Mid-term evolution of Chronic Chagas disease patients hospitalized due to COVID-19

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Fecha de recepción: febrero de 2021.

Fecha de aceptación: junio de 2021.

ABSTRACT

This is the first report of mid-term evolution of patients with COVID-19 and Chagas Disease (CD). General characteristics, in-hospital evolution, and mid-term follow up of 12 consecutive patients at a single center is described. A call for action is needed to screen for CD, especially in endemic areas, as the interaction of both diseases may lead to worse cardiac outcomes.

KEYWORDS

COVID-19, Chagas disease, SARS-COV-2, Pneumonia, Arrhythmias, Heart failure, Trypanosoma Cruzi

Evolución a medio plazo de los pacientes con enfermedad de Chagas crónica hospitalizados por COVID-19

RESUMEN

Este es el primer reporte de la evolución a medio plazo de pacientes con COVID-19 y enfermedad de Chagas (EC). Se describen las características generales, evolución hospitalaria y seguimiento a medio plazo de 12 pacientes consecutivos en un solo centro. Estos resultados deben generar un llamado de atención, para incrementar la pesquisa de la EC, especialmente en áreas endémicas, ya que la interacción de ambas enfermedades puede conducir a desenlaces cardíacos adversos.

PALABRAS CLAVE

COVID-19, Enfermedad de Chagas, SARS-COV-2, Neumonía, Arritmias, Insuficiencia cardíaca

INTRODUCTION AND AIMS

Chagas disease (CD) is a neglected tropical disease affecting 6 to 7 million people worldwide (1). First discovered more than a century ago, a lack of interest from the scientific community, in concordance to its affection mainly to poor people from rural Latin America, led to a long-delayed understanding of its physiopathology, diagnosis, classification and treatment, being considered a neglected tropical disease. Currently, there are several guidelines and roadmaps (1), and new drugs are under research. However, chronic CD is a frequent finding even in urban areas of Latin America due to migration and non-vectorial transmission. On the other hand, recently a novel coronavirus, SARS-CoV-2, has emerged and driven to a pandemic (3). COVID-19 disease leads to interstitial pneumonia, and also has been related with direct and indirect cardiac damage in some reports (4). We sought to describe the clinical characteristics and mid-term outcomes of hospitalized patients with COVID-19 who also had chronic CD.
For this paper, EQUATOR Network CARE guidelines were followed.

RESULTS, CASE REPORTS

Among hospitalized patients at Sanatorio Güemes University Hospital (large third level referral hospital in Buenos Aires, Argentina) during the pandemics, we identified the first 12 patients with both diseases (table). All the patients had a confirmed SARS-CoV-2 by polymerase chain reaction method on nasopharyngeal swab. CD diagnosis was done with two indirect methods (enzyme-linked immunosorbent assay ELISA, indirect hemagglutination IHA, or indirect immunofluorescence IIF). Patients had a confirmed chronic CD as a medical history or were screened during hospitalization due to high risk factors (epidemiology, electrocardiographic findings).
A typical bilateral peripheral interstitial pneumonia with elevation of inflammatory biomarkers was diagnosed in 11 out of 12 cases (table 1).
Patient 1 had a history of stage A CD and leukemia, was admitted due to COVID-19 pneumonia and required oxygen supply by mask. After 22 days was discharged with oxygen requirements at home. Patient restarted cancer treatment after pneumonia resolution.
Patient 2 had COVID-19 pneumonia, a torpid evolution, developed respiratory distress, septic shock, required intubation and pronation but died on day 12. Her ECG had AF and repolarization abnormalities and was born in an endemic area, so was tested for CD being positive (ELISA and IIF). Her echocardiogram revealed mild left ventricular dysfunction with apical hypokinesis.
Patient 3 had chronic Chagas cardiomyopathy and renal failure, requiring in-hospital dialysis, had a positive SARS-CoV-2 swab, developed bilateral pneumonia but not worsening heart failure, and had later good evolution.
Patient 4 had a known CD with right bundle branch block but was in stage B1. The patient developed an acute coronary event in the context of SARS-CoV-2 infection, didn´t develop pneumonia, and required coronary intervention.

Patient 5 had COVID-19 pneumonia, was from an endemic province and had RBBB in the ECG, he was tested positive to CD. The patient had mecagolon, developed intestinal occlusion requiring surgery, but died in-hospital due to sepsis.
Patient 6, had a known stage B2 CD, with severe left ventricle dilation and reduced ejection fraction. He developed bilateral pneumonia and died 8 days after admission.
Patient 7, had a known serology for CD (stage A), was admitted due to COVID pneumonia requiring oxygen supplementation by mask. He was discharged at 20th day with an acceptable ambulatory status.
Patient 8, had stage A Chagas disease and COVID-19 pneumonia. During hospitalization developed GI bleeding, and a colonoscopy found colon cancer. The patient had a surgery and good evolution, being discharged after 59 days.
The 9th patient had CD at stage B2, but only was at hospital for 4 days due to non-severe pneumonia and had good evolution. However, he later had progressive dyspnea requiring two hospitalizations for heart failure, changing to stage C of Chagas disease.
The 10th patient is the brother of the 9th patient, both from an endemic province. He had a baseline CD dysautonomia with alternating 1st and 2nd degree AV block. While hospitalized due to moderate COVID-19 pneumonia, he developed a complete AV block so a permanent pacemaker was implanted.
The 11th patient had stage C CD, and developed severe pneumonia requiring intubation. During hospital stay developed severe sinus bradychardia and septic shock with multiple organ failure, dying at day 36
Last patient had a stage A CD, was hospitalized due to non-severe pneumonia with early discharge, but required rehospitalization due to progression of dyspnea.
Among the four deceased patients, two cases were strongly related to the severe acute pneumonia, but the other two were related to prolonged hospitalization and in-hospital infections.

DISCUSSION

As far as we know, this is the first report of the post COVID-19 events in a cohort of CD patients. This information is crucial, as currently there is an increase in the number of COVID-19 patients in Latin America, where CD is endemic. Both diseases are related to cardiac damage and they could interact at different levels (5). Even more, some of the proposed treatments for coronavirus are related to arrhythmias. Of note, opposite to Brazil or other neighboring countries, social distancing and closure of the country by authorities delayed and flattened initially the curve of cases of COVID-19 in Argentina, and none of the patients from our series received experimental and potentially harmful treatments like chloroquine, hydroxychloroquine or lopinavir-ritonavir (6). However, some of the patients received dexamethasone, which is linked to fluid retention, metabolic and long term cardiovascular adverse events (7), and azithromycin (related to QT prolongation and cardiovascular death even in a short 5-days course) (8). Of note, no side effects from these treatments were found in the patients described.
A recent publication from Brazilian investigators found similar in-hospital prognosis between Chagas and non-Chagas COVID-19 patients (matched cohort, preprint, 9), however, CD patients surviving a hospitalization have a variety of symptoms and there seems to be a vulnerable phase after discharge, so having a chronic disease as CD may potentially put patients at a higher risk, especially regarding worsening cardiac events during that phase.
Prior to this pandemic, there were reports of reactivation of CD in patients that received immune modulators for chronic rheumatic conditions, cancer, or organ transplants, so if it is the case during a severe or critical COVID-19 pneumonia (using steroids and interleuquin inhibitors), a potential for reactivations exists, thus symptoms of acute CD may be screened in these patients during sub-acute phase. By depressing the immune system, T. Cruzi may increase its replication and develop parasitaemia with neurological or myocardial involvement. The most comprehensive review in this aspect was published by Pinazo et al (10).
The days of hospitalization were heterogeneous; half of patients had a severe or critical disease and had oxygen requirements. That percentage is higher than general estimates of COVID-19 severity, however the small sample size does not allow us to establish strong affirmations in that regard. Nevertheless, the findings in our patients of worsening stage of CD after a COVID-19 pneumonia, or worsening of conduction abnormalities and bradyarrhythmias should

be considered a sign of alert.

As a limitation, not all patients had an echocardiogram during hospitalization, and the risk assessment for CD and COVID-19 heart involvement based only on cardiomegaly at X-rays is not specific (11). As all patients were from one center in a non-endemic area, larger multi-centric registries involving different areas and T. Cruzi strains as well as SARS-CoV-2 mutations may help understanding the severity and implications of the coexistence of both diseases. In that sense, Argentinian Society of Cardiology, Interamerican Society of Cardiology, as well as World Heart Federation, are currently gathering information related to CD status among COVID-19 patients. Information derived from COVID-19 registries elsewhere, show that patients with cardiac comorbidities like heart failure and arrhythmias are at most risk of having a complicated course of pneumonia (12) and therefore, with coexisting CD a worse outcome may be expected.

Conclusion

We believe that more investigation is needed regarding the interaction of CD and SARS-CoV-2, because of the complexity of both diseases and the not-near end of COVID-19 pandemics.

Financial disclosure and COI: This article had no financing and authors have no conflict of interests to declare related to this investigation.

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TABLE 1. CLINICAL CHARACTERISTICS AND OUTCOMES OF THE PATIENTS.

Patient	Age, sex	Baseline characteristics	CD stage	Admissionlaboratory	Admission ECG	Disease severity (WHO scale)	Days of hospitalization	Status at day 14	Status at day 28	90 days follow up	120 days follow up
1	44, M	HTN - SAVR (Biol) - splenectomized - AML	A	ferritin 3665/ TnTus 15/ CRP 273	SR	Severe, bilateral pneumonia	22 days	At hospital, in recovery with oxygen through nasal cannula	Discharge with home oxygen. Chemotherapy restart	At home, asymptomatic	At home, asymptomatic
2	70, F	HTN - COPD - T2DM -	A	ferritin 991 / TnT us 433/ CRP 165 / D- dimer 0,81	SR	Critical, bilateral pneumonia	12 days	Mechanical ventilation, respiratory distress, Death at day 12	Not applicable	Not applicable	Not applicable
3	64, M	obesity - CAD	A	ferritin 3065- CRP 13-	SR	Severe, bilateral pneumonia	26 days	At hospital, in recovery with oxygen mask	Discharge on day 26. Mild dyspnea	At home, asymptomatic	At home, asymptomatic
4	63, M	CAD	B2	CRP 33 D- dimer 0,3 - TnT us 5	SR , Right Bundle Branch Block And Left Anterior Fascicle Block	Non Severe	21 days	At the hospital, myocardial revascularization surgery performed on day 12.	At home, asypmtomatic	At home, asymptomatic	At home, asymptomatic
5	77, M	HTN - T2DM – COPD	B1	CRP 188- TnTus 58- Ferritin 6698	SR and Right Bundle Branch Block	Critical, bilateral pneumonia and intestinal subocclusion	26 days	At hospital in recovery of the devolvulation	Died on day 26 of admission because of a septic shock to abdominal focus.	Not applicable	Not applicable
6	64, M	HTN -DM -ESRD- kidney cancer- PAD amputation- HF	C	ferritin 1110- CRP 128-	SR	Non Severe	4 days	Discharge on day 4th, asymptomatic.	At home, asymptomatic	Mild dyspnea	Pleural effusion, died.
7	64, F	HTN	A	CRP 212, D - dimer 2.2, ferritin 814	SR	Non Severe	20 days	At hospital, in recovery with oxygen supplementation	At home, asymptomatic	Mild dyspnea	At home, asymptomatic

Patient	Age, sex	Baseline characteristics	CD stage	Admissionlaboratory	Admission ECG	Disease severity (WHO scale)	Days of hospitalization	Status at day 14	Status at day 28	90 days follow up	120 days follow up
8	63, F	HTN	A	CRP 8.85, LDH 618	SR	Critical, bilateral pneumonia	59 days	At hospital, developed digestive bleeding, colon cancer was diagnosed and surgery was performed	At the hospital, colonic surgery, stable.	At home, asymptomatic	At home, asymptomatic
9	47, M	None	B1	CRP 118 / LDH 708 / D dimer 2.1 / TnT us 20	SR and Right Bundle Branch Block	Non Severe	4 days	At home, asymptomatic	At home, asymptomatic	At home, asymptomatic	Heart Failure hospitalization
10	60, M	Smoking	C	CRP 43,9 / LDH 299	Second degree AV blocka	Non severe bilateral pneumonia. Developed 2nd degree AV block, required permanent pacemaker	12 days	At home, without oxygen requirement	At home, asymptomatic	At home, asymptomatic	At home, asymptomatic
11	59, F	Obesity	A	CRP 369, LDH 373, TnTus 6,31	SR , bradychadia	Critical, bilateral pneumonia	36	Mechanical ventilation, respiratory distress. AKI, dialysis	Mechanical ventilation, multiple organ failure	died at day 36, in-hospital infections	Not applicable
12	57, F	Rheumatoid arthritis	A	CRP 21, LDH 672, Ferritin 530, D-dimer 0.66	SR	Non severe bilateral pneumonia	6	At home, without oxygen requirement	At home, mild dyspnea	60 days rehospitalization, worsening dyspnea	At home, mild dyspnea

ABBREVIATIONS: AKI=ACUTE KIDNEY INJURY, AV= ATRIOVENTRICULAR, CRP=C REACTIVE PROTEIN, DM=DIABETES MELLITUS, HTN= HYPERTENSION, LDH=LACTIC DEHIDROGENASE, SR=SINUS RHYTHM, TNTUS=ULTRASENSITIVE TROPONIN T.