

## Case Report

# Successful Treatment of Embolic Aortic Valve Endocarditis in a Patient Affected by COVID-19 Pneumonia

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**Abstract:** The COVID-19 pandemic has required reorganization of the cardiac surgery system in the Italian region of Lombardy during early 2020. As a consequence, the hub-and-spoke (H&S) model was introduced to manage emergent/urgent cardiac surgery cases. In this challenging scenario, in which thousands of people were affected by the novel coronavirus, we present the case of a successful treatment of a middle-aged patient affected by both COVID-19 pneumonia and subacute aortic endocarditis. Learning objective: How to treat endocarditis during the COVID-19 pandemic.

**Keywords:** COVID-19; endocarditis; aortic valve



**Citation:** Belluschi, I.; Melisurgo, G.; Campana, C.; Castiglioni, A. Successful Treatment of Embolic Aortic Valve Endocarditis in a Patient Affected by COVID-19 Pneumonia. *Surgeries* **2021**, *2*, 113–118. <https://doi.org/10.3390/surgeries2010010>

Academic Editors: Michael S. Firstenberg and Cornelis F. M. Sier

Received: 27 January 2021

Accepted: 26 February 2021

Published: 2 March 2021

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## 1. Introduction

In early 2020, the SARS-CoV-2 outbreak spread in Europe and especially in Lombardy, a northern region of Italy. Since all hospitals were involved in the treatment of COVID-19 patients, a different system to manage emergent/urgent cardiac surgery cases was established by identifying hub-and-spoke units, i.e., a model in which spoke patients needing more intensive care are routed to their relative hub center [1,2]. This highly efficient program should guarantee patient access and hospitalization by providing four adult surgery hubs and one pediatric cardiac surgery hub in the whole region of Lombardy, as recently described [1]. The hub centers fulfilled the following criteria: the presence of 24/7 operating rooms (ORs, at least three simultaneously, of which one is dedicated to COVID patients, i.e., COVID-OR) and the presence of COVID-free post-operative cardiovascular intensive care units (ICUs, in addition to COVID-ICUs).

According to the Center for Disease Control (CDC), the SARS-CoV-2 mean incubation period is almost 2–14 days [3]. It sometimes could be pauci- or asymptomatic, but in the worst cases it causes a severe acute respiratory distress syndrome (ARDS) named COVID-19 (COorona, Virus, Disease, 19). Age and underlying comorbidities (hypertension, diabetes mellitus, etc.), represent important risk factors for unfavorable outcomes [4]. Currently, several vaccines are now available against SARS-CoV-2 and more efficient therapies (i.e., hyperimmune plasma, monoclonal antibodies, and antiretroviral drugs) have been extensively studied and are still under investigation worldwide. However, at the very beginning of the Italian outbreak, COVID pathophysiology and specific treatments were mostly unknown, thus, most therapies targeted only symptoms and provided support in case of complications.

In this difficult scenario, the efficient treatment of a middle-aged patient affected by COVID-19 pneumonia and a concomitant aortic valve endocarditis was considered to be a successful and concrete example of a well-functioning new Lombardy Cardiac Surgery hub-and-spoke system, together with the expertise of a multidisciplinary endocarditis team.

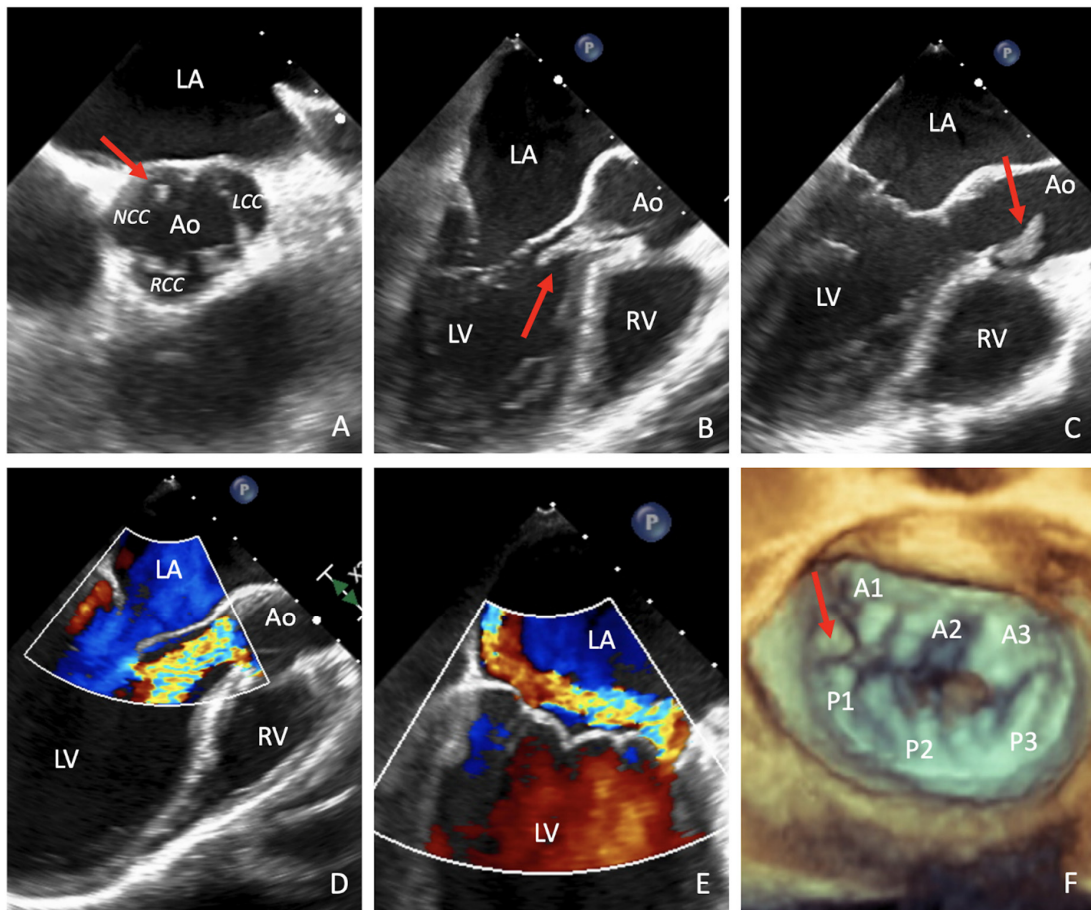
## 2. Case Report

A 50-year-old man with no co-morbidities presented with pneumonia after unsuccessful empirical treatment at home with levofloxacin 750 mg/day. The patient was first admitted in the pneumology department, but the main infectious disease analyses (H1N1, HIV, quantiferon, and legionella-pneumococcal-mycoplasma antigens), as well as the first nasopharyngeal swab test for SARS-CoV-2 results were negative. Due to the sudden development of heart failure, the patient was transferred to the cardiac-ICU, where a trans-oesophageal echocardiography (TOE) showed a tricuspid aortic valve affected by endocarditis, with multiple motile vegetations above the cusps (the major one of  $2 \times 0.5 \text{ cm}^2$  on the non-coronary cusp), resulting in severe aortic regurgitation (AR) (Figure 1 and Supplemental Video S1). A concomitant severe mitral regurgitation (MR) due to prolapse/flail of the myxomatous antero-lateral scallop of the posterior leaflet (P1) and a mildly reduced left ventricle ejection fraction (LVEF) (50%) were also observed. Later, a second SARS-CoV-2 nasopharyngeal swab test result was positive and a total-body computed tomography (CT) scan confirmed the presence of a COVID-19 pneumonia, with bilateral apical and midfield ground glass pattern (Figure 2A and Supplementary Video S2), with hepatic and also splenic endocarditis embolizations. The patient was initially treated with i.v. 2 g vancomycin and 360 mg gentamicin daily, followed by 700 mg of daptomycin and 3 g meropenem per day, although the first six sets of blood culture results were negative. The presence of abundant pleural effusion required percutaneous bilateral drainage, while high-dose inotropic support and non-invasive ventilation (NIV) with continuous positive airway pressure (CPAP, 10 cmH<sub>2</sub>O, F<sub>IO<sub>2</sub></sub> 0.6) were started due to progressive hemodynamic and respiratory deterioration, obtaining adequate gas exchange, thus, avoiding the need for orotracheal intubation (OTI) and prone positioning [5,6]. Then, the patient was transferred from the spoke unit (Sant'Anna Hospital, Como) to the central hub (San Raffaele University Hospital, Milan), since urgent surgery was indicated, despite increased surgical risk (STS, 4.8%) [1,7]. Here, after exclusion of QT interval abnormalities, immunomodulation therapy against SARS-CoV-2 with hydroxychloroquine 200 mg twice a day was added [8]. Contemporarily, the patient underwent an aortic valve replacement with a 23 mm Perimount bioprosthesis (Edwards Lifesciences Inc., Irvine, CA, USA) and a concomitant mitral valve repair with an antero-lateral para-commissural edge-to-edge (A1-P1) technique and a 37 mm Simulus partial flexible posterior prosthetic ring (Medtronic Minneapolis, MN, USA). Extra-corporeal circulatory (crystalloid Custodiol cardioplegia) and aortic cross-clamp times were 96 and 83 min, respectively. The patient entered the hub hospital in a dedicated COVID-19 pathway, which consisted of a specific COVID-19 negative pressure OR, with a postoperative stay reserved in the COVID-ICU/ward. In addition, healthcare personnel directly involved were required to use specific protections (i.e., FFP2/3 mask) to prevent droplets/contact transmission.

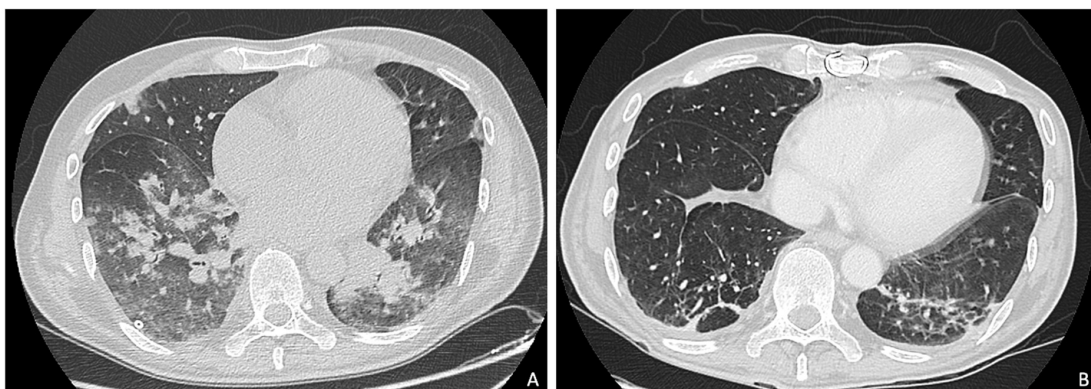
On the one hand, cultures and real-time polymerase chain reaction (PCR) of the patients' native valve explanted result was negative to both bacteria/fungi and SARS-CoV-2. On the other hand, histopathological analysis of the explanted valve revealed the presence of a few Grocott-Gomori's methenamine silver stain positive small yeast-like microorganisms, suggestive of fungi.

During the ICU post-operative stay, the patient required circulatory high-dose inotropic ( $\geq 0.1 \text{ mcg/kg/min}$  of epinephrine and norepinephrine) and mechanical support with IABP due to severe biventricular dysfunction. One cycle of levosimendan  $0.4 \text{ mcg/kg/min}$  was successfully performed over 96 hrs. After six days, the respiratory function progressively recovered, and the patient was extubated. Further application of CPAP guaranteed optimal oxygen saturations. Development of post-operative fever and evidence of *Candida parapsilosis* on the tip of the central venous catheter and blood cultures as well, required the introduction of 100 mg/day anidulafungin first, followed by antibiogram-guided 400 mg per day of fluconazole, with a subsequent decrease of inflammation parameters. After three weeks, the SARS-CoV-2 test finally resulted negative as well as blood cultures and a thoracic CT scan showed an almost complete resolution of COVID-

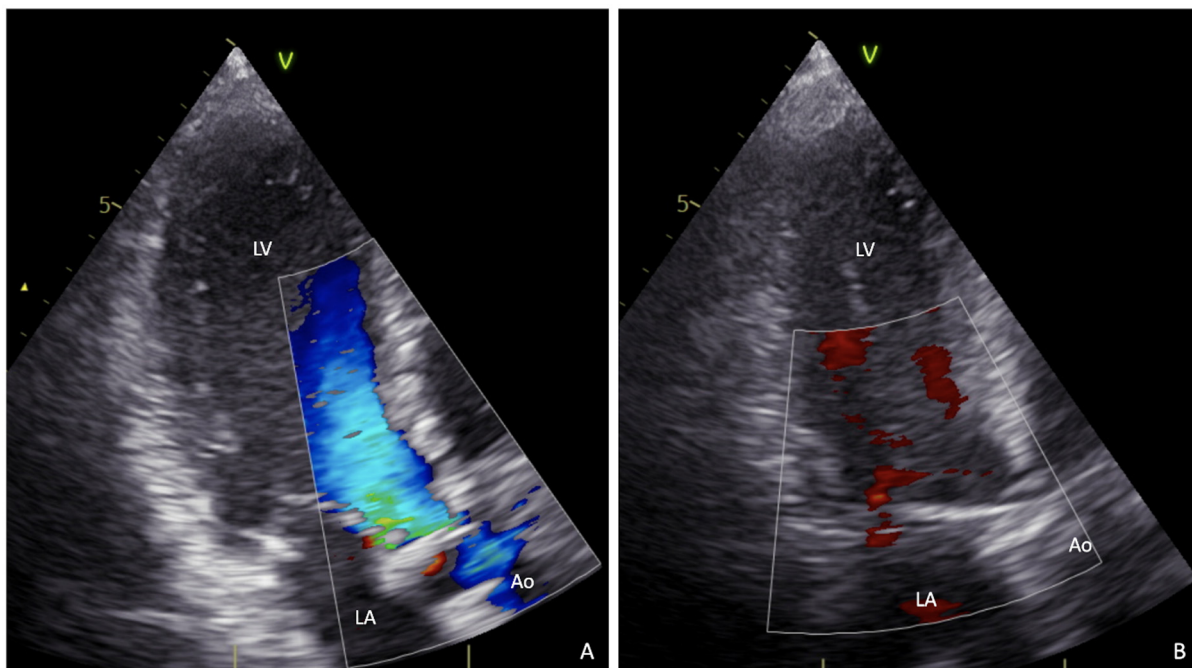
19 pneumonia (Figure 2B and Supplemental Video S2). The pre-discharge transthoracic echocardiography (TTE) showed a good post-operative result of the aortic bioprosthesis (mean transvalvular gradient 12 mmHg), no paravalvular leaks, and a residual mild MR without increased gradient (Figure 3 and Supplemental Video S3).



**Figure 1.** Pre-operative trans-oesophageal echocardiography (TOE). Four-chambers TOE showing a motile vegetation (red arrow) on the non-coronary cusp of the aortic valve (A) during diastole (B) and systole (C), resulting in severe aortic regurgitation (AR) (D); Color doppler (E) and four-dimensional (4D) TOE (F) reported a concomitant severe MR due to P1 flail.



**Figure 2.** Pre- and post-operative thoracic computed tomography (CT) scan. CT imaging showing COVID-19 pneumonia (A) and its resolution (B) after three months.



**Figure 3.** Post-operative transthoracic echocardiography (TTE). Long-axis three-chambers view in late diastole (A) and systole (B) at color doppler TTE showing no paravalvular leak (PVL) of the AVR and good result of the mitral valve repair.

After 36 days, the patient was finally discharged home with antibiotic treatment of linezolid 1200 mg/day, amoxicillin 3 g/day, and fluconazole 400 mg/day, for 3 months. The one-month later TOE excluded appearance of new vegetations, while no signs of fungal infection were shown at the ophthalmologic evaluation. At eight months, the patient maintained a good clinical status, with normal pulmonary function and 6-min walking tests.

### 3. Discussion

During the COVID-19 pandemic, the entire health care system, especially in northern Italy, has faced difficult challenges, therefore, the introduction of a different organization model was considered pivotal to satisfy all the emergency needs, especially in the cardiovascular field [1,2]. In this scenario, we reported a case which offers a concrete example of capable cooperation between the hub and the spoke units, maintaining the best healthcare possible even during the Lombardy outbreak of such a devastating pandemic.

In this complex and intriguing case of endocarditis following COVID-19, pre-operative blood cultures and PCR analysis on the native valve explanted result were negative, while the histopathological test was suggestive for fungi and post-operative blood cultures were positive for *Candida parapsilosis*. Although still questionable, it is unlikely that the patient suffered fungal endocarditis, while a bacterial endocarditis of unknown microorganism is a more reasonable hypothesis. Indeed, we suggest that the presence of fungi at the histopathological test was a contaminant, thus causing a false positive. In addition, the patient finally revealed he had undergone some dental care just a few months before surgery without adequate antibiotic prophylaxis. Therefore, antibiotic treatment with vancomycin and gentamicin first, followed by daptomycin and meropenem, in association with fluconazole after evidence of candidemia, proved to be an efficient therapy to treat this case of endocarditis, as recommended by the 2015 ESC guidelines [6]. In other words, this intricate and puzzling scenario of unknown origin endocarditis shows the importance of following the evidence, just like a famous detective does.

Furthermore, in the setting of a new and previously unknown pulmonary disease such as COVID-19, the initial differential diagnosis of pleural effusion caused by acute heart failure or interstitial SARS-CoV-2 pneumonia became very difficult during early evaluation.

#### 4. Conclusions

In conclusion, we reported a case of successful treatment of infective endocarditis of unknown origin involving the aortic valve with visceral embolization in a patient affected by COVID-19 pneumonia during the dramatic Italian outbreak in Lombardy of SARS-CoV-2. Despite the high surgical risk and the off-label adoption of an immunomodulation drug, which had shown encouraging results in the treatment of SARS-CoV-2 positive cases only at the very beginning of the pandemic, the patient finally underwent an efficient double-valve surgery for endocarditis and ultimately healed from COVID-19 pneumonia, without mid-term respiratory complications. Long-term follow-up is necessary to assess for the eventual presence of SARS-CoV-2 chronic hidden and yet unknown respiratory limitations.

**Supplementary Materials:** The following are available online at <https://www.mdpi.com/2017-2017/2/1/10/s1>.

**Author Contributions:** I.B. wrote the manuscript; G.M., C.C., and A.C. reviewed the manuscript. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Institutional Review Board Statement:** Ethical review and approval were waived for this report, due to its intrinsic medical/educational activity that does not meet the DHHS definition of “research”.

**Informed Consent Statement:** Informed consent was obtained from the patient for publication.

**Data Availability Statement:** No new data were created or analyzed in this study. Data sharing is not applicable to this article.

**Conflicts of Interest:** The authors have nothing to disclose.

#### Abbreviations

AR	Aortic regurgitation
ARDS	Acute respiratory distress syndrome
CDC	Center for Disease Control
COVID-19	COrona VIRus Disease 19
CPAP	Continuous positive airway pressure
CT	Computed tomography
ICU	Intensive care unit
LVEF	Left ventricle ejection fraction
MR	Mitral regurgitation
NIV	Non-invasive ventilation
OR	Operative room
OTI	Orotracheal Intubation
PCR	Polymerase chain reaction
TOE	Trans-oesophageal echocardiography
TTE	Transthoracic echocardiography

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