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The course and treatment of COVID-19 in heart transplant recipients

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Dear Editor,

Thank you very much for the opportunity to contribute to the current discussion on post-transplant patients with COVID-19, by referring to the letter of Anna Drohomirecka and Tomasz Zieliński [1] published in the *Kardiologia Polska (Kardiol Pol, Polish Heart Journal)* as a commentary on our article entitled: “The course and treatment of COVID-19 in heart transplant recipients: A case series from the late phase of the pandemic”. Given the high risk of infectivity and mortality due to COVID-19 among heart transplant recipients and the need to improve the care of our patients, the exchange of institutional experience between transplant centers is of great importance. We believe that the *Kardiol Pol* is an excellent platform for sharing knowledge and experience in this field for the cardiac and transplant community.

Below we refer to the questions that have arisen during the discussion: *Pulmonary aspergillosis in heart transplant recipients with COVID-19*.

COVID-19 associated fungal infections, including COVID-19 Associated Pulmonary Aspergillosis (CAPA) have been well described [2] and defined as secondary (fungal-after-viral) infections; however the data on the prevalence of invasive pulmonary aspergillosis preceding to COVID-19 are limited. We described 2 cases of HT recipients with COVID-19 initially infected with aspergillosis. The diagnosis in both cases was established in the early

post-transplant period, according to the guidelines of the International Society for Heart and Lung Transplantation [3], including clinical and laboratory (positive bronchoalveolar lavage testing for *Aspergillus galactomannan*) criteria, and the results of computed tomography of the chest. Both patients were treated with voriconazole and had a tacrolimus concentration of 17.3 ng/mL and 10.2 ng/mL at the time of COVID-19 diagnosis, respectively (compared to the other 2 patients with a tacrolimus concentration of 10.3 ng/mL and 13.3 ng/mL, respectively). Referring to the observation of kidney transplant recipients with COVID-19, we also noted a trend towards higher tacrolimus concentrations during COVID-19 compared to earlier periods in our patients.

The management of immunosuppressive regimens during anti-COVID treatment

Treatment of post-transplant patients, especially immunosuppressive management, always requires an individual approach. Moreover, in the absence of established rules, decisions are often made on the basis of individual and institutional clinical experience. During the pandemic, it was common practice to discontinue or reduce the treatment with antimetabolites, however reports on the effect of mycophenolate on the course of infectious diseases are contradictory. While some studies suggest an impaired immune response to Sars-Cov2 vaccination in individuals treated with mycophenolate [4], others show a beneficial effect of the drug administration on the course of COVID-19, and indicate the antiviral properties of mycophenolate itself [5].

Referring to immunosuppressive management during anti-COVID treatment, we considered the actual intensity of immunosuppression, time from transplant or rejection event, and the type of anti-COVID treatment (antivirals or biologics). Our overall strategy for early post-transplant patients on antiviral therapy was to maintain background therapy with tacrolimus and mycophenolate mofetil and closely monitor drug levels with dose adjustments. In cases of neutropenia, we temporarily discontinued anti-metabolite treatment.

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