Immunosuppressants

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COVID-19 and COVID-19-pneumonia: 19 case reports

An observational study of liver transplant patients consecutively diagnosed with COVID-19 at a hospital in Spain between 15 March 2020 and 5 May 2020, described 14 men and four women, aged 55–72 years, who developed COVID-19 or COVID-19-pneumonia during immunosuppressive treatment with azathioprine, everolimus, mycophenolate-mofetil, mycophenolic-acid, prednisone or tacrolimus [*routes, dosages and durations of treatments to reaction onsets not stated*].

The patients, who had HBV cirrhosis, hepatocellular carcinoma, cryptogenic cirrhosis, HCV cirrhosis, acute liver failure or alcoholic cirrhosis, underwent liver transplant (18 patients) and liver-kidney transplant (1 patient). Additionally, the patients had comorbidities like hypertension, diabetes mellitus or lung disease. The patients were maintained on immunosuppressive therapy with everolimus (2 patients), mycophenolate mofetil and everolimus (1 patient), mycophenolate mofetil (6 patients), tacrolimus (5 patients), azathioprine, everolimus and prednisone (1 patient), tacrolimus and prednisone (1 patient), tacrolimus, mycophenolate mofetil and prednisone (1 patient), mycophenolic acid (1 patient) and tacrolimus and mycophenolate mofetil (1 patient). Following 2–314 months of transplant (in the year 2020), the patients presented to the hospital in Spain with symptoms including cough, fever, dyspnoea, thoracic pain, diarrhoea, nausea, vomiting, olfactory and taste disorders, weakness or myalgia for 1–21 days. Only one of these patients was already admitted for a liver biopsy and a percutaneous transhepatic cholangiography without any symptoms of COVID-19. Lung infiltrates were present on chest X-ray at presentation in 13 patients indicating pneumonia. All had positive reverse transcription polymerase chain reaction (rRT-PCR) for SARS-CoV-2 except two patients. All the patients were diagnosed with COVID-19 (n=6) and COVID-19-pneumonia (n=13). Their respective immunosuppressive therapies along with comorbidities were considered as the risk factors for the development of SARS-CoV-2 infection. Two patients had unusual thrombotic complications. One of these patients showed a right hepatic vein branch thrombus and a second degree right portal vein branch thrombus in a Liver CT, probably related to a percutaneous transhepatic cholangiography procedure. Another patient had an intermittent right upper quadrant pain for a week at the time of admission, and at abdominal CT scan revealed an acute thrombus partially occupying the inferior vena cava from the hepatic veins-caval anastomosis area to the left renal vein. The role of SARS-CoV-2 infection in these two thrombotic events could not be ruled out.

Fourteen of these patients received inpatient treatment for COVID-19, while remaining five patients were treated on outpatient basis. Out of five patients, who received outpatient treatment, two were treated with off-label hydroxychloroquine monotherapy, while remaining three received no antiviral therapy. None of these five patients required respiratory support or change in immunosuppressive regimen. Fourteen patients, who received inpatient treatment, received off-label hydroxychloroquine monotherapy (5 patients), off-label tocilizumab monotherapy (1 patient), off-label hydroxychloroquine plus tocilizumab (1 patient), off-label hydroxychloroquine plus lopinavir/ritonavir (1 patient), off-label hydroxychloroquine, lopinavir/ritonavir plus interferon-beta (1 patient), off-label hydroxychloroquine plus interferon-beta (1 patient) and no antiviral treatment (4 patients). The patients received hydroxychloroquine at dose of 400mg every 12 hours during the first day, then 200mg every 12 hours during 4–9 days, lopinavir/ritonavir at dose of 200/100mg twice a day for 14 days, SC interferon-beta at dose of 250µg every 48 hours or a single IV dose of tocilizumab. Nine of these 14 patients required respiratory support via nasal cannula (7 patients), invasive mechanical ventilation (1 patient) and non-rebreather oxygen mask (1 patient). The patient, who required invasive mechanical ventilation, rapidly deteriorated, without receiving any specific antiviral treatment and with discontinuation of immunosuppressive therapy. This patient eventually died due to pulmonary embolism and respiratory failure. The patient receiving respiratory support via non-rebreather oxygen mask also died eventually due to respiratory failure. In two of these 14 patients, who were treated with lopinavir/ritonavir, immunosuppressive therapy was changed to tacrolimus and mycophenolate mofetil or tacrolimus monotherapy due to the possibility of interaction between everolimus and ritonavir. No other patient required changes in the immunosuppressive treatment. At the time of this report writing 15 patients were at home in good condition and two patients were still in hospital. Out of these two patients one was recovering from a severe cholangitis and without showing any symptoms of COVID-19 and with a SARS-CoV-2 PCR negative, while the remaining one (recently admitted) was on respiratory support via nasal cannula, correctly evolving, with good prognosis.

Loinaz C, et al. Varied clinical presentation and outcome of SARS-CoV-2 infection in liver transplant recipients: Initial experience at a single center in Madrid, Spain. Transplant Infectious Disease 22: No. 5, Oct 2020. Available from: URL: http://doi.org/10.1111/tid.13372 803536052

» **Editorial comment:** Details of four patients (Patient 1, 2, 3 and 5 from table 1) have previously been published and processed for Adis PV [see Reactions 9999; 803491842]. In the current report authors have considered respective maintenance immunosuppressive therapies (everolimus, mycophenolate mofetil, azathioprine, prednisone or tacrolimus) and comorbidities as risk factors for COVID-19 or COIVD-19 pneumonia. At the time of this report writing three of these patients were at home in good condition, while one died of respiratory failure. Additional laboratory tests were provided.