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Case Series

Cardiovascular Dysautonomy as a Sequel of SARS COV 2. Case Series

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Abstract: The impact of COVID-19, caused by the SARS-CoV-2 virus, a pandemic that originated in Wuhan, China, can lead to serious complications, in addition to mild symptoms, with special interest in the autonomic nervous system (ANS). Damage to the ANS by SARS-CoV-2 can cause dysautonomia, an imbalance between the sympathetic and parasympathetic system, with unclear mechanisms such as cytokine storm, excessive inflammation, and virus neurotropism. A significant sequelae of COVID-19 is cardiac dysautonomia, which affects heart rate, blood pressure and other autonomic reflexes, causing postural tachycardia, orthostatic hypotension, arrhythmias and fatigue. There is decreased heart rate variability (HRV) in patients, suggesting dysautonomia. Long COVID syndrome can also include cardiac dysautonomia. To diagnose cardiac autonomic neuropathy, at least two of six criteria must be met, such as an SDNN less than 50 ms and an RMSSD less than 15 ms. The cases of cardiac dysautonomia below present several of these criteria met. Methods to evaluate cardiac dysautonomia include the COMPASS 31 scale and the orthostatic hypotension questionnaire (OHQ), but more research is still needed, especially in Mexico. The case study shows that those who followed non-pharmacological recommendations such as cardiovascular exercise, increased water intake and BMI control had improvement, while cases that did not follow these recommendations did not show significant improvements. Cardiac dysautonomia is a post-COVID-19 sequelae with high prevalence, highlighting the importance of non-invasive methods for its diagnosis. Even without symptoms, people can have this sequelae, so it is important to suspect cardiovascular disorders. The need for early intervention and monitoring of hygienic-dietary measures is emphasized to avoid the worsening and chronicity of cardiac dysautonomia, with the hope of preventing the development of chronic diseases and fatal outcomes.

Keywords: Dysautonomia, ANS, orthostatic hypotension, COVID-19, HRV.

INTRODUCTION

Coronavirus disease 2019 (COVID 19), caused by the SARS CoV 2 coronavirus that emerged in Wuhan, China, spread rapidly throughout the world, rapidly becoming a pandemic that caused morbidity and mortality worldwide. SARS CoV 2 leads to a wide spectrum of clinical manifestations ranging from asymptomatic, mild symptoms (fever, headache, myalgia, sore throat, cough, anosmia), through to severe symptomatic viral pneumonia, which generally progresses to syndrome of acute respiratory distress and multiple organ failure, leading to death.

One of the claims about SARS COV 2 is that it affects the autonomic nervous system (ANS), however, the mechanism by which it does so has not yet been clarified. Various mechanisms have been proposed by which nerve damage is generated by this virus; The most accepted to date are the cytokine storm and excessive inflammation in addition to the neurotropism of the virus itself, which produces damage at the level of the autonomic regulatory centers present in the brain stem. The damage generated in the ANS leads to an imbalance between its two branches, sympathetic and parasympathetic, which is known as dysautonomia.

Cardiac dysautonomia constitutes one of the most studied post-COVID 19 sequelae. In this pathology, heart rate, blood pressure and other reflex mechanisms involved in correct cardiac autonomic functioning are affected. So far, the key symptoms presented by patients suffering from this condition have been described, such as orthostatic hypotension, postural orthostatic tachycardia, arrhythmias, among others. However, the long-term implications of this sequelae are unknown, that is, whether the nerve damage will be permanent, will subside or worsen; Furthermore, it represents an underdiagnosed sequelae because it is difficult to recognize and requires expensive diagnostic tests [1-4, 9].

It is physiologically correct to say that there is a variation in the duration between one beat and another, we call this heart rate variability (HRV), this characteristic in turn gives the ability to increase or decrease the heart rate as necessary, maintaining thus the necessary reflex homeostasis. HRV is an indicator of the regulatory function of the ANS on the heart and its analysis represents a reliable non-invasive method that is widely used around the world. The reports found in the literature consulted collectively point to a decrease in HRV in patients who had COVID 19, which in turn supports the existence of a deregulation in the autonomic system secondary to the infection.

During COVID 19 infection, the patient presents an increase in parasympathetic activity with respect to cardiac control of HRV. [3] Long covid syndrome includes the presence of cardiac dysautonomia with symptoms mainly of orthostatic hypotension, tachycardia, fatigue, among others. [4, 5, 15, 16]. However, the mechanism by which damage to the ANS is generated secondary to SARS CoV 2 infection and why it continues to be present even after acute infection remains to be clarified [7, 16]. It is necessary to establish a better diagnosis of the sequelae of covid, including cardiac dysautonomia, in addition to more prospective studies and establishment of measures to avoid permanent damage [4-7].

In addition, there are other non-invasive diagnostic support methods for the suspicion and search for autonomic disorders at different levels, because it is well known that cardiac dysautonomia can occur in conjunction with other dysautonomia. The symptoms presented by dysautonomia in different organs are evaluated using the COMPASS 31 scale. On the other hand, cardiac dysautonomia frequently causes orthostatic hypotension for which the Orthostatic Hypotension Questionnaire (OHQ) is useful; it is composed of two parts, the first evaluates the symptoms presented corresponding to orthostatic hypotension (OHSA), while the second evaluates orthostatic hypotension and its impact on daily activities (OHDAS) [17, 18].

Based on the various studies carried out to date, the relationship between the function of the ANS and the severity of the damage caused by COVID 19 is accepted. However, there are no concrete data about the status of cardiac autonomic regulation by long-term COVID 19. distance and in the Mexican population there are no reports in this regard.

CASE 1

This is a previously healthy 21-year-old male patient. Upon direct examination, he stated that he did not engage in any kind of physical activity and denied any significant pathological history. The patient comments that he has had mild COVID 19 on two occasions, both confirmed by an antigen test. The first infection occurred in August 2020, presenting diarrhea, anosmia, headache, asthenia, adynamia, odynophagia; He was treated with ivermectin, corticosteroids, aspirin, B complex, and paracetamol. The second infection occurred in September 2021, on this occasion he presented cough, fever and hyaline rhinorrhea lasting seven days, his treatment on this occasion consisted only of paracetamol. One year after the last confirmed infection with COVID 19, you come to us to take a 12-lead electrocardiogram and perform a study that evaluates the variability of your basal heart rate.

An anthropometry was performed, which resulted in a height of 174 centimeters and a weight of 78 kilograms, which results in a BMI (Body Mass Index) of 25.8 corresponding to overweight, a waist-hip index (WHR) of 0.97, which refers to at a low risk of developing cardiovascular diseases.

In the electrocardiogram taken, no electrophysiological alterations were observed with a sinus rhythm, frequency of 80 bpm and a normal axis.

The most outstanding finding in this case was the decrease in variability in basal heart rate. In the time domain analysis, STD RR was obtained: 27.9 s, RMSSD (Root mean square of the differences of the sum of the squares between adjacent RR intervals): 13.1 s, NN50: 0, PNN50: 0 % ; in the frequency domain it was obtained, LF: 48.9, HF: 50.9 and LF/HF ratio: 1.643. Regarding the nonlinear analysis, SD1: 9.3 and SD2: 38.4 were obtained.

Hygienic dietary measures were indicated to the patient, a structured diet to reduce fat percentage accompanied by low-impact cardiovascular exercise for 30 minutes to an hour daily. However, it was not possible to comply with these measures. In addition, he mentions that during these months he has had 3 episodes of weakness in his lower limbs when standing immediately after waking up, sometimes causing falls, without losing consciousness at any time.

A control study was carried out nine months later, in addition to the application of the COMPASS 31 scale and the OHQ questionnaire. Regarding the COMPASS 31 evaluation, orthostatic intolerance (28/40 points); vasomotor (0/5 points); secretomotor (4/15 points); gastrointestinal (10/25 points); bladder (1/10 points) and pupillomotor (3/5 points), total score of 46 out of 100. Referring to the COMPASS 31 evaluation, orthostatic intolerance (24/40 points); vasomotor (4/5 points); secretomotor (6/15 points); gastrointestinal (8/25 points); bladder (0/10 points) and pupillomotor (3/5 points), total score of 45 out of 100. Presenting an OHSA of 46/60 points and an OHDAS of 16/40 points, a total of 62/100 points.

In the time domain analysis, STD RR: 46.9 s, RMSSD: 23.4 s, NN50: 15, PNN50: 3.9% were obtained; in the frequency domain it was obtained, LF: 48.9, HF: 50.9 and LH/HF ratio: 1.89. Regarding the nonlinear analysis, SD1: 16.6 and SD2: 64.2 were obtained.

CASE 2

This is a previously healthy 22-year-old female patient. Upon direct questioning, she stated that she did not do any kind of physical activity, and that she was allergic to pollen, dust, humidity, and pineapple; Their allergies manifest themselves through rhinitis and allergic conjunctivitis. The patient states that she has had an increase in her allergies since the second episode of COVID-19. The patient comments that she has had mild COVID 19 on two occasions, both confirmed by an antigen test. The first infection occurred in July 2020, presenting gastrointestinal symptoms such as diarrhea and vomiting, he denies respiratory symptoms; He was treated with paracetamol and oral electrolytes. The second infection occurred in January 2022, on this occasion he presented cough, headache and hyaline rhinorrhea lasting three days, his treatment was the same as in the previous episode. Eight months after the last confirmed COVID-19 infection, you come to us to take a 12-lead electrocardiogram and perform a study that evaluates the variability of your basal heart rate.

An anthropometry was performed, which obtained a height of 157 centimeters and a weight of 64 kilograms, which results in a BMI of 26.6 corresponding to overweight, an ICC of 0.89 that refers to a high risk of developing cardiovascular diseases.

In the electrocardiogram taken, no electrophysiological alterations were observed with a sinus rhythm, frequency of 79 bpm and a normal axis.

The most outstanding finding in this case was the decrease in variability in basal heart rate. In the time domain analysis, STD RR: 16.6 s, RMSSD: 12.2 s, NN50: 0, PNN50: 0% were obtained; in the frequency domain it was obtained, LF: 48.9 ms 2, HF: 50.9 ms 2 and LF/HF ratio: 0.981. Regarding the nonlinear analysis, SD1: 8.6 and SD2: 21.8 were obtained.

Hygienic dietary measures were indicated to the patient, a structured diet to reduce the percentage of fat accompanied by low-impact cardiovascular exercise for 30 minutes to an hour daily. However, it was not possible for her to comply with these measures; she also reported feeling more fatigued than normal during her daily life, even when climbing stairs.

A control study was carried out nine months later, in addition to the application of the COMPASS 31 scale and the OHQ questionnaire. Regarding the COMPASS 31 evaluation, orthostatic intolerance (24/40 points); vasomotor (4/5 points); secretomotor (6/15 points); gastrointestinal (8/25 points); bladder (0/10 points) and pupillomotor (3/5 points), total score of 45 out of 100. Presenting an OHSA of 26/60 points and an OHDAS of 12/40 points, a total of 38/100 points.

In the time domain analysis, STD RR: 25.9 s, RMSSD: 21.5 s, NN50: 6, PNN50: 1.6 % were obtained; in the frequency domain it was obtained, LF: 32.7, HF: 67.2 and LH/HF ratio: 0.487. Regarding the nonlinear analysis, SD1: 15.2 and SD2: 33.3 were obtained.

CASE 3

This is a previously healthy 23-year-old male patient. Upon direct questioning, he affirms that he performs aerobic physical activity for one hour a day and denies any significant pathological history. The patient comments that he has had mild COVID-19 on two occasions, both confirmed by an antigen test. The first infection occurred in May 2020, he denies symptoms. The second infection occurred in February 2022, on this occasion he presented asthenia, adynamia, myalgia, fever, headache and hyaline rhinorrhea lasting seven days, his therapeutic management was only with paracetamol. Six months after the last confirmed COVID-19 infection, you come to us to take a 12-lead electrocardiogram and perform a study that evaluates the variability of your basal heart rate.

An anthropometry was performed, which obtained a height of 181 centimeters and a weight of 65 kilograms, which results in a BMI of 19.8 corresponding to a normal value, an ICC of 0.84, which refers to a very low risk of developing cardiovascular diseases.

In the electrocardiogram taken, no electrophysiological alterations were observed with a sinus rhythm, frequency of 82 bpm and a normal axis.

The most outstanding finding in this case was the decrease in variability in basal heart rate. In the time domain analysis, STD RR: 15.6 s, RMSSD: 9.7 s, NN50: 0, PNN50: 0% were obtained; in the frequency domain it was obtained, LF: 50.6, HF: 49.4 and LH/HF ratio: 1.023. Regarding the nonlinear analysis, SD1: 6.9 and SD2: 20.9 were obtained.

Hygienic dietary measures were indicated to the patient, a structured diet to reduce the percentage of fat accompanied by low-impact cardiovascular exercise for 30 minutes to an hour daily. These measures were carried out satisfactorily. At no time does the patient state that he or she presents any type of symptomatology that is important to him or her.

A control study was carried out nine months later, in addition to the application of the COMPASS 31 scale and the OHQ questionnaire. Regarding the COMPASS 31 evaluation, orthostatic intolerance (0/40 points); vasomotor (0/5 points); secretomotor (4/15 points); gastrointestinal (9/25 points); bladder (4/10 points) and pupillomotor (3/5 points), total score of 20 out of 100. Presenting an OHSA of 12/60 points and an OHDAS of 1/40 points, a total of 13/100 points.

In the time domain analysis, STD RR: 33 s, RMSSD: 36.3 s, NN50: 55, PNN50: 15.9 % were obtained; in the frequency domain it was obtained, LF: 21.7, HF: 78.3 and LH/HF ratio: 0.276. Regarding the nonlinear analysis, SD1: 25.7 and SD2: 38.9 were obtained.

DISCUSIÓN

In the exposed cases, cardiac dysautonomia is evident as a sequel to mild COVID-19, ranging from the absence of symptoms typical of the pathology to manifestations that gradually worsen. Which coincides with what the literature shows about cardiac dysautonomia as a post-covid disorder.

In order to diagnose cardiac autonomic neuropathy, at least 2 of the following 6 criteria must be met: SDNN < 50 ms, SDANN < 40 ms, RMSSD < 15 ms, PNN50 < 75%, LF < 300 ms2, HF < 300 ms2 [10]. Patients meet 4 of the 6 criteria; a RMSSD < 15 ms, a PNN50 < 75%, a LF < 300 ms2, a HF < 300 ms2. Therefore they were diagnosed with cardiac autonomic neuropathy.

The PNN50 refers to the percentage of RR intervals that are more than 50 milliseconds apart. It is necessary to highlight that so far no cases have been reported that show a PNN50 of zero as these three cases did, so we can think that involvement to this degree may be more common than is thought; in addition to the danger represented by having a PNN50 of zero.

Corresponding to the COMPASS 31 questionnaire, its evaluation is carried out through six weighted domains, resulting in a total of 100 points, the higher the score, the greater the autonomic dysfunction. The same applies to the OHQ, with a total of 100 points and a directly proportional relationship between score and orthostatic hypotension [17, 18]. In both cases, the highest score was case one and the lowest was case three, who from the beginning was asymptomatic and who managed to improve their HRV values by following the indicated measures, while cases one and two who did not carry out the indications, noticed a worsening of the symptoms and changes in the values in the HRV were almost imperceptible.

Special attention must be paid when contrasting the different evolution that each of them had. It should be noted that by properly following the non-pharmacological therapeutic management measures that include, performing cardiovascular exercise for at least 30 minutes a day, increasing water intake, decreasing the amount of food per meal, maintaining a BMI <25, among others, demonstrated a notable improvement in case number three compared to cases one and two.

Graph 1. The change that the three cases had in their HRV is observed compared to a patient without covid or nervous alteration. The decrease in dispersion is notable in each of the cases, especially in number three; In all of them the comet shape is lost. Which in turn makes the PNN50 of zero that the three showed more evident. A. Baseline HRV Poincaré diagram for a representative COVID-negative patient. B. Basal HRV Poincaré diagram CASE 1. C. Basal HRV Poincaré diagram CASE 2. D. Basal HRV Poincaré diagram CASE 3.

Graph 2. It is observed that the patients still maintain a low dispersion in contrast to the non-covid patient. Case three was the one who followed the non-pharmacological measures that were given to him. If it is compared with his previous result, it can be seen that he was the one who obtained the most progress and therefore a better improvement, compared to the other patients who, yes. shows a slight improvement in their HRV but they are increasingly symptomatic.

A. Baseline HRV Poincaré diagram for a representative COVID-negative patient. B. Baseline HRV Poincaré diagram CASE 1 follow-up. C. Poincaré diagram baseline HRV CASE 2 follow-up. D. Baseline HRV Poincaré diagram CASE 3 follow-up.

CONCLUSION

Cardiac dysautonomia represents one of the most prevalent post-COVID-19 sequelae today. Among its manifestations we find mainly postural orthostatic tachycardia and, to a lesser extent, a decrease in heart rate variability.

We present these cases to denote the importance of dysautonomia within post-COVID sequelae and its detection through non-invasive methods. Furthermore, the presence of a sequela of this type should not be ruled out just because of the absence of symptoms. Making it evident that no matter how healthy a person is, as was case 3, they are not exempt from presenting this sequel.

It is important to suspect a cardiovascular alteration as a post-COVID-19 sequel, since dysautonomia has relevance at different levels in medicine and in the patient's style and quality of life. If there is a decrease in HRV and cardiac dysautonomia, one should begin with hygienic-dietary measures that, if not respected, would represent the maintenance and probable worsening of cardiac dysautonomia, which could become irreversible, thus becoming a disease chronic and representing the loss of reflex regulation of heart rate.

The pathophysiology of this condition and the consequences it can cause needs to be studied in a deeper and more extensive manner. COVID-19 is a new entity that still needs extensive data collection. We propose that emphasis be placed on carrying out the relevant therapeutic indications in case of suspecting and having met parameters to diagnose cardiac dysautonomia, observing if it gives them a notable improvement and thus the ability to reverse the damage caused by COVID 19; In this way, early attention can prevent the development of a chronic disease and a fatal outcome.

Ethical Responsibilities: Protection of People and Animals: The authors declare that no experiments on humans or animals have been performed for this research.

Data Confidentiality: The authors declare that they have followed the protocols of their workplace regarding the publication of patient data.

Right to Privacy and Informed Consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

Use of Artificial Intelligence to Generate Texts: The authors declare that they have not used any type of artificial intelligence in the writing of this manuscript or for the creation of figures, graphs, tables or their corresponding legends.

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