Case Report

The Exacerbation of Lutembacher Syndrome in the Setting of COVID-19 Infection: A Rare Case Report

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ABSTRACT

Lutembacher syndrome is a rare cardiac condition characterized by a combination of the atrial septal defect (ASD; congenital or iatrogenic) and mitral stenosis (MS; congenital or acquired). Patients with Lutembacher syndrome and adults with congenital heart disease (ACHD) in general may be at high risk when accompanied by coronavirus disease 2019 (COVID-19). Since there is no published study on the impact of COVID-19 on ACHD, little is known about management strategies in this subset of patients. Herein, we report a young adult female presented with abdominal discomfort, swollen legs, fever, cough, and dyspnea. The patient had developed palpitation and exercise intolerance five years ago but paid it no attention. Echocardiography revealed large secundum type ASD with severe MS (Wilkins score of eight) and a nasopharyngeal swab confirmed SARS-COV-2 infection. The patient was diagnosed with Lutembacher syndrome and COVID-19. Intensive treatment was given to relieve symptoms due to heart failure and to treat COVID-19 pneumonia. Patients with Lutembacher syndrome are at a higher risk of being infected with COVID-19 and manifest into severe infections. Therefore, determining the risk of infection and the severity of COVID-19 in ACHD patients are required during the pandemic.

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Introduction

Lutembacher syndrome is first credited with a paper by the French physician Rene Lutembacher in 1916, describing the combination of the atrial septal defect (ASD) with mitral stenosis (MS) [1]. Currently, consensus describes Lutembacher syndrome as a combination of ASD (congenital or iatrogenic) and MS (congenital or acquired). In developing countries, the majority of mitral valve (MV) pathologies are associated with secondary rheumatic heart disease (RHD) [2].

Since first emerged in Wuhan, China, in December 2019, the coronavirus disease 2019 (COVID-19) has rapidly spread across countries until the World Health Organization declared a pandemic in March.
Patients with SARS-CoV-2 infection often present with mild respiratory manifestations \([4]\). Nevertheless, a small proportion of patients develops into complications such as pneumonia and acute respiratory distress syndrome, which increases intensive care admission and mortality \([5]\). While much of the focus is on the complications that occur in the lungs, recent reports suggest that cardiac involvement can be present in COVID-19 \([6,7]\).

Adults with congenital heart disease (ACHD) may be at high risk when accompanied by COVID-19. However, the individual risk profile is not uniform due to the heterogeneity of the anatomical abnormalities and complications that develop over the course of the disease \([8]\). Since there is no published study on the impact of COVID-19 on ACHD, little is known about management strategies in this subset of patients. Currently, all management strategies are extracted from studies on the impact of COVID-19 in adult patients and adult patients with cardiovascular disease.

**Case Presentation**

A 21-year-old Javanese woman presented to the emergency department with a chief complaint of abdominal discomfort and swollen legs for five days before admission. These symptoms were accompanied by fever, nonproductive cough, dyspnea, and a slight limitation of physical activity. The patient developed palpitation, fatigue, and exercise intolerance for five years but paid it no attention. There were no complaints of chest pain, orthopnea, paroxysmal nocturnal dyspnea, hemoptysis, illness indicating rheumatic fever, or any other urinary tract and gastrointestinal problem.

On arrival to the emergency department, vital signs showed a blood pressure of 90/60 mmHg, regular heart rates of 117 beats per minute, respiration rates of 24 times per minute, oxygen saturation of 98% on ambient air, and temperature of 37.7°C. Physical examination revealed conjunctival pallor, elevated jugular venous pressure, fixed wide split-second heart sound, grade III/VI ejection mid-systolic murmur at the left upper parasternal region, and grade III/IV early-to-mid diastolic murmur at the apex. Crackles were found over the entire lung field, and the abdomen was mildly distended with hepatomegaly. Bilateral pitting edema was found on the lower limbs. Based on the severity of symptoms and exercise capacity, the patient was categorized as New York Heart Association (NYHA) class III.

Laboratory results showed a hemoglobin level of 6.8 g/dL with a microcytic hypochromic, leucocyte level of 9x10^3/uL with neutrophil-lymphocyte ratio (NLR) of 6.1, platelet level of 253 x10^3/uL, albumin level of 3.0 g/dL, D-dimer of 3213.9 ng/mL, and reactive IgM of SARS-COV-2. A nasopharyngeal swab confirmed for SARS-CoV-2 infection using real-time reverse transcriptase-polymerase chain reaction (RT-PCR) assay.

A twelve-lead electrocardiogram (ECG) indicated sinus tachycardia 120 bpm with right axis deviation (RAD) and right ventricular hypertrophy (RVH) (Figure 1). Findings on chest radiography showed pulmonary consolidation, increased pulmonary vascularity, and significant cardiomegaly, indicating right atrial and right ventricular enlargement (Figure 2). Transthoracic echocardiography revealed large secundum type ASD (diameter 1.6 cm) with a left to right shunt and severe MS (MV area planimetry of 0.9 m²) with a Wilkins score of eight, including the forward movement of valve leaflets in diastole (2), mid-leaflet thickening (2), chordal thickening (2), and calcification confined to leaflet margins (2). In addition, there were moderate tricuspid regurgitation (TR; max PG 40.25), dilated right atrial (RA) and right ventricular (RV), and moderate probability pulmonary arterial hypertension (PAH; PASP 48 mmHg) (Figure 3).
The patient was admitted to the isolation ward with a diagnosis of Lutembacher syndrome, SARS-CoV-2 infection, and anemia. Intravenous furosemide was used to stabilized and relieve symptoms and sign of congestion. The patient was treated with a COVID-19 regimen, which consisted of oseltamivir (75 mg twice a day), azithromycin (500 mg three times a day), chloroquine (500 mg twice a day), isoprinosine (500 mg three times a day), vitamin C (1500 mg once daily), and subcutaneous enoxaparin (40 mg twice a day). Additional treatments were spironolactone (25 mg once a day), digoxin (0.25 mg once a day), and transfusion of packed red blood cells with the hemoglobin target level of 10g/dL.

During the second week of hospitalization, the condition of the patient had worsened and required intensive care admission. However, the clinical course gradually improved, and the patient progressively stabilized. In the fourth weeks of hospitalization, the patient had no complaints, SBP was ranging between 90-110 mmHg, respiratory rates 20-22 times per minute with a saturation of 97-98% without oxygen supplementation, the temperature of 36.5ºC, and the nasopharyngeal swab RT-PCR test resulted negative. The patient was discharged and planned for a follow-up at the outpatient clinic a week later.

Discussions

Here we report a case of newly diagnosed congenital heart disease in young adults with COVID-19. The main complaints were abdominal discomfort, swollen legs, fever, nonproductive cough, dyspnea, and a slight limitation of physical activity. The patient developed palpitation, fatigue, and exercise intolerance in the past five years ago but paid it no attention. Echocardiography revealed congenital ASD complicated by MS, most likely due to RHD. On admission screening for COVID-19, the patient was suspected of SARS-CoV-2 infection, and subsequently, a nasopharyngeal swab confirmed the diagnosis of COVID-19. The patient was diagnosed with Lutembacher syndrome and COVID-19.

Due to the decompression of LA through the bloodstream via the ASD to the right atrium, Lutembacher syndrome is well tolerated by many patients for years, and patients often present to the hospital in an advanced state [9]. They often present with palpitations, fatigue, and exercise intolerance due to left-to-right shunts and reduced cardiac output.

On physical examination, the manifestation of both ASD and MS confounded each other. The characteristics of MS, such as first heart sound, opening snap, and a mid-diastolic rumbling murmur, may be difficult to find due to LA decompression through ASD.

Meanwhile, ejection mid-systolic murmur and fixed wide split-second heart sound as a sign of large ASD can be easily found in the left upper parasternal [10]. Two-dimensional echocardiography with Doppler color flow remains the gold standard for diagnosis and evaluation of Lutembacher syndrome [11,12].

Based on the criteria for echocardiographic diagnosis of RHD by the World Heart Federation (WHF), an MS with at least two morphological changes of RHD of the MV and a mean gradient ≥ four mmHg is defined as subcategory B of definite RHD. Classically, the thickened posterior leaflet moves parallel with the anterior MV leaflet and is relatively immobile during diastole [13]. Open heart surgery is the gold-standard treatment for Lutembacher syndrome.

As technology advances, percutaneous transcatheter therapy in the form of a special
closure device for ASD and balloon mitral valvuloplasty (BMS) for MS have become the favored treatment options [14,15]. However, the management of ACHD based on 2020 European Society of Cardiology (ESC) Guidelines states that ASD closure is not recommended in patients with PAH and pulmonary vascular resistance (PVR) more than five Wood units despite targeted PAH treatment or decreased oxygen saturation during activity [16].

In the general population with COVID-19, severe infection and mortality are mainly dominated by elderly patients. This is different from the population of ACHD patients, which are mostly young adults. Despite these facts, most deaths in COVID-19 patients are those who have one or more comorbidities, and one of the most common comorbidities is cardiovascular disease [17,18]. Reflecting on the experience of ACHD patients with previous viral infections, including respiratory viruses and influenza, it is reasonable to predict that patients with severe ACHD are at a higher risk of being infected with COVID-19 and manifest into severe infections [19,20]. ACHD patients are also known to have a higher tolerance for dyspnea and desaturation, so they may present later with more severe symptoms [21].

Based on the AHA/ACC guidelines, to determine the risk of infection and the severity of COVID-19 in ACHD patients can be classified based on anatomical and physiological assessment (AP). Patients with complex congenital anatomy or patients who have a physiological stage B, C, or D are most likely to be at risk of having a poor prognosis with COVID-19 due to reduced functional reserve [22]. Our patient was considered as a high-risk patient due to significant heart valve disease and moderate PAH. In addition, the British Congenital Cardiac Association has released criteria to identify ACHD patients who are susceptible to COVID-19 infection. Patients with PAH are included in this category because a respiratory disease will increase PVR, which will lead to right heart failure and low output cardiac (23). This mechanism is most likely to cause exacerbations in this patient. COVID-19 pneumonia in patients with underlying PAH will induce hypoxia, causing further vasoconstriction of the blood vessels and an increase in PVR. Abdominal discomfort, swollen legs, and physical activity limitation are the symptoms that develop in this patient due to right heart failure and low output cardiac.

SARS-CoV-2 infection should be suspected in ACHD patients who present with fever, acute respiratory symptoms, desaturation, new-onset arrhythmia, or unexplained deterioration of heart function [27]. A chest radiography or chest computerized tomography (CT) scan can provide additional information for certain patients. Employment of echocardiography and cardiac enzymes are recommended to assess the cardiac injury. In patients with confirmed COVID-19, management should be guided by risk stratification and the clinical status of the patient. Monitoring of oxygenation, heart rate, blood pressure, ECG, and basic laboratory tests are required [8,28].

The complexity of underlying heart defects in ACHD patients is greatly related to the degree of pulmonary impairment when they suffer from COVID-19. High-risk patients or those with signs of severe respiratory or cardiovascular problems generally require hospitalization in an isolation ward [29].

Another important aspect of COVID-19 is the disruption of the coagulation profile, leading to thrombotic complications [24]. In this case, the condition is worsened by the stasis in the left atrium and slowed blood flow in patients with rheumatic
mitral valve stenosis, making it prone to thrombus formation causing embolic complications [25].

Our patient had increased D-dimer during hospitalization. Thus, in accordance with the ESC Guidance 2020 [26], we administered a higher than prophylactic doses of anticoagulation with low molecular weight heparin (LMWH) of enoxaparin.

**Conclusion**

Patients with Lutembacher syndrome are at a higher risk of being infected with COVID-19 and manifest into severe infections. Determining the risk of infection and the severity of COVID-19 in ACHD patients are required during the pandemic.

**Acknowledgement**

There is no conflict of interest.

**References**


Supplementary Data

Figure 1. Twelve-lead electrocardiography shows sinus tachycardia 120 bpm with right axis deviation and right ventricular hypertrophy

Figure 2. Chest X-ray posterior-anterior view shows pulmonary consolidation, increased pulmonary vascularity, and significant cardiomegaly
Figure 3. (a) Transthoracic echocardiography (TTE) in apical four-chamber view and (b) TTE in subcostal four-chamber view show large secundum type ASD (diameter 1.6 cm) with good margin and left to right shunt; (c) TTE in short axis view shows MV area of 0.9 cm² by planimetry with thickening on the anterior mitral leaflet (AML) and posterior mitral leaflet (PML) and fusion of anterolateral and posteromedial commissures; (d) TTE in apical four-chamber view shows moderate TR (TR max PG 40.25); (e) TTE in parasternal long-axis view shows left atrial to aortic root (LA/Ao) ratio of 3.0 suggestive for pulmonary hyperperfusion; (f) TTE in apical four-chamber view shows dilated RA and RV with normal RV function (TAPSE 2.8 cm); (g) TTE in parasternal short-axis view shows normal kinetic left ventricle (LV) with ejection fraction (EF) of 70% (by Teich).

Table 2. Parameters measured in all subjects. BP = blood pressure, LDL = low density lipoprotein, HDL = high density lipoprotein, TG = triglyceride, BMI = body mass index, SAT = subcutaneous adipose tissue, VAT = visceral adipose tissue

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ACS NSTEMI 11 15.7
Recent MI 6 8.6
STEMI 49 70.0
UA 4 5.7

Smoking
Yes 47 67.1
No 23 32.9

History of diabetes mellitus
Yes 27 38.6
No 43 61.4

History of hypertension
Yes 22 31.4
No 48 68.6

Table 3. Correlation between BIA-BF%, VAT, SAT, WC, and BMI with blood pressure. BP = blood pressure, BIA-BF% = percentage of bioelectrical impedance analysis – body fat, SAT = subcutaneous adipose tissue, VAT = visceral adipose tissue, WC = waist circumference, BMI = body mass index.

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Table 4. Correlation between BIA-BF%, VAT, SAT, WC, and BMI with lipid profile. BIA-BF% = percentage of bioelectrical impedance analysis – body fat, SAT = subcutaneous adipose tissue, VAT = visceral adipose tissue, WC = waist circumference, BMI = body mass index, LDL = low density lipoprotein, HDL = high density lipoprotein, TG = triglyceride.

<table>
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Table 5. Correlation between BIA-BF%, VAT, SAT, WC, and BMI with blood glucose, HbA1c, and fibrinogen levels. BIA-BF% = percentage of bioelectrical impedance analysis – body fat, SAT = subcutaneous adipose tissue, VAT = visceral adipose tissue, WC = waist circumference, BMI = body mass index.

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