SARS-CoV-2 Infection and Brugada Syndrome: A Case Report

Infeção por SARS-CoV-2 e Síndrome de Brugada: Relato de Caso

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Abstract

The world is facing a new pandemic – SARS-CoV-2 infection. Fever is one of the most common presentations of SARS-CoV-2 infection.

We bring you the case of a 61-year-old female which Brugada syndrome was uncovered presumably for the first-time during fever caused by SARS-CoV-2 infection.

Fever due to SARS-CoV-2 infection may uncover Brugada syndrome, therefore attention must be paid to the electrocardiogram when the patients present with lipotimia/syncope.

Keywords: Brugada Syndrome; COVID-19; SARS-CoV-2

Resumo

O mundo enfrenta uma nova pandemia – a infeção a SARS-CoV-2. Uma das apresentações mais frequentes da infeção a SARS-CoV-2 é a febre.

Reportamos o caso de uma mulher de 61 anos cuja síndrome de Brugada se manifestou presumivelmente pela primeira vez durante um episódio de febre no contexto de infeção a SARS-CoV-2.

A febre em contexto de infeção a SARS-CoV-2 pode desmascarar a síndrome de Brugada, pelo que se deve prestar particular atenção aos doentes que se apresentam com lipotimia/síncope.

Palavras-chave: COVID-19; SARS-CoV-2, Síndrome de Brugada

Introduction

The world is facing a new pandemic since December 2019, the COVID-19 lung disease, caused by a member of coronavirus viruses' family, the SARS-CoV-2.[1] The clinical spectrum of SARS-CoV-2 infection varies from asymptomatic or mildly symptomatic to severe clinical conditions characterized by respiratory failure and multiorgan failure, need to mechanical ventilation and admission in an Intensive Care Unit. One of the most frequent symptoms is fever.[2]

Brugada syndrome is an inherited arrhythmic disease that predisposes to ventricular fibrillation and sudden cardiac death in a structurally normal heart.[3,4] Brugada syndrome seems to be associated with mutations in the cardiac sodium channels, and mutations in the *SCN5A* gene have been estimated to account

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to up to 30% of the cases.[4] Patients with Brugada syndrome are generally healthy, young and ignorant of their predisposition. Consequently most patients are asymptomatic and those who are symptomatic present with arrhythmic syncope or aborted sudden cardiac death precipitated by vagotonia, fever or medications.[5] Given the unknown prevalence of asymptomatic patients, it is difficult to estimate the prevalence of Brugada syndrome, however, studies report that it ranges between 1 in 1000 to 1 in 10 000, being higher in Southeast Asian men.[5,6] The diagnosis of Brugada syndrome is based on a specific pattern found on the electrocardiogram (ECG).

Case Report

A 61-year-old female was admitted to the emergency room due to nausea, vomiting and asthenia complaints that had started 24 hours prior. Additionally, the patient referred an episode of loss of consciousness that lasted a few seconds, with no prodromes and with no other accompanying symptoms. At admission, the patient was hemodynamically stable and apyretic. An ECG was performed and showed no significant findings. Additional exams suggested a urinary tract infection and, therefore, it was assumed loss of consciousness due to dehydration and the patient was discharged with amoxicillin clavulanate. Two days later, the patient suffered a new loss of consciousness episode, with the same characteristics, but did not return to the emergency room, and two days after that, the patient presented another episode of loss of consciousness that lasted about a minute. The episode was immediately preceded by sweating and shivering. The patient denied accompanying chest pain, palpitations, or any other symptoms. At admission, she presented with fever (38.4ºC) and the ECG showed coved type ST-segment elevation of approximately 1 mm, followed by a negative T-wave in lead V2 (type-3 pattern – type-1 ECG morphology but without voltage criteria) (Fig. 1). It is important to refer that the ECG at presentation was performed at the 4th intercostal level. Blood tests were all normal, including troponin, potassium and magnesium levels. The patient reported another episode of loss of consciousness 3 years prior, not being able to provide further details, and denied previous episodes of syncope with fever. The patient also denied family history of heart conditions or sudden cardiac death. Syncope due to fever unmasking Brugada syndrome was suspected, and the patient was hospitalized for further monitoring and evaluation. A fast SARS-CoV-2 test was performed and a positive result was received in a couple of hours. The radiography showed no signs of pneumonia. The patient was placed in a room with airborne isolation and monitored with telemetry. Measures to prevent new episodes of fever were thoroughly applied. During the hospital stay, the patient had no respiratory

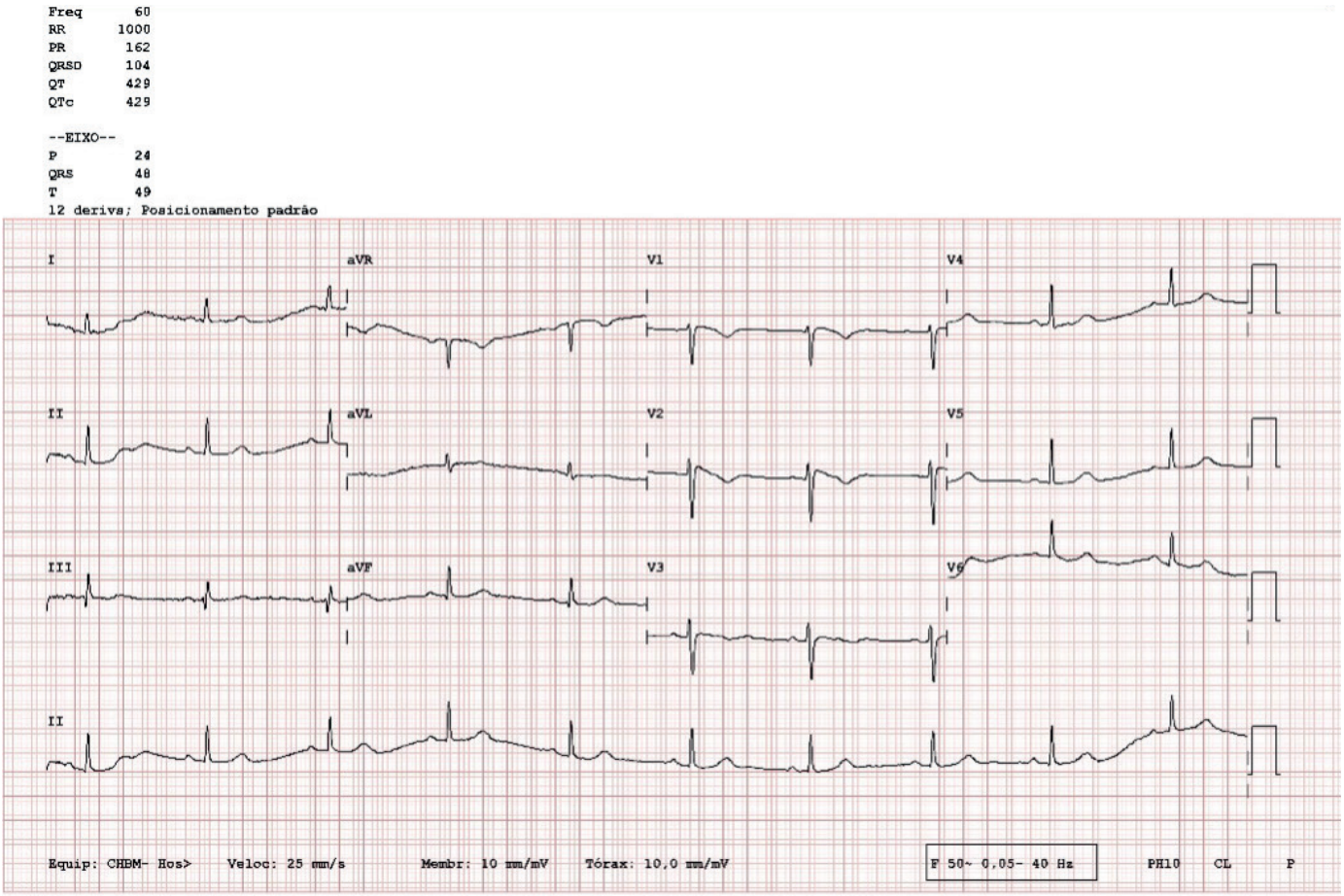

Figure 1. Patient's ECG at admission, with fever, at the 4th intercostal space.

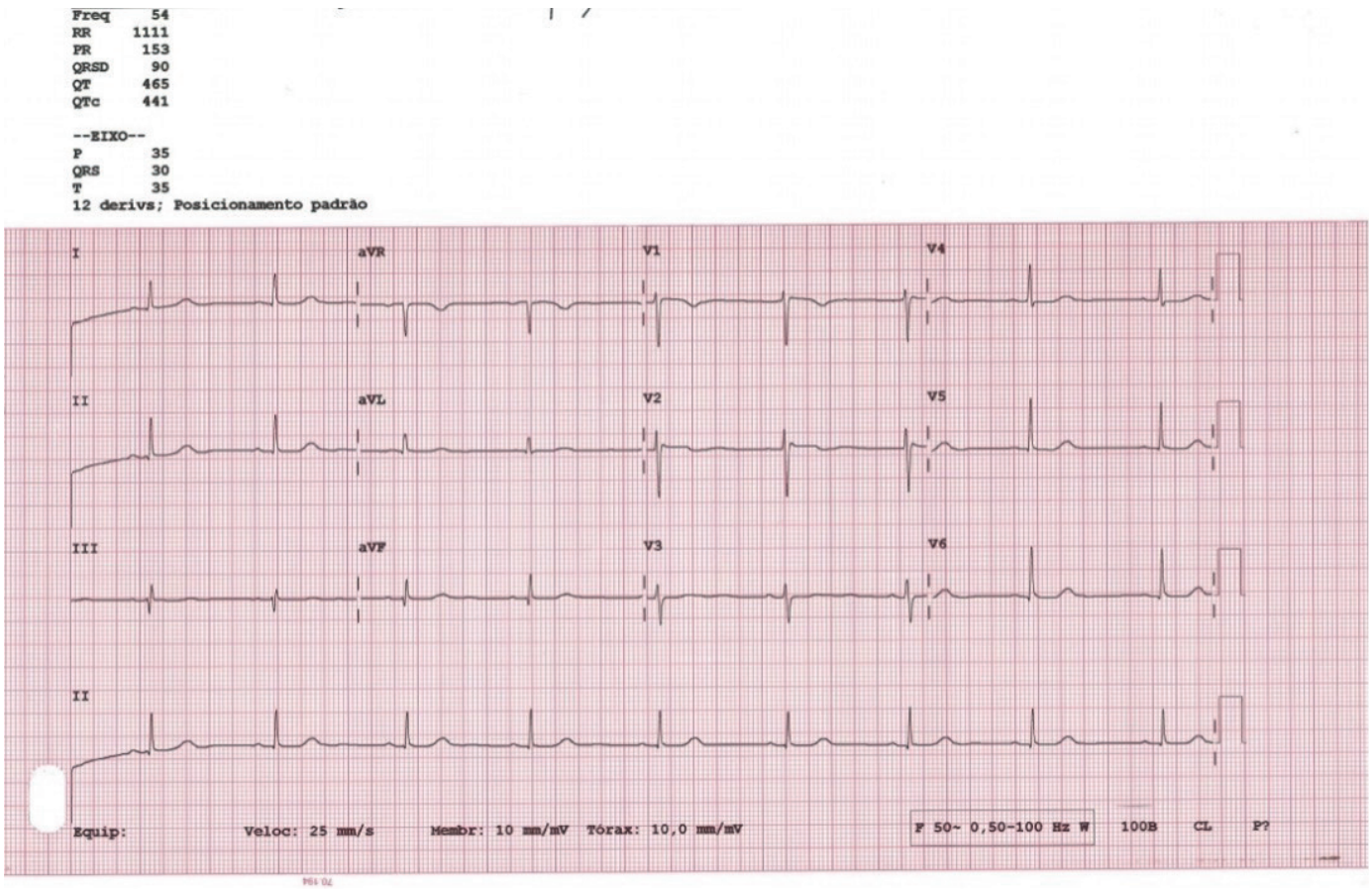

Figure 2. Patient's ECG before flecainide protocol, without fever, at the 2nd intercostal space.

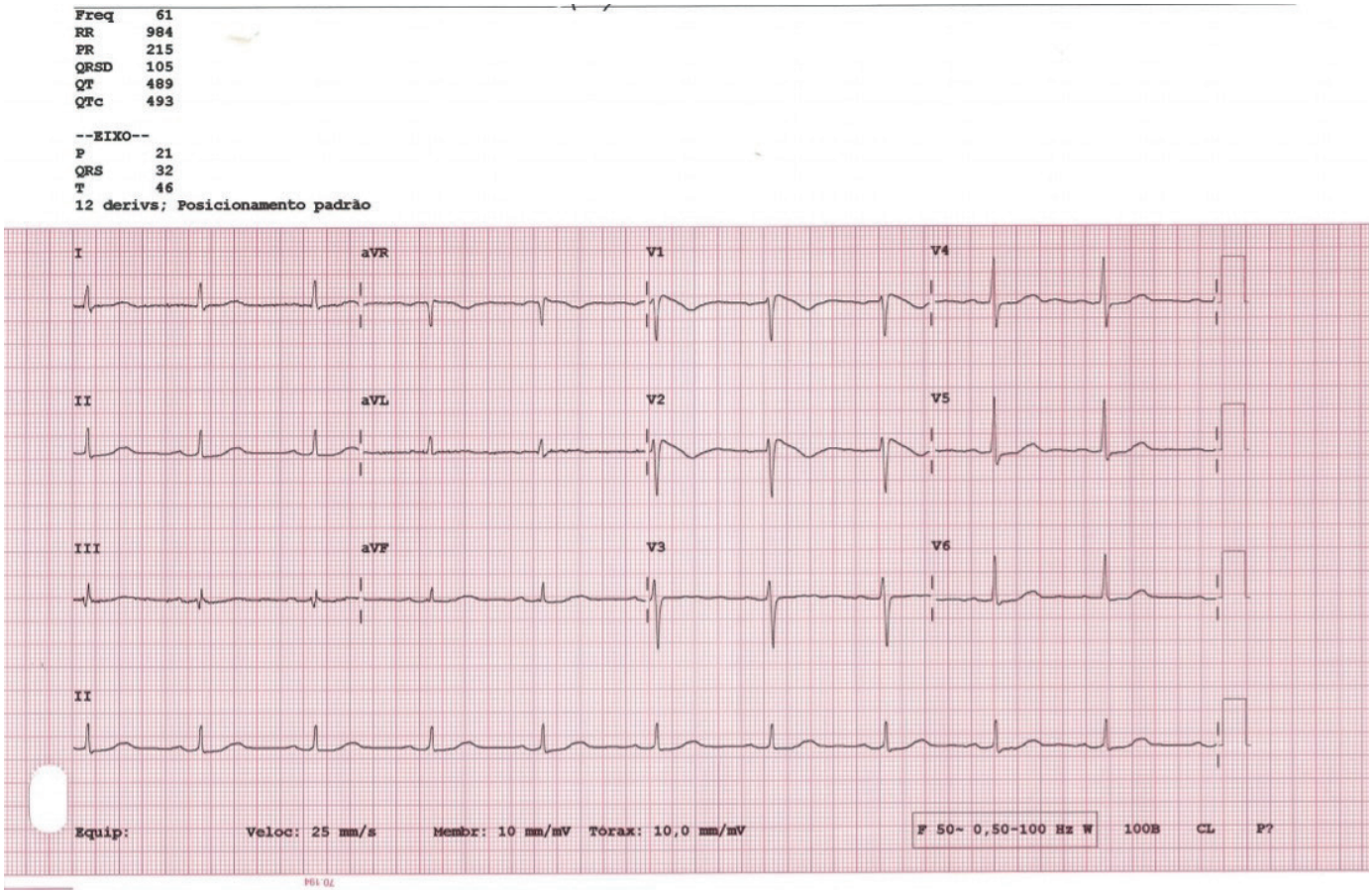

Figure 3. Patient's ECG at minute 10 of flecainide protocol, without fever, at the 2nd intercostal space.

symptoms, no further episodes of fever, no dysrhythmias in the telemetry and no alterations on blood tests. Two weeks later, the patient was negative for SARS-CoV-2 infection and underwent a provocative test with flecainide. Fig. 2 is the patient's ECG before flecainide protocol (no Brugada syndrome pattern) and Fig. 3 is the patient's ECG in the 10th minute of the protocol, both ECG in the 2nd intercostal space. Therefore, Brugada syndrome was assumed and, after discussion with colleagues specialized in arrhythmology, the patient underwent implantation of a defibrillator.

Discussion

The diagnosis of Brugada syndrome is based on a specific pattern found on the ECG: a coved type ST-segment elevation ≥2 mm followed by a negative T-wave in ≥1 of the right precordial leads V1 to V2. This pattern on the ECG - also called type-1 pattern - may be observed either spontaneously or during a provocative test with a sodium-channel blocker.[4] When Brugada syndrome is suspected, leads V1 and V2 should always be recorded both from the 4th intercostal space as well as from the 3rd and 2nd intercostal space, as these higher positions increase the sensitivity of leads V1 and V2 for detecting type-1 pattern preserving specificity.[7] The ECG pattern of Brugada syndrome may be dynamic: it may only be unmasked when precipitant conditions occur (such as fever or bradycardia) and patients may present patterns other than type-1 pattern. Type-2 ("saddle-back type") pattern is only suggestive of Brugada syndrome and is characterized by an ST-segment elevation ≥0.5 mm (generally ≥2 mm in V2) in ≥1 right precordial lead (V1 to V3), followed by a convex ST-segment. Finally, type-3 ECG pattern refers to ST-segment elevation ≤1 mm in ≥1 right precordial leads (V1-V3) with either saddleback or coved-type morphology in the 2nd, 3rd or 4th intercostal space. When type-2 or type-3 patterns are present, a provocative test unmasking a type-1 pattern establishes the Brugada syndrome diagnosis.[5,8]

In our patient's case, although fever unmasked a type-3 pattern in ECG and we were not able to register any arrhythmia, the patient presented with syncope and provocative flecainide test confirmed Brugada syndrome, therefore our decision to proceed to the implantation of a defibrillator. Also, the ECG at admission was performed only at the 4th intercostal space level, revealing a type-1 morphology without voltage criteria. An ECG at 2nd intercostal space level would have been important.

Evidence on the management of patients with Brugada syndrome with SARS-CoV-2 infection is lacking. However, Gregory Dendramis *et al*[9] suggested that high risk patients (spontaneous type-1 pattern, aborted sudden death and history of syncope due to ventricular tachycardia) should be managed carefully, being monitored for arrhythmias with external defibrillation pads on place, avoiding fever, periods of bradycardia and drugs known to have the potential to induce arrhythmias. Asymptomatic patients with type-1 pattern were suggested to be at intermediate risk, needing to be observed in the hospital until fever and major symptoms resolve. Low risk patients, including asymptomatic patients with type 3 pattern, were considered to be safe to discharge and attend the hospital if symptoms such as syncope developed. At the time we admitted our patient, little information was available and although we were not sure the syncope had been due to an arrhythmic event, we decided to keep our patient in the hospital for observation for some days, until fever subsided and considering that no events were registered during hospital stay.

At least 12 genes have been associated with Brugada syndrome, being *SCN5A* the most relevant gene. This gene encodes the subunit of sodium channels responsible for phase 0 of the cardiac action potential.[4] Dumaine *et al*,[10] showed that these sodium channels expression is sensitive to temperature, therefore suggesting that patients with Brugada syndrome are at higher risk of arrhythmias during febrile states. Such association has been further reported.[11] Therefore, the most probable interpretation for this case is that fever alone was the cause for the unmasking of Brugada syndrome in our patient. However, it is yet to understand if the SARS-CoV-2 itself interact directly with the myocardial cells and sodium channels, inducing the Brugada syndrome patterns.

Responsabilidades Éticas

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