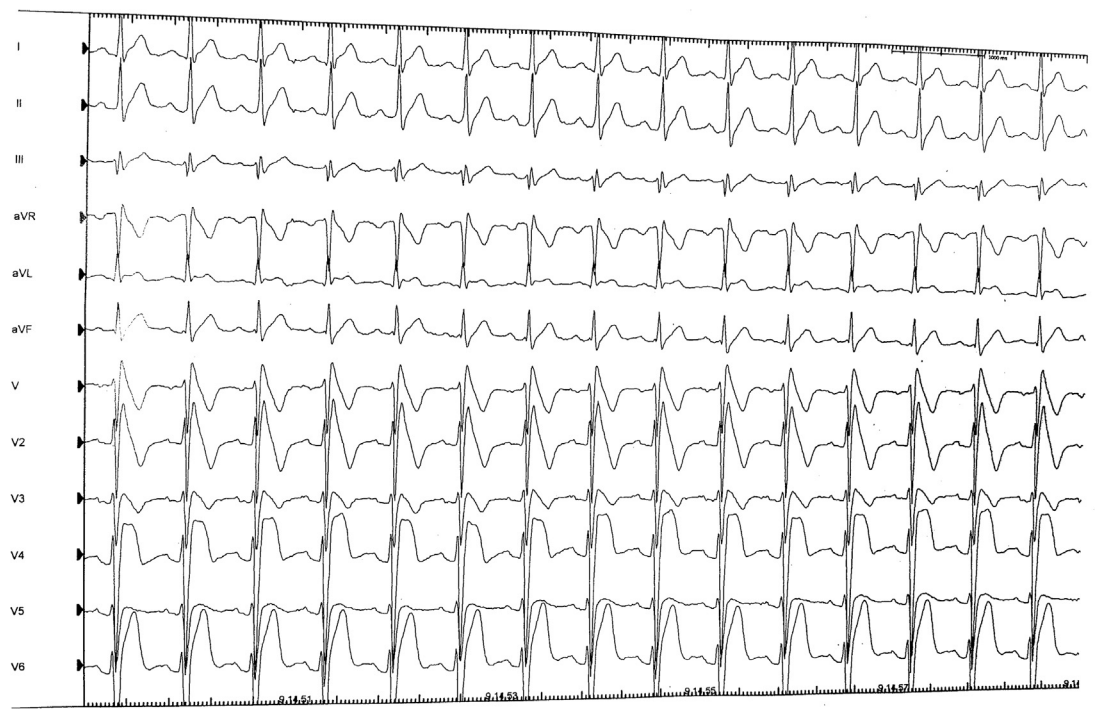
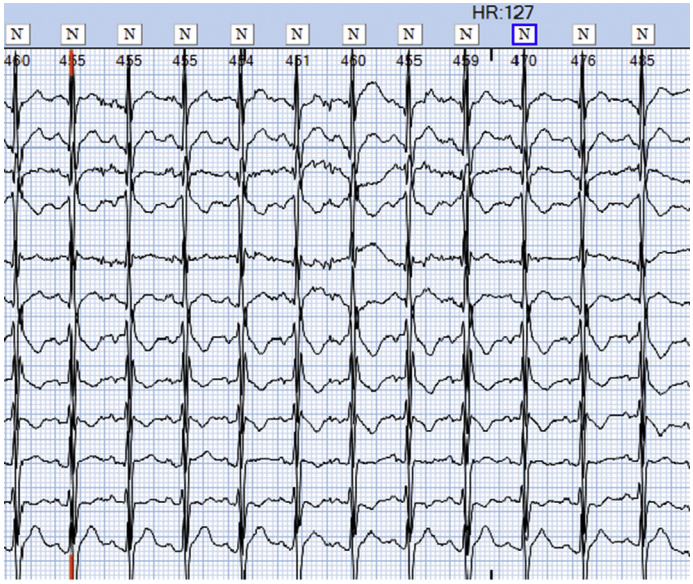


FIGURE 4 Electrocardiogram on Admission



During follow-up at 1 to 3 and 6 months after discharge, the patient did not report any symptoms, the physical examination was unremarkable, and basal ECG findings were normal. Holter ECG monitoring at 6 months with MPLs to a higher intercostal position (second to fourth intercostal space) registered sinus rhythm right bundle branch block and ST-segment elevation ≤2 mm (Figure 6).

DISCUSSION

SARS-CoV-2 infection has demonstrated a wide range of clinical manifestations. Although the course of acute disease is commonly mild in children, MIS-C has been well described.[1] Several case reports describe new onset of coved ST-segment elevation in right precordial leads in patients hospitalized for coronavirus disease 2019 so far, even in the absence of fever,[2] giving rise to the hypothesis that SARS-CoV-2 itself may provoke electric remodeling through direct infection of cardiomyocytes or because of inflammation and elicit cardiac arrhythmias. Some investigators have reported cardiac conduction abnormalities related to MIS-C, such as first-degree or advanced atrioventricular block, but just 2 patients developed atrial tachyarrhythmia.[3,4] Moreover, SARS-CoV-2 can induce an autonomic imbalance that can persist many months after healing. Alterations in the vagal system causing modification of T-wave amplitude were described by Regan et al[3] and Dionne et al[4] and were also evidenced by our ECG data (not yet published). It was demonstrated that autonomic

FIGURE 5 Brugada Type 1 Pattern

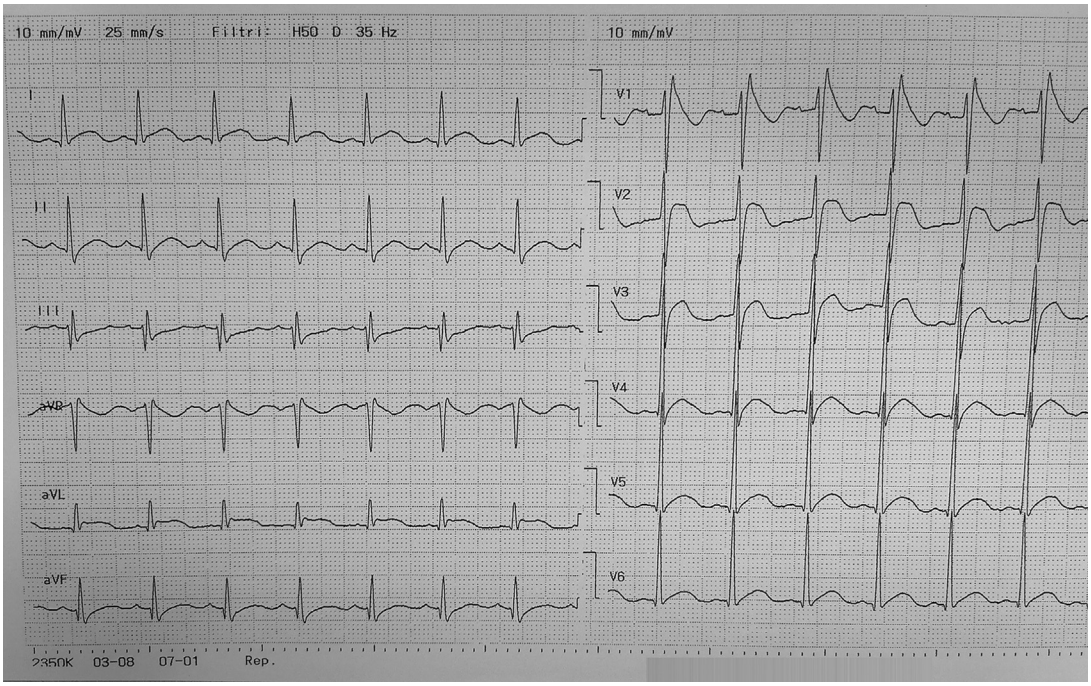
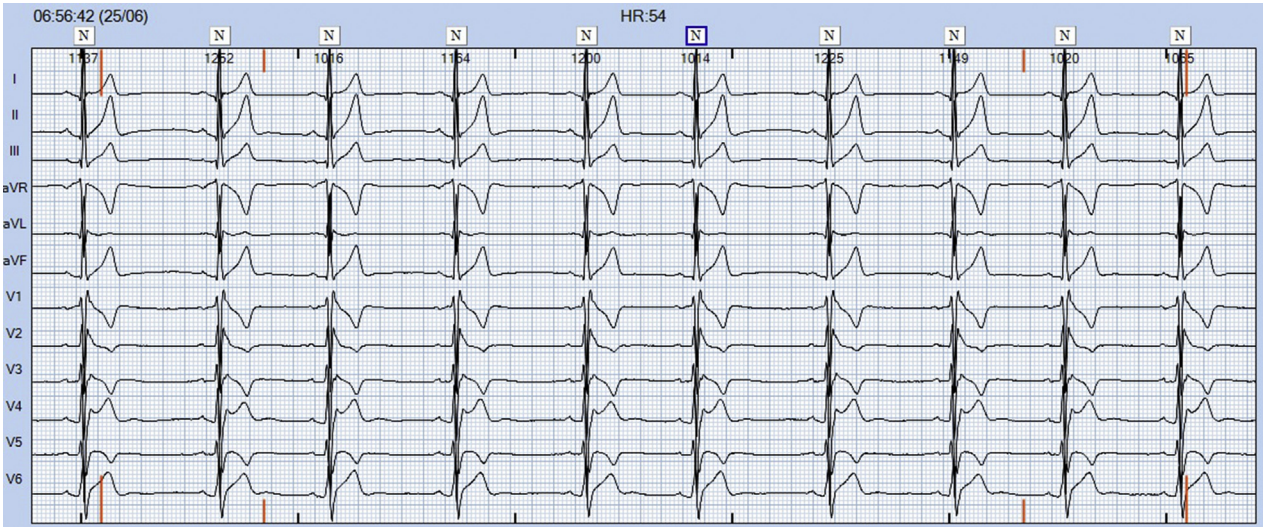


FIGURE 6 Sinus Bradycardia: Right Bundle Branch Block and ST-Segment Elevation ≤2 mm in Modified Precordial Leads



imbalance in patients with BrS, because of decreased adrenergic tone, results in predominant parasympathetic tone. Acetylcholine is known to affect ionic currents such as Ito and ICa, which are more prominent in the right ventricular outflow tract epicardium. When vagal tone increases, these currents may be modulated, resulting in the loss of the spike-and-dome shape of the action potential in the epicardium, with the development of ST-segment elevation on right precordial surface electrocardiography.[5-7]

The term "Brugada phenocopy" was introduced to describe Brugada-like ECG patterns in the absence of congenital dysfunction of ion channels. Findings that support the suspicion of BP include the presence of an identifiable underlying condition, disappearance of the pattern with resolution of the condition, a negative family history, the absence of symptoms, and negative results on sodium channel-blocker challenge.[8] They are related to certain incompletely understood conditions that alter the homeostasis of inward and outward currents in right ventricular outflow tract myocytes. BS does not carry a higher risk for malignant arrhythmia, although the real outcome remains unknown.[9]

The coved ST-segment elevation seen during the hospitalization of our patient was initially interpreted as a BP. Indeed, he had never had symptoms related to BrS, nor did he have a suspicious family history. The transient ECG pattern could have been related to an inflammatory state causing myocardial damage or to autonomic imbalance that could have altered myocardial repolarization. Piazza et al[10] described a 5-year-old patient whose Brugada-like pattern was considered secondary to myocarditis without further investigations.

Conversely, we considered that it was important to rule out the diagnosis of BP and thus decided to perform an ajmaline test.

To the best of our knowledge, this is the first case of atrial fibrillation in a patient with MIS-C and the second of a new-onset Brugada type 1 pattern during hospitalization. This case report is the only one in which the diagnosis of BrS was confirmed through a provocative test.

FOLLOW-UP

At 10-month follow-up, no symptoms, arrhythmias, or syncope was reported.

Given the absence of high-risk criteria and symptoms at ambulatory follow-up, genetic testing and lifestyle modifications were indicated.

CONCLUSIONS

MIS-C may elicit Brugada type 1 pattern during the acute or subacute phase of the disease. In such a condition, the differential diagnosis between true BrS and BP is complex, so that in selected cases with low pretest probability for BrS, pharmacologic challenge could be a way to discriminate an acquired condition from a congenital disease. We suggest careful ECG monitoring not only in the acute inflammatory phase of MIS-C but also in the subacute phase and during postdischarge follow-up.

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