The course and treatment of COVID-19 in heart transplant recipients: A case series from the late phase of the pandemic

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INTRODUCTION

COVID-19, infectious severe acute respiratory syndrome caused by coronavirus 2 (SARS-CoV-2), has spread worldwide since December 2019, with varying intensity in different geographical regions and with diverse clinical presentations [1, 2]. According to previous studies, heart transplant (HT) recipients are a particularly vulnerable population, with the COVID-19 mortality rate ranging from 24% to 43% in hospitalized patients [3–5]. Therefore, the COVID-19 course in this unique group still requires a better understanding to ensure a more effective medical treatment.

METHODS

We retrospectively reviewed the data of 1896 adult (≥18 years) patients hospitalized with a diagnosis of COVID-19 at Heliodor Swiecicki Clinical Hospital (Poznań, Poland) between November 2021 and May 2022. Patients with a history of heart transplantation (five identified cases) were included in the study. Hospitalization criteria for HT recipients with COVID-19 are listed in Supplementary materials.

Data on the medical history, laboratory and radiological findings, clinical course, and outcomes were collected from the electronic medical records. The severity of the illness was classified according to the World Health Organization (WHO) definition [6].

The diagnosis of COVID-19 and patient infectivity after treatment were confirmed using the established methods of either real-time reverse transcriptase-polymerase chain reaction (RT-PCR) or the rapid antigen test (RAT) with nasopharyngeal swabs.

This study was retrospective and observational; therefore, the approval of the Bioethics Committee and written consent were not required.

Statistical analysis

Statistical analysis was performed using the PQStat v.1.8.4 software (PQStat, Poznań, Poland). Continuous variables are presented as medians with interquartile ranges (IQRs).

RESULTS AND DISCUSSION

All patients were white men at the median (IQR) age of 52 (47–58) years. The median (IQR) time from HT to presentation was 5 (5–17) months.

In all cases, HT was performed because of end-stage heart failure. All patients had comorbidities, including hypertension (n = 5), diabetes mellitus (n = 4), and chronic kidney disease (n = 4).

Four patients were symptomatic while one patient (case 4) tested positive during screening but was asymptomatic on presentation. The median (IQR) duration of symptoms before presentation was 2 (2–4) days. The most commonly reported symptom was fatigue (n = 4); less-common symptoms included fever (n = 2), cough (n = 2), dyspnea (n = 2), and chills (n = 2). Two patients (cases 3 and 5) were admitted with respiratory failure and required oxygen supplementation via a nasal cannula (maximum of 6–10 l).

On admission, all patients had lymphopenia and elevated C-reactive protein levels

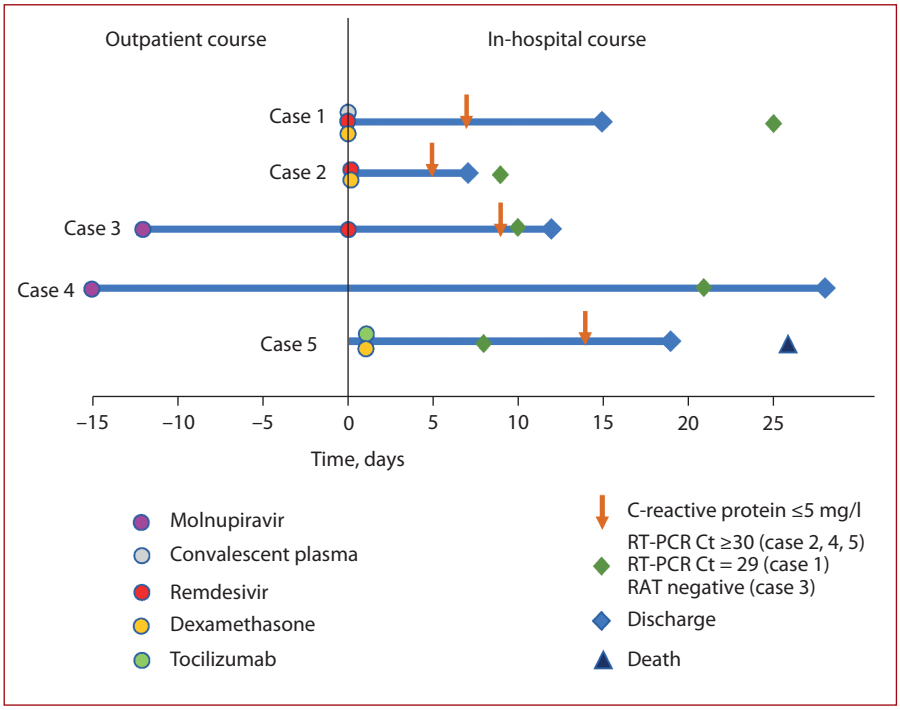

Figure 1. Graphic representation of the clinical course, administered therapy, infectivity, and outcomes for five heart transplant recipients with COVID-19

Abbreviations: RAT, rapid antigen test; RT-PCR Ct, reverse transcriptase-polymerase chain reaction cycle threshold value

with a median (IQR) peak of 60 (49–177) mg/l. In all cases, echocardiography showed ejection fractions comparable to those in previous examinations.

Data on the demographics, clinical characteristics, administered therapies, and outcomes are detailed in Supplementary material, *Table S1*.

Two patients (cases 3 and 4) were initially treated with molnupiravir as outpatients and required hospitalization within 15 days because of the development or worsening of COVID-19 symptoms. Three patients (cases 1–3) received remdesivir for 5 days from day 0. One patient (case 5) received a single dose of tocilizumab (800 mg) on day one. Three patients (cases 1, 2, and 5) received intravenous dexamethasone. One patient (case 1), who was not vaccinated against COVID-19, received an infusion of convalescent plasma on day 0.

The management of immunosuppressive regimens during anti-covid treatment is presented in Supplementary material, *Table S1*.

All patients were discharged within 29 days in good condition on a basal prehospital immunosuppression regimen. The median hospitalization duration was 16 (IQR, 12–19) days. The median duration of infectivity, based on the RT-PCR cycle threshold value and RAT, was 22 (IQR, 9–25) days and was longest (36 days) in a patient treated with molnupiravir as the only antiviral (case 4). The in-hospital course was mainly complicated by coinfections: cases 1 and 4 were diagnosed with urinary tract infections, and case 4 had a bacteriemia early on admission; case 5 had a cytomegalovirus infection from day 5.

None of the patients required mechanical ventilation, extracorporeal membrane oxygenation support, or intensive care unit admission. No episodes of clinically significant rejections were observed. One patient (case 5) was readmitted after one week with neutropenia and septic shock and suddenly died on day 0. An autopsy was not performed.

Data on the clinical course, administered therapy, infectivity, and outcomes are summarized in Figure 1.

Considering the dominance of the Delta and Omicron variants in the general population during the period of our study and their common symptoms [1, 2], we noticed fewer typical manifestations of the disease in our patients. The most common comorbidities and laboratory findings, including lymphopenia on admission, are comparable with those previously reported [3]. Similarly, the median hospitalization duration and high prevalence of coinfections are comparable to those in previous studies [4]. Regarding the illness severity, two of our patients (40%) were ultimately classified as severe according to the WHO scale, which confirms previous data indicating a high prevalence of severe cases in hospitalized HT recipients with COVID-19 [7].

Compared to a Silesian report from the early phase of the pandemic [5], we noticed lower mortality in our hospitalized cohort. The difference may reflect the declining trend in COVID-related mortality during the pandemic in solid organ transplant (SOT) recipients [8].

The results from a recent study [3] suggest a more severe course of COVID-19 in HT recipients on a triple immunosuppressive regimen. In our study, of four patients treated with intense triple immunosuppressive regimens, all had good outcomes although one case was severe. However, in two cases, the hospital course was complicated by coinfections, which agrees with the conclusions of the previous study [3]. This reflects the paradoxical effect of immunosuppressive therapy on the course of infectious diseases and the challenge of maintaining the balance

between cytokine storm mitigation and an increased risk of coinfections.

Following the recommendations of the Polish Association of Epidemiologists and Infectiologists [9], we administered molnupiravir as outpatient therapy in one asymptomatic patient and one patient with mild disease. In both cases, that therapy was ineffective, and the patients required hospitalization for deterioration in their general condition, with one case progressing to severe disease. However, both patients were ultimately discharged with good outcomes. The real-world data verifying the efficacy of molnupiravir administration among HT recipients with COVID-19 are still limited. Contrary to the outpatient strategy, two other patients with mild disease, who were inpatients, were treated with intravenous remdesivir and dexamethasone, as recommended for more advanced disease in the general population [9]. Additionally, we used remdesivir as the second antiviral agent in one severe case after ineffective molnupiravir therapy. Compared to previous studies [10,11], the administration of remdesivir was associated with good final results even when applied two weeks after the disease onset, and no significant side effects or drug-to-drug interactions were observed. Regarding immunomodulatory therapy, following the recommendations [9], we administered tocilizumab with dexamethasone in one patient with severe disease, rapid progression of respiratory failure, and high levels of inflammatory markers who presented late in the course of disease. Despite a rapid improvement in clinical and inflammatory parameters and discharge, the outcome was ultimately fatal owing to a secondary infection. Taking into consideration data suggesting the beneficial effects of tocilizumab administration in SOT recipients with COVID-19 [11], as well as numerous predictors of poor prognosis and co-administration of valganciclovir in the case of our patient, we considered the cause of death to be multifactorial.

Our study had certain limitations. First, it was a single-center, retrospective study with small sample size. Second, we did not identify the type of COVID; therefore, our observations were incomplete.

However, data on COVID-19 among HT recipients are limited, especially data on the best treatment option. Our observation of different anti-COVID treatment strategies advances the clinical knowledge on this issue.

In conclusion, the key to the successful treatment of COVID-19 in HT recipients is their early presentation to receive care for symptoms and the early onset of treatment. Among other antivirals, remdesivir appears to be an effective and safe option for these patients. More studies are needed to verify the efficacy of molnupiravir in this population.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska

Article information

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