

Giant Inverse T-Wave in a Patient with COVID-19

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ABSTRACT

It has been described that COVID-19 is a dynamic behavior and systemic affection entity, so it is essential to develop the diagnostic and prognostic tools which allows to specifically identify target organ damage. The electrocardiographic finding of an inverse T-wave suggests transient apical dysfunction of the left ventricle, generating confusion among different heart diseases. However, despite the lack of troponin elevation and other myocardial injury signs, this finding is unspecific, especially in the patient with COVID-19. The aim of this manuscript is to present the case of a patient with COVID-19 without a previous diagnosis of heart disease, which manifests an isolated inverse T-wave.

KEYWORDS: COVID-19, electrocardiography, heart diseases, takotsubo cardiomyopathy

INTRODUCTION

A T-wave inversion (TWI) is defined as any wave measuring ≥ 1 mm in depth in two or more contiguous leads, excluding electrocardiographic lead aVR, III, and V1 leads. The clinical relevance of this finding depends largely on its location on the 12-lead electrocardiogram (ECG).^[1] The importance of identifying TWI on the ECG lies on its differential diagnoses discarding. It must be remembered that TWI confined to V1–V2 is a common finding in the general population and can also be seen in high-performance athletes (14%–28%).^[2] Nevertheless, studies have estimated that the incidence of TWI in the middle-aged population is approximately 0.7%, and it is associated with an increase in the risk of arrhythmias and cardiac death.^[1] In another hand, TWI in the inferolateral leads is always abnormal and indicates underlying cardiac pathology.^[1] In relation to the above and in the current attempt to explain the different manifestations of COVID-19 disease, an association has been found between cardiovascular alterations and the presence of low-grade endocardial interstitial inflammation with the presence of viral particles in the myocardium of infected patients.^[1] Due to this, considering that COVID-19 is an entity of dynamic behavior and systemic affection, so it is essential to develop the diagnostic and prognostic tools which allows to specifically identify target organ damage. Hence, the aim of this manuscript is to present the case of a patient with COVID-19 without a previous diagnosis of heart disease, who manifests an isolated inverse T-wave.

CASE REPORT

A 60-year-old male patient with a history of controlled arterial hypertension came to the emergency room with a clinical picture of respiratory distress. Chest X-ray showed pulmonary consolidation with interstitial pattern compatible with pneumonia, and polymerase chain reaction (PCR) to confirm the suspicion of severe acute respiratory syndrome-coronavirus-2 (SARS-Cov-2) infection, testing positive. An ECG was performed showing giant inverse T-waves in V2, V3, V4, and V5 leads (extensive anterior wall) [Figure 1], so troponin

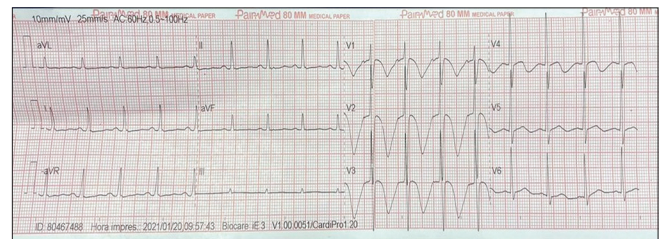


Figure 1: Electrocardiogram showing regular RR interval; with a heart rate of 110 beats/min; PR interval 120 ms; QRS 80 ms; prolonged QT interval – 480 ms; sinus rhythm; normal cardiac electrical axis; giant negative T-waves from V2 to V5; left ventricular hypertrophy

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tests were requested due to the suspicion of myocardial ischemic event, obtaining negative results in both tests with a 6-h interval. Ionogram, D-dimer, creatine kinase-MB, and N-terminal prohormone BNP were found to be normal. Based on the above, a presumptive diagnosis of mild myocarditis secondary to COVID-19 was made.

For this case, treatment of myocarditis was started with immunoglobulins (80 mg/day) for 4 days and methylprednisolone (500 mg/day) in a descending regimen for 14 days and antiviral treatment: interferon beta-1a 0.25 mg/48 h and ritonavir 400 mg/lopinavir 100 mg/12 h. Once medical management with hemodynamic, medical, and respiratory support was established, normalization of T-waves and significant reduction of the QTc interval (460 ms) were evidenced. The markers of cardiac damage such as troponins, MB, and BNP remained in their normal ranges.

The patient evolved satisfactorily from the hemodynamic point of view, progressively improving his clinical condition. He was left with pulmonary rehabilitation with therapies for optimal recovery of this disease. After 3 months of follow-up, the patient presented only dyspnea on slight exertion, which progressively decreased thanks to the use of physical exercise and respiratory therapies. A control electrocardiographic report is observed without significant findings.

DISCUSSION

Troponin elevation in patients with COVID-19 is presumed to be due to cardiomyocyte damage by SARS-CoV-2 rather than the typical coronary artery occlusion.^[5] Moreover, in histopathological studies of patients with moderate–severe COVID-19 phenotype, low-grade endocardial interstitial inflammation with the presence of viral particles, in addition to loss of cytoplasmic membrane integrity, has been found. In these patients, there is no evidence of arterial obstruction in coronary studies, so it is presumed that the development of cardiogenic shock is directly related to myocarditis.^[1] The presence of diffuse TWI with or without troponin elevation in this group of patients has been associated with very high mortality rates.^[1] These findings allow us to observe the direct cardiac affection because of SARS-CoV-2, and alert us to possible different pathogenic mechanisms of this virus. Among the cases reported in the literature [Table 1], arterial hypertension, diabetes mellitus type II, and coronary heart disease are the most frequent comorbidities.^[4] A recent study showed that elevation of proinflammatory molecules, such as high-sensitivity C-reactive protein and IL-6, as well as markers of myocardial damage such as hs-cTnI and NT-proBNP, were associated with an increase in in-hospital mortality in all severe cases.^[5] However, increased cardiac indicators

had more important values than inflammatory factors in the prognostic assessment of patients with COVID-19,^[4] which may possibly indicate direct myocardial affection by the viral infection other than the damage suffered by the myocardium due to systemic vascular and coronary involvement.

In presence of a TWI, a differential diagnosis with Takotsubo syndrome^[6] and Wellens' syndrome,^[7] which have described the presence of this same alteration, must be made. Although studies in this regard are growing and there is too much to be clarified, there are possible explanations for a possible myocardial injury that may cause this electrocardiographic finding. It has been proposed that this damage arises mainly from two processes: first, due to the inflammatory response secondary to the presence of cytokine storm in the presence of infection,^[8] and second, due to alterations in coagulation, causing thromboembolic complications that affect cardiac microcirculation.^[9] More importantly, the direct mechanism that triggers myocarditis cannot be neglected.

The TWI location correlates well with the location of the segments with transmural edema which seems to be a prerequisite for TWI and therefore may be an indicator of underlying myocardial injury in these segments. On the other hand, diffuse TWI can be associated with global myocardial injury, as well as fulminant myocarditis in some cases.^[1] Results need to be evaluated in a larger sample of patients, comparing the presence of diffuse TWI versus nondiffuse TWI, and determine whether any specific intervention can reduce mortality in these cases. Contrasting with the cases summarized in Table 1, Romero *et al.*^[1] Published in their case series a mean age of the study population of 66 ± 7 years, of which 51% were male and 71% of total TWI were observed in lateral leads. On the other hand, Barman *et al.*^[4] in their original study classified their study population into severe and nonsevere groups with respect to the manifestation of the pathology and reported a mean age of 65 ± 13.8 years in the severe group with a higher mortality rate, no gender significance between both the groups, and electrocardiographic findings such as the presence of TWI and ST–T changes in this group. Therefore, we can find a relationship between the age of the patients and the cardiovascular manifestations with electrocardiographic alterations. In addition, it can be observed that all patients had comorbidities affecting the cardiometabolic system and were middle aged, so that the inflammatory process together with hemodynamic stress could have triggered the destabilization of an established atherosclerotic plaque secondary to the endothelial dysfunction generated by these cardiometabolic diseases, leading to vascular stasis, symptomatic myocarditis, and coronary obstruction.

Table 1: Summary of studies reporting inverted T-wave in patients with coronavirus disease-2019

Author	Description	Electrocardiographic findings
Romero <i>et al.</i> ^[1] Case series	195 patients. 51% were men versus 49% women. 72% of the total patients had arterial hypertension, 43% diabetes mellitus type II, 23% chronic kidney disease, 14% coronary heart disease, 10% chronic obstructive pulmonary disease, and 2% obstructive sleep apnea. All with confirmed diagnosis of SARS-CoV-2 PCR	Presence of TWI in septal face in 26% of patients, 64% in anterior face, 71% in lateral face, 57% in inferior face, 31.3% in a single cardiac wall, 33% in two cardiac walls, 24.1% in three cardiac walls, and 11.8% in four cardiac walls. 18% of patients presented QTc >460 ms
Barman <i>et al.</i> ^[4] Original study	219 patients. 59% were men versus 41% women. 212 had chronic disease: 53% hypertension, 28% diabetes mellitus type II, 20% hyperlipidemia. All with confirmed diagnosis of SARS-CoV-2 PCR	TWI was present in 22% of the total number of patients reported. In this group, 8% presented this finding in the anterior face, 5% in the inferior face, and 9% in the lateral face. Of this group, 4% of patients presented ST-segment elevation, 20% ST4 depression, 5% QT >500 ms, 14% QRS >120 ms, 2% PR >200 ms, 4% PR <120 ms. 5% presented right bundle branch block
Manzur-Sandoval <i>et al.</i> ^[5] Case report	A 54-year-old woman with a history of diabetes mellitus type II and hypertension, treated with oxygen with a mask for respiratory symptoms due to COVID-19. The patient developed acute chest pain, hypotension, and pulmonary edema. Diagnosis of Takotsubo syndrome associated with COVID-19 infection	Giant inverted T-waves from V2 to V6, DI and aVL (extensive anterior face); Q waves in DII and aVF; prolonged QT
Suryawan <i>et al.</i> ^[6] Case report	85-year-old man with a history of diabetes mellitus type II, presented with oppressive chest pain, fever, dyspnea, and fatigue. Diagnosed with Wellens syndrome with suspicion of COVID-19 infection	Nonspecific ST-T segment changes from V2 to V5, which evolved into biphasic TWI and minimally elevated ST-segment in leads V2 and V3, and then deeply inverted T waves in lead from V2 to V4
Doyen <i>et al.</i> ^[7] Case report	A 69-year-old man with a history of arterial hypertension. He presented acute respiratory distress syndrome requiring mechanical ventilation. PCR positive for COVID-19. Diagnosis of myocarditis secondary to SARS-CoV-2	Presence of TWI in anterior face derivatives that later progressed to a diffuse character

PCR: Polymerase chain reaction, TWI: T-wave inversion, COVID-19: Coronavirus disease-2019, SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2

The direct involvement of viral particles has been reliably related to the myocardial damage present in patients with COVID-19, the plasma concentration of interleukin-6 (IL-6) increases markedly in those with cardiac injury as well as the amino-terminal fraction of N-terminal brain natriuretic peptide (NT-proBNP) and cardiac troponins (cTnI/T). Considering that cytokine storm is also the central pathophysiological mechanism in fulminant myocarditis, it is logical to think of cardiac damage by COVID-19.^[10-12] Patients with COVID-19 are at risk for cardiac arrhythmias, acute coronary syndromes, heart failure-related events, and fulminant myocarditis. Myocardial injury can occur at different phases of COVID-19 (e.g. viral, pulmonary, inflammatory, and recovery phases), even late after symptom onset. In addition, SARS-CoV-2 has been shown to establish a receptor-binding domain with angiotensin-converting enzyme 2 (ACE2) before entering the host cells via endocytosis. Since more than 7.5% of myocardial cells have positive ACE2 expression, this could influence the entry of SARS-CoV2 into cardiomyocytes and cause direct cardiotoxicity.^[13]

In addition, SARS-CoV-2 viral particles have been identified in cardiac tissue by real-time PCR testing, which has provided

evidence to strengthen this theory.^[13-15] On the other hand, IL-6 may provide a determining factor in explaining this phenomenon, as observed in the first case report of COVID-19 complicated with fulminant myocarditis; the patient in this case had significantly elevated IL-6, suggesting the presence of cytokine storms.^[16] Cytokine storms may lead to increased vascular wall permeability and myocardial edema, which may explain the thickened interventricular septum in this patient. In addition, hypoxia may result in early and substantial inflammatory responses and cellular damage, which may cause rapid and substantial damage to the heart.^[16] Based on these findings, the effects of underlying cardiovascular comorbidities and myocardial damage on the prognosis of patients with COVID-19 are significant. To exclude the impact of other confounders, multivariable-adjusted models have shown independent associations between cardiac injury and mortality, with hazard ratios ranging from 4.26 to 10.90.^[17,18]

Finally, it is important to note that these ECG findings were associated with higher rates of mechanical ventilation and mortality, particularly in the presence of troponin elevation.^[1] Proper and timely identification of this ECG pattern could play an important role in identifying patients

with COVID-19 at a higher risk of adverse events such as intubation and death. This phrase means that in those patients who have an incidental finding of inverted T wave, but who do not present any clinical manifestation, follow-up should be performed to evaluate whether in the short or medium term any manifestation may occur in patients who have and do not have a history of cardiovascular disease.

CONCLUSION

High troponin levels accompanied by the presence of TWI are signs of bad prognosis in patients with COVID-19. Likewise, the appearance of ECG abnormalities such as TWI in the absence of respiratory symptoms suggests SARS-Cov-2 infection with myocardial affectation. This must be an alarm sign to execute the COVID-19 protocol and evaluate the cardiac and metabolic stability of the patient.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal the identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Romero J, Alviz I, Parides M, Diaz JC, Briceno D, Gabr M, *et al.* T-wave inversion as a manifestation of COVID-19 infection: A case series. *J Interv Card Electrophysiol* 2020;59:485-93.
- D'Ascenzi F, Anselmi F, Adami PE, Pelliccia A. Interpretation of T-wave inversion in physiological and pathological conditions: Current state and future perspectives. *Clin Cardiol* 2020;43:827-33.
- Inciardi RM, Lupi L, Zaccone G, Italia L, Raffò M, Tomasoni D, *et al.* Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). *JAMA Cardiol* 2020;5:819-24.
- Barman HA, Atici A, Alici G, Sit O, Tugrul S, Gungor B, *et al.* The effect of the severity COVID-19 infection on electrocardiography. *Am J Emerg Med* 2020;46:317-22.
- Manzur-Sandoval D, Carmona-Levario P, García-Cruz E. Giant inverted T waves in a patient with COVID-19 infection. *Ann Emerg Med* 2021;77:264-7.
- Suryawan IG, Bakhriansyah J, Puspitasari M, Gandi P, Intan RE, Alkaff FF. To reperfuse or not to reperfuse: A case report of Wellens' syndrome with suspected COVID-19 infection. *Egypt Heart J* 2020;72:58.
- Doyen D, Mocerri P, Ducreux D, Dellamonica J. Myocarditis in a patient with COVID-19: A cause of raised troponin and ECG changes. *Lancet* 2020;395:1516.
- He X, Wang L, Wang H, Xie Y, Yu Y, Sun J, *et al.* Factors associated with acute cardiac injury and their effects on mortality in patients with COVID-19. *Sci Rep* 2020;10:20452.
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497-506.
- Lodigiani C, Iapichino G, Carenzo L, Cecconi M, Ferrazzi P, Sebastian T, *et al.* Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. *Thromb Res* 2020;191:9-14.
- Irabien-Ortiz Á, Carreras-Mora J, Sionis A, Pàmies J, Montiel J, Tauron M. Fulminant myocarditis due to COVID-19. *Rev Esp Cardiol* 2020;73:503-4.
- Lozada-Martínez ID, Torres-Llinás DM, Moscote-Salazar LR. Myocardial lesion in patients with COVID-19: Not all is in the lung. *J Taibah Univ Med Sci* 2021;16:303-4.
- Caballeros Lam M, de la Fuente Villena A, Hernández Hernández A, García de Yébenes M, Bastarika Alemañ G. Cardiac magnetic resonance characterization of COVID-19 myocarditis. *Rev Esp Cardiol* 2020;73:863-4.
- Standl E, Schnell O. Heart failure outcomes and Covid-19. *Diabetes Res Clin Pract* 2021;175:108794.
- Caro-Codón J, Rey JR, Buño A, Iniesta AM, Rosillo SO, Castrejon-Castrejon S, *et al.* Characterization of myocardial injury in a cohort of patients with SARS-CoV-2 infection. *Med Clin (Bare)* 2021;S0025-7753(21)00092-0.
- Zeng JH, Liu YX, Yuan J, Wang FX, Wu WB, Li JX, *et al.* First case of COVID-19 complicated with fulminant myocarditis: A case report and insights. *Infection* 2020;48:773-7.
- Alzahrani SH, Al-Rabia MW. Cardiac injury biomarkers and the risk of death in patients with COVID-19: A systematic review and meta-analysis. *Cardiol Res Pract* 2021;2021:9363569.
- Zhao YH, Zhao L, Yang XC, Wang P. Cardiovascular complications of SARS-CoV-2 infection (COVID-19): A systematic review and meta-analysis. *Rev Cardiovasc Med* 2021;22:159-65.