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Reflex cardioinhibitory syncope potentially related to SARS-CoV-2 infection: a case report

Síncope cardioinibitória reflexa potencialmente relacionada à infecção por SARS-CoV-2: um relato de caso

Maria Emilia C. Andraus[1,2,3] , Gil F. Salles[1], Roberto P. Santos[2], Thalles C. Gomes[4], Jhonata S. Silva[4], Cesar F. Andraus[3,5] , Arjune Sen[6]

ABSTRACT

Autonomic dysfunction related to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection is increasingly described in the literature. We report the case of a 30-year-old male with a background of asthma and migraine who experienced a second episode of SARS-CoV-2 infection characterized by mild respiratory symptoms. Twenty-four days after the symptom onset, he developed acute syncope. A tilt test revealed a neuromediated cardioinhibitory response with asystole (Vasovagal Syncope International Study – VASIS type 2B). The temporal association between SARS-CoV-2 infection and syncope seems to indicate a probable causal relationship, which requires corroboration by future studies.

Keywords: autonomic dysfunction, cardioinhibitory syncope, COVID-19, post-Covid syndrome, SARS-CoV-2, vasovagal syncope.

RESUMO

Disfunção autonômica relacionada à infecção por coronavírus-2 da síndrome respiratória aguda grave (SARS-CoV-2) vem sendo cada vez mais descrita na literatura. Relatamos o caso de um homem de 30 anos de idade, com histórico de asma e enxaqueca, que apresentou um segundo episódio de infecção por SARS-CoV-2 caracterizado por sintomas respiratórios leves. Vinte e quatro dias após o início dos sintomas, desenvolveu um quadro agudo de síncope. Um teste de inclinação revelou uma resposta cardioinibitória neuromediada com assistolia (Vasovagal Syncope International Study – VASIS tipo 2B). A associação temporal entre infecção por SARS-CoV-2 e síncope parece indicar uma provável relação causal, a qual requer corroboração por estudos futuros.

Palavras-Chave: disfunção autonômica, síncope cardioinibitória, COVID-19, síndrome pós-Covid, SARS-CoV-2, síncope vasovagal.

[1]Internal Medicine Department, School of Medicine, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil
[2]Neurology Service, Clementino Fraga Filho University Hospital, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil
[3]Fuzzy Logic Laboratory (LabFuzzy), Coordination of Post-Graduate Engineering Programs (COPPE/UFRJ), Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil
[4]Scientific Initiation Program (PINC), Internal Medicine Department, School of Medicine, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil
[5]Deolindo Couto Institute of Neurology, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil
[6]Oxford Epilepsy Research Group, NIHR Biomedical Research Centre, Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital, Oxford OX3 9DU, UK

Corresponding author: Prof. Maria Emilia C. Andraus. Departamento de Clínica Médica, Hospital Universitário Clementino Fraga Filho, Universidade Federal do Rio de Janeiro, Rua Rodolpho Paulo Rocco 255, 11º andar, Bloco F, Sala 05, 21941-617, Rio de Janeiro, RJ, Brazil
E-mail: cosenzaandraus@ufrj.br
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INTRODUCTION

Syncope is a sudden and transient clinical manifestation, characterized by complete loss of consciousness and postural tone with rapid and spontaneous recovery, secondary to global and transient cerebral hypoperfusion[1]. Syncope represents around 3-5% of cases seen in emergency departments, of which 40% result in hospitalization[2].

Vasovagal syncope is the most common cause of syncope, in which the cardioinhibitory component is marked and can be severe enough to produce asystole [1,2] . According to the modified Vasovagal Syncope International Study (VASIS) Classification[3], cardioinhibitory syncope is classified into four types:

- Type I or mixed: bradycardia occurs at the time of syncope, but to not less than 40 beats per minute, or the heart rate is less than 40 beats per minute for less than 10 seconds with or without asystole of fewer than three seconds and arterial hypotension occurs before the bradycardia
- Type 2A: bradycardia of fewer than 40 beats per minute occurs without asystole of more than three seconds, and arterial hypotension occurs before the bradycardia
- Type 2B: cardioinhibition occurs with asystole for more than three seconds, and bradycardia coincides with, or precedes arterial hypotension
- Type 3: a vasodepressor response occurs, and the heart rate does not fall by more than 10% from its peak at the time of syncope

Vasovagal syncope results from a reflex leading to hypotension and bradycardia, triggered by being in one position, especially standing, for a prolonged period or exposure to emotional stress, pain or medical procedures[1]. This cardioinhibitory syncope relates to excessive bradycardia or asystole owing to a parasympathetic response [1,2] . Typically, such syncope is associated with a prodrome of sweating, feeling hot and pallor, with some fatigue after the event. Some patients require an effective treatment, such as implantation of a cardiac pacemaker, especially when they experience recurrent episodes of syncope with prolonged spontaneous cardiac pauses1. Nonetheless, given its benign nature and frequent spontaneous remissions, non-pharmacological conservative measures are usually sufficient [1,2,4] .

Recent studies have increasingly described autonomic dysfunction related to severe acute respiratory syndrome coronavirus-2 (SARS-CoV2) infection [5,6,7]. Possible mechanisms involved would be a direct action of the virus on autonomic pathways or by immune-mediated mechanisms during or after infection [7,8] .

CASE REPORT

This case report was submitted and approved by the Research Ethics Committee of the Deolindo Couto Institute of Neurology of the Federal University of Rio de Janeiro under the number 5.844.687.

We present the case of a 30-year-old male with a history of bronchial asthma and migraine. There was no background of syncope and no risk factors for epilepsy were identified. He was taking long-term formoterol fumarate and salbutamol sulfate.

The patient reported two previous episodes of SARS-CoV-2 infection, confirmed by polymerase chain reaction (PCR) from nasal swab samples. During his first bout of COVID-19, in December 2020, he presented with mild respiratory symptoms and hyposmia. He had already received two doses of the anti-COVID-19 vaccine when he contracted COVID-19 once more in January 2022, experiencing mild respiratory symptoms over about five days. Nineteen days after the resolution of the symptoms from this second episode, he presented a sudden 'fainting' and was referred to a neurologist.

At the initial review, the patient reported that he had experienced a sudden episode of discomfort in the sternal region and a sensation of 'strong pulsation' in the oropharynx, with generalized weakness. A family member, who is a health professional, explained that at the time of the event the patient had a blood pressure of 70/40 mmHg and a heart rate measured by pulse oximeter of 40 beats per minute. The event evolved with loss of consciousness, pallor, sweating and initially cephalic muscle jerks that were generalized, with a total duration of five minutes. The patient regained consciousness about ten seconds later, with a sensation of the need to open his bowels. There was no urinary and/or fecal sphincter incontinence.

The patient underwent cardiological and neurological outpatient investigation, with the main diagnostic hypothesis being vasovagal syncope leading to an anoxic seizure. Laboratory blood tests, electrocardiogram, two-dimensional transthoracic echocardiograms, carotid and vertebral arteries duplex ultrasound, treadmill stress test, electroencephalogram and brain magnetic resonance imaging were all normal. A 24-hour Holter electrocardiogram recorded a period of sinus bradycardia (44 beats per minute) without associated symptoms. We performed a tilt test with non-invasive blood pressure monitoring in a room with a stable temperature of around 20ºC. The patient was kept in a supine position at 0° for 10 minutes, followed by an inclination of the table at 70° for a maximum period of 35 minutes. Isosorbide dihydrate was administered at a dose of 12.5mg sublingually at the 20th minute of tilt. The patient had a sudden and significant drop in blood pressure and heart rate (Figure 1), with an asystolic pause of 9.8 seconds (Figure 2) followed by syncope, with rapid recovery after being placed in the Trendelenburg position. The tilt test was therefore positive for the presence of neuromediated cardioinhibitory response with asystole (VASIS type 2B).

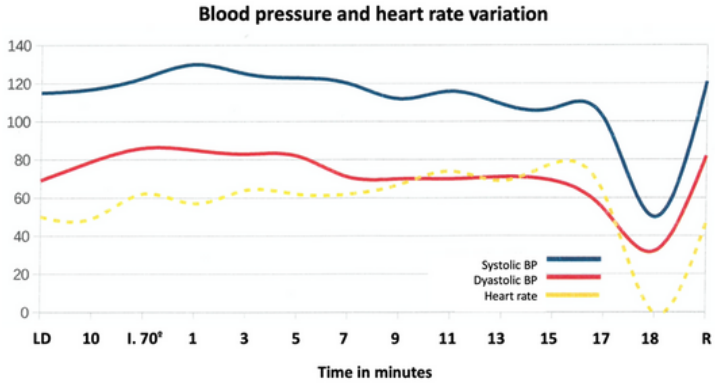

Figure 1. Values obtained for blood pressure in mmHg and heart rate in beats per minute during the tilt test. Eighteen minutes after 70degree head up tilt, there is a marked drop in blood pressure and asystole at the time of syncope.
Blue line represents the systolic blood pressure; red line represents the diastolic blood pressure; yellow dotted line represents heart rate.
BP – Blood pressure; LD – lying down; I.70° – Inclination at 70°; R – Return.

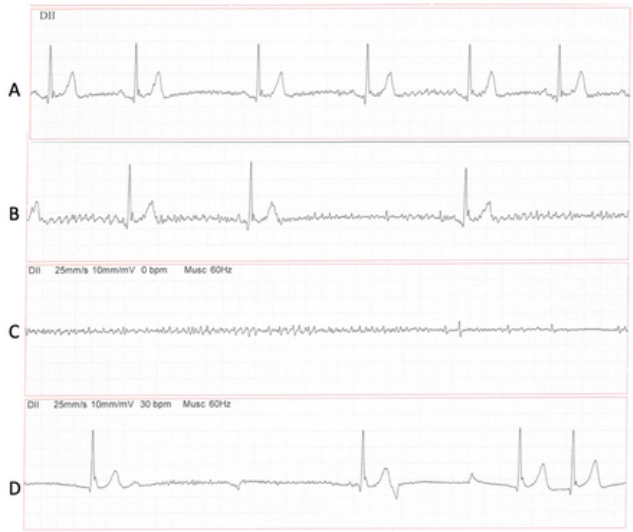

Figure 2. Example electrocardiogram tracings during the tilt test: A – Basal sinus rhythm of 50 beats per minute; B – cardioinhibitory response with bradycardia (heart rate 38 beats per minute) which coincided with presyncope state; C – 9.8 second asystole which coincided with syncope; D – onset of recovery after the patient is placed in Trendelenburg position. Paper speed 25mm/s.

Currently, the patient is under outpatient clinical follow-up. No specific cardiovascular medication has been initiated. The patient remains well and, through adhering to conservative measures such as good hydration and standing slowly from the sitting posture, has not experienced any further syncopal episodes. There were also no reports of subsequent seizures.

DISCUSSION

An association between autonomic manifestations and SARS-CoV-2 infection has been increasingly reported[5,6,7] . Manifestations related to autonomic dysfunction may occur during the acute phase of the disease and/or be part of a post-COVID-19 syndrome when symptoms extend beyond four weeks[5,9]. Some authors hypothesize an anti-inflammatory cholinergic response as the genesis of this autonomic dysfunction, which consists of an increase in vagal tone in contrast to the sympathetic stimulus of inflammatory cytokines[7]. In addition, the COVID-19 virus can directly cause immune-mediated neurological syndromes[7,8] .

This report presents a case of syncope secondary to neuromediated cardioinhibitory response with asystole temporally associated with SARS-CoV-2 infection. The syncopal episode occurred within four weeks of the onset of respiratory symptoms. The 24-hour Holter performed 45 days after testing positive for COVID-19, still showed sinus bradycardia. The tilt test, performed on the 55th day after infection, demonstrated cardioinhibitory syncope. This may indicate that the patient developed post-acute COVID-19 syndrome.

According to The Center for Disease Control (CDC), post-COVID conditions can be characterized by the persistence of health issues more than four weeks after SARS-CoV-2 infection[10]. The long-term duration of such manifestations, however, is still unclear, and symptoms may last for months, weeks or longer [9,10]. Here, we consider that the temporal association with SARS-CoV-2 infection, and the absence of other etiological factors that can better explain the clinical manifestations presented by the patient, favor the diagnosis of cardioinhibitory syncope related to SARS-CoV-2 infection.

Although autonomic dysfunction and SARS-CoV-2 infection has been reported both in the acute and chronic phases, as far as we know, there is only one previous report of cardioinhibitory reflex syncope associated with SARS-CoV-2 infection[7]. In that individual, syncope occurred during the acute phase of the disease and the asystolic periods were repetitive and severe requiring temporary transvenous pacemaker implantation. In our patient, the cardioinhibitory syncope occurred nearly three weeks after the acute COVID-19 symptoms, with an altered tilt test performed after four weeks. Taken together these data suggest that vasovagal reflex syncope may occur either in acute or post-acute COVID-19 syndromes. In both our case and the previous report, the reflex syncope was classified as VASIS type 2B by the tilt test, and there appeared to be a full cessation of the syncopal episodes.

CONCLUSION

This case report evidences a potential association between SARS-CoV-2 infection and the development of cardioinhibitory syncope. Although a causal relationship cannot be proved by this case report, we believe that highlighting this, hitherto rarely described phenomenon, should encourage clinicians to further consider COVID-19 as being contributory to syncope even once the acute infection has subsided. Future studies should prospectively follow people experiencing syncope in the post-acute phase of COVID-19 and try to better determine a mechanistic basis for the observed syncope.

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