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Liver Transplant in a Polymerase Chain Reaction—Positive COVID-19 Recipient: A Case Report

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ABSTRACT

The severe acute respiratory syndrome coronavirus 2 coronavirus disease 2019 (COVID-19) global pandemic has ushered in an era of hesitation in performing transplants in affected patients. This stems from the paucity of data regarding the testing modalities, long-term implications, and uncertain prognosis in this group of patients. Current guidance from the Centers for Disease Control recommends assessing symptoms rather than polymerase chain reaction (PCR) positivity. In light of these recommendations, we describe a case of an orthotopic liver transplant in a patient infected with COVID-19 with persistent PCR positivity for 40 days before retransplant. The patient’s perioperative and postoperative course was uncomplicated. Our experience leads us to advocate for liver transplants in patients who are PCR positive for COVID-19 after careful individualized and multidisciplinary evaluation regarding their liver disease and COVID-19 symptomatology.

CASE

Presentation and Pretransplant Course

A 65-year-old man with a medical history significant for type 2 diabetes mellitus and nonalcoholic steatohepatitis cirrhosis complicated by ascites, nonbleeding esophageal varices, and hepatocellular carcinoma within the Milan criteria underwent OLT from a donation after circulatory death donor in March 2020. He was maintained on immunosuppression with tacrolimus, mycophenolate, and prednisone taper. During workup of persistently elevated liver enzymes, he underwent a liver biopsy that was consistent with biliary outflow impairment, along with periportal fibrosis without any features of rejection. Imaging studies confirmed biliary strictures, which led to multiple endoscopic retrograde cholangiopancreatographies with minimal improvement. His liver enzymes continued to rise with total bilirubin ranging up to 35 mg/dl, alkaline phosphatase of 1485 U/L, and aminotransferases ranging 2 to 3 times the upper limit of normal.

Because of the rapid progression to cholestatic graft failure, he was relisted for liver transplant in August 2020. He was...
continued on tacrolimus monotherapy while he waited for an organ offer. He was found to be SARS-CoV-2 PCR positive on August 13, 2020, while he was evaluated for a potential organ offer. The transplant was aborted owing to the concerns of active infection, and his listing was changed to status 7: inactive for transplant. The patient was completely asymptomatic with a stable physical examination maintaining normal oxygen saturation. He denied fever, cough, shortness of breath, diarrhea, or alterations in his sense of taste or smell. Chest x-ray (Fig 1) and computed tomography without intravenous contrast were performed (Fig 2), despite lack of symptoms, to ensure any signs of disease activity and showed patchy ground glass opacities along the peripheral aspects of the upper, as well as the left lower, lobe, in association with architectural distortion mild bronchiectasis in the right upper lobes and partly in the lower lobes. These findings were thought to represent pulmonary manifestations of COVID-19 pneumonia, and after further review with our infectious disease colleagues, consensus was made to check the SARS-CoV-2 PCR weekly, until negative, to make the patient stay active on the list. Serial testing over 40 days confirmed persistent positivity of the SARS-CoV-2 PCR, as summarized in Table 1 and Fig 3. All molecular testing was performed on nasopharyngeal swabs collected by a health care professional and in viral transport media. Two different emergency use authorized testing platforms were used over the course of this patient’s repeated testing: the Abbott (Abbott park, IL) m2000 SARS-CoV-2 RealTime assay and the Cepheid (Sunnyvale, CA) GeneXpert SARS-CoV-2 PCR. As a result, cycle threshold values are not directly comparable between instruments, with the m2000 assay producing cycle threshold values typically 10 cycles lower than the GeneXpert assay. Of note, the patient was staying at a hotel with his wife and son who did not develop COVID-19 and were completely asymptomatic. Furthermore, detection of SARS-CoV-2 antibodies on September 9, 2020, suggested evidence of immunity and low transmissibility.

The case was reviewed by the liver transplant multidisciplinary team, and in the setting of progressive liver disease, rising Model for End-Stage Liver Disease score, and lack of COVID-19 symptoms, the patient was re-activated for transplant. Two days after being activated on the transplant list, he underwent liver retransplant with a donation after brain death, public health service increased risk organ in late September.

OLT and perioperative management

The patient’s surgery was performed in a negative pressure air cleaning system operation room. All the surgical staff had appropriate personal protective equipment (N-95 masks, gowns, hats, and shoe covers) for precaution. General endotracheal anesthesia was administered. Methylprednisolone 500 mg was given intravenously in the operating room prior to reperfusion following to the protocol. The donor liver was mounted in piggyback fashion by sewing the donor suprahepatic cava to the anterior wall of the recipient vena cava at the left, middle hepatic vein orifices. The portal vein was anastomosed to the recipient’s portal vein. The recipient had the small replaced right hepatic artery. The hepatic arterial inflow was via an infrarenal aortic conduit using an iliac artery of the same donor and was anastomosed to the donor celiac artery, resulting in a good pulse. The biliary anastomosis was done as an Roux-en-Y hepaticojjunostomy. He tolerated the procedure well, and no complications occurred. Cold ischemic time was 6 hours and 20 minutes. The immediate postoperative ultrasound demonstrated good arterial flow with the patent portal vein and hepatic vein. His postoperative course was significant for acute blood loss anemia, which required a return to the operating room for a washout on postoperative day (POD) 1. A hematoma around...
the liver was identified without any major bleeding. He was weaned from mechanical ventilation on POD 2 without any respiratory complication. He was not kept in airborne isolation precautions post-transplant. Mycophenolate mofetil 2000 mg/d, weight-based tacrolimus, and a standard steroid taper were prescribed according to hospital protocol. We did not change our protocol especially to this patient. The rest of the postoperative course was unremarkable. He was discharged home with home health services on POD 10. The last follow-up visit was on POD 30 when his COVID-19 PCR was negative. He was in an excellent clinical status.

DISCUSSION

We report a case of an OLT in a patient with persistently positive SARS-CoV-2 PCR with no symptoms of COVID-19. The transplant was successful, and no viral transmission was documented. Our case helps shed light on the dearth of data concerning identifying the optimal time for transplantation in patients with positive SARS-CoV-2 PCR.

According to the latest American Association for the Study of Liver Diseases (AASLD) expert consensus for transplants in candidates who are SARS-CoV-2 positive, they should be delayed for at least 14 to 21 days after symptom resolution and for 1 or 2 negative SARS-CoV-2 diagnostic tests [9]. The likelihood of a replication-competent virus after 10 days of mild to moderate COVID-19 is very low [10,11]. In some cases of severe COVID-19 infection, mostly complicated by immunocompromised state, recovery of replication-competent virus has been reported beyond 10 days but it is usually undetectable 20 days after symptom onset [12]. The recovered patient can continue to have SARS-CoV-2 RNA detected in their upper respiratory specimens for up to 12 weeks, even though there is no replication-competent virus and no reported secondary infections from such patients [13].

Since this transplant was performed, there have been reported cases of isolation of replication-competent virus for longer than 20 days in intensely immunosuppressed patients with cancer (viable virus isolated on days 21, 25, and 64) [14] and in a severely immunocompromised patient with lupus [15].

The CDC Guidelines for Discontinuation of Transmission-Based Precautions and Disposition of Patients with COVID-19 emphasize that “disease severity factors and the presence of immunocompromising conditions should be considered in determining the appropriate duration for specific patient populations” [16]. Considering this, our patient seems to be a case of true asymptomatic SARS-CoV-2 infection, not a case of COVID-19.

The exact proportion of asymptomatic SARS-CoV-2 infections is not known, but recent estimates are up to 40% to 45% [17]. In the small but well-studied cohort of passengers of the Diamond Princess cruise ship, 33 of 104 patients followed for 14 days after diagnosis were completely asymptomatic.

| Date         | 8/13/20 | 8/17/20 | 8/28/20 | 9/2/20 | 9/8/20 | 9/15/20 | 9/22/20 | 9/25/20 | 9/26/20 |
|--------------|---------|---------|---------|--------|--------|---------|---------|---------|---------|
| SARS-CoV-2 PCR (rapid) | Detected | Detected | Detected | Detected | Detected | Detected | Detected | Detected | Negative |
| SARS-CoV-2 PCR | Detected | Detected | Detected | Detected | Detected | Detected | Detected | Detected |          |
| SARS-CoV-2 Ab | Detected | Detected | Positive |         |         |         |         |         |          |

COVID-19, coronavirus disease 2019; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
throughout the observation period [18]. Asymptomatic patients are sometimes conflated with “presymptomatic” patients, in part owing to difficulties with study design [11]. This makes it difficult to ascertain the degree of infectiousness of both categories, which may be biologically dissimilar. Of note, our patient never had any symptoms, and his wife and son, who were staying with him at close quarters in a hotel room, did not develop symptoms of COVID-19 either. Although a false-positive PCR result is conceivable, the persistently positive PCR, development of anti-nucleocapsid SARS-CoV-2 antibodies, and characteristic chest computed tomography findings support asymptomatic infection rather than a persistently false-positive PCR result.

In our case, continued immunosuppression since his previous transplant may have contributed to the persistent positivity of the SARS-CoV-2 PCR. Keeping this in mind, we roughly doubled the waiting period recommended by AASLD. This is also double the amount of time recommended by the CDC for severely immunocompromised patients who were asymptomatic throughout their infection [16].

Additionally, our patient had developed antibodies against SARS-CoV-2 3 weeks after the PCR was detected. The presence of antibodies indicates a previous infection and some level of immunity or protection against COVID-19 re-infection, albeit for an unknown duration [19]. A serum-neutralizing antibody titer of at least 1:20 has been independently associated with noninfectious SARS-CoV-2 [12]. Our patient’s antibody titers were later found to be undetectable; hence he was advised to proceed with the COVID-19 vaccination when it became available to him. He has done phenomenally well since his transplant with no major complications.

We face an unusual challenge during the pandemic with the scarcity of empirical evidence to guide solid organ transplants for patients positive for COVID-19. Although there was a decrease in the number of organ transplants performed in the United States amid the COVID-19 outbreak, the number is beginning to increase [7]. The consensus in the transplant community has been the systematic use of PCR-based testing for both donors and recipients, and in cases where recipients have a suspicious or active SARS-CoV-2 infection, it is advised to defer the transplant for at least 4 weeks and after 2 negative tests at least 24 hours apart [20]; however, the optimal disease-free interval for a potential transplant recipient is not known. The decision should be individualized through a multidisciplinary approach to thoroughly evaluate all aspects of the case. The severity of SARS-CoV-2 infection as well as the appropriate use of quantitative viral load and serologic assays should be considered to assess patient eligibility. It is equally important to take into account the severity and progression of the underlying liver disease and the risk of mortality if the transplant is delayed.

CONCLUSIONS

It is encouraging to see increasing data revolving around outcomes in solid organ transplant recipients who acquired the SARS-CoV-2 infection. However, limited studies are available to provide evidence-based guidance regarding the time duration and eligibility of patients who get plagued by this disease before transplant. We hope this case report, with its very favorable outcome, serves to fill the void currently faced by the transplant society.

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