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CASE IMAGE

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Sars-Cov-2 infection as a possible risk factor for prosthesis endocarditis: A challenging redo-Bentall for subvalvular abscess

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Abstract

Background: Candida Parapsilosis is an unusual agent of prosthetic endocarditis in immunocompetent individuals but Coronavirus disease 2019 is reported to be associated with a transient immunodeficency that exposes patientes to opportunistic infections.

Case Report: We describe a dreadful case of Candida Parapsilosis endocarditis in a transient immunosuppressed patient recently infected with severe acute respiratory syndrome-Coronavirus 2019.

Conclusion: Considering that the symptoms of Candida Parapsilosis infection and the symptoms of Coronavirus disease-2019 may overlap, it is important never to understimate the non-specific symptoms to improve patient outcome, especially in patient with previous Coronavirurs disease-2019 infection and with prosthetic material grafting.

KEYWORDS
Bentall procedure, Covid-19, fungal endocarditis, prosthesis endocarditis

1 | INTRODUCTION

Coronavirus disease 2019 (Covid-19) describes a complex and multisystemic syndrome that preferentially involves the lower respiratory tract. In the majority of cases and in its mild presentation, the most common symptoms included fever, cough, myalgia, fatigue, and dyspnea. Severe Covid-19, however, is accompanied by acute respiratory distress syndrome with respiratory failure and hyperinflammatory syndrome characterized by a fulminant and fatal hypercytokinemia also with multiorgan failure and a marked possibility of thrombus formation.

Immune dysregulation is caused by the cytokine storm, an imbalance between proinflammatory and anti-inflammatory cytokines that predisposes the immune system to an immunodeficiency and that contributes to developing opportunist infections.[1] *Candida parapsilosis* (CP) infections are usually uncommon in immunocompetent individuals, despite the presence of a prosthetic valve, but it can be life-threatening in patients with immunodeficiency.

CP is the leading agent of candidemia (43%) in patients hospitalized in the intensive care units (ICUs), with an 80% mortality rate related to comorbidities.[2] The most frequent conditions for the development of candidemia are prolonged hospitalization, long-term or broad-spectrum antibiotics therapy, central venous catheters, parenteral nutrition, mechanical ventilation and corticosteroid therapy, and intravenous drug abuse.[3]

Among Covid-19 patients, the development of *Candida* infection is around 2.6% during the ICU stay; therefore, a patient with prosthetic heart valve endocarditis can present a clinical pattern where associated fungal coinfections may not be detected or misdiagnosed due to the temporary immunosuppression related to Covid-19. Hence, this results in a delayed therapy or in the

development of catastrophic infections, which increases the mortality risk.[4]

2 | CASE PRESENTATION

We report the case of a 55-year-old man with a clinical history of the bicuspid aortic valve and ascending aortic aneurysm treated 10 years earlier with a Bentall procedure. The postoperative follow-up was uneventful. During the second pandemic severe acute respiratory syndrome coronavirus-2 (Sars-Cov-2) outbreak, the patient suffered from a severe pattern of Covid-19, manifesting pneumonia and severe cytopenia and lymphopenia, requiring hospitalization in a specific Covid unit. During the prolonged ICU stay, our patient was treated with corticosteroids, long broad-spectrum antibiotic therapy, and immunosuppressors to reduce the consequences of immune dysregulation.

A few days after healing and discharge, the patient manifested high fever again and was rehospitalized in the infectious disease ward. Blood culture tests were positive for CP. Laboratory tests showed C-reactive protein 68 mg/L, white blood cell 2.32×10^9/L, neutrophil 65%, and lymphocyte 30%.

Considering the previous cardiovascular pathologies, the patient performed a transesophageal echocardiogram (TEE), which showed good functioning of the aortic valve prosthesis, but revealed the presence of an endocarditic infiltration of the posterior aortic wall, and a pedunculated structure (12 × 30 mm) at the ring of the mechanical valve prosthesis level protruding into the outflow tract of the left ventricle (LVOT) (Figure 1).

To evaluate the extent of infiltration into the tubular prosthesis, a total body contrast positron emission tomography/computed tomography (PET/CT) was performed revealing the presence of an hypercaptating mass on the ventricular side of the aortic prosthesis (Figure 2A).

According to the antibiogram, antifungal therapy with caspofungin and fluconazole was started, without clinical improvement; therefore; it was decided to modify the therapy with lysosomal amphotericin-B.

Assessd the voluminous dimensions of the pedunculated vegetation and the poor response to antifungal therapy, according to guidelines,[5] surgical treatments became mandatory to avoid the risk of embolic events.

Evaluating the complexity of the surgery, to optimize the hematological setting, the patient was treated preoperatively with transfusions of concentrated red blood cells, granulocyte-stimulating factor, and erythropoietin-α.

The patient underwent a redo-Bentall procedure, with aortic root replacement and coronary ostia reimplantation, using a new composite mechanical valve/graft.

Intraoperatively, the prosthetic valve ring was covered with a friable/yellowish vegetations (Figure 2B) that the microbiological tests confirmed positive for CP. In addition, the infection was found to be extended also in the LVOT, where it caused erosive lesions and subannular abscess that required a partial patch reconstruction in a double-layer fashion.

The postoperative course was uneventful; on the 12th postoperative day, the patient was transferred to the infectious disease ward to continue the antifungal therapy with Ceftobiprole and was discharged home after 30 days without any signs of prosthetic reinfection.

3 | DISCUSSION

Fungal prosthetic valve endocarditis is a rare but devastating disease. Typical risk factors for CP endocarditis include prosthetic valve implantation, cardiac implantation devices, and invasive intravenous procedures. According to the literature, the prevalence of fungal infections in immunocompetent patients is very unusual as many reports refer largely to immunosuppressed patients.

This coinfection may be associated with Covid-19 as there are few reports that correlate immune dysregulation in Covid-19 patients to fungal infections. Long ICU stay, treatment of the overexpression of inflammatory mediators, immunosuppressive therapy, monoclonal antibodies, and interleukin-6 inhibitors to mitigate the cytokine storm has been reported to promote candidemia among severely ill

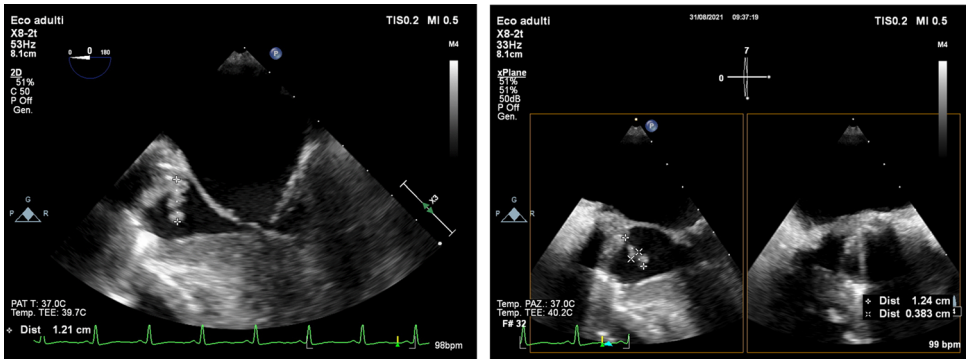

FIGURE 1 Transesophageal echocardiogram showed pedunculated and mobile vegetations anchored to the aortic annulus and protruding into the outflow tract of the left ventricle.

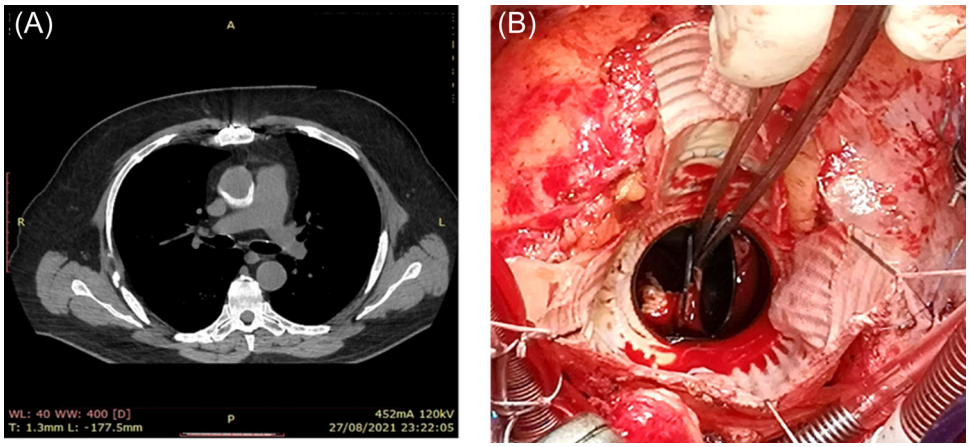

FIGURE 2 (A) Computed tomography scan showed vegetations in the lumen of the aortic graft. (B) Intraoperative view of yellowish and friable vegetations located to the annulus of the mechanical valve.

Covid-19 patients. In our case, the patient manifested a severe systemic CP infection with ocular, skin, urinary tract, and previously implanted valve graft involvement, causing a severe Candida endophthalmitis treated with intravitreal injection of an antifungal agent, and a catastrophic endocarditis characterized by large mobile vegetations with a high risk of embolization. For a better management of the systemic dissemination of the infection, the patient was followed with a multidisciplinary approach by a team composed of cardiologists, infectious disease specialists, hematologists, and cardiac surgeons. Since fungal endocarditis on mechanical valve prosthesis has a very rare incidence, even more accountable to CP species, we cannot exclude that the recent Sars-Cov-2 infection is correlated with the onset of endocarditis. We assume that there may be the possibility that Covid-19 disease and/or immunosuppressive therapies with corticosteroids, immunosuppressive drugs, interleukin inhibitors, monoclonal antibodies, and broad-spectrum antibiotics may trigger a transient immunodeficiency that exposes the patient to typical diseases of immunocompetent patients. Two other cases of CP endocarditis involving prosthetic materials in patients with the Covid-19 disease have been reported in the literature by Quarti et al.[6] and Segrelles-Calvo et al.[7] This finding could suggest a possible role of the SARS-CoV-2 in the predisposition of patients to infective endocarditis. Therefore, we assume that Covid-19 disease may act as an additional risk factor in patients with cardiovascular prosthetic material, increasing the possibility of developing uncommon pathogenic endocarditis. Covid-19 disease and fungal endocarditis symptoms overlap, so it may be difficult to make a differential diagnosis and there may be a risk that Covid-19 disease hide endocarditis symptoms, resulting in a silent development of heart infection. Based on our experience, the best strategy for the treatment of this type of fungal infection is surgery associated with early recognition of candidemia and an appropriate and timely antifungal therapy. Performing a redo-Bentall procedure to implant a new mechanical valve/graft is a difficult surgical procedure, but it is necessary in cases of very extensive infection, poor response to antifungal therapy, and when pedunculated vegetations with a high risk of embolization are present. Our case highlights the need for an early diagnosis of endocarditis in patients with valve/graft prosthesis and reinforces the importance of not underestimating nonspecific symptoms such as fever, cough, fatigue, and dyspnea, especially in patients with the previous Covid-19 disease, which in patients with prosthetic material it may behave as an additional risk factor.

AUTHOR CONTRIBUTIONS

Maria Grazia Romeo wrote the paper. Maria Grazia Romeo, Giuseppe Comentale, Emanuele Pilato, and Vera Cirillo revised and accepted the final manuscript.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICS STATEMENT

IRB approval is not necessary. The patient's consent was obtained.

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