ACG CASE REPORTS JOURNAL

CASE REPORT | LIVER

Orthotopic Liver Transplantation in a Cirrhotic Patient With Recent COVID-19 Infection

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ABSTRACT

The coronavirus disease 2019 (COVID-19) pandemic has led to a decrease in liver transplantation because of concerns regarding safety and healthcare resource utilization. There are scant data regarding the safety, optimal timing, and preferred postsurgical immunosuppression regimens for liver transplantation in patients recovered from COVID-19 infection. We describe our experience with one of the first reported cases of orthotopic liver transplantation in a patient who had recently recovered from COVID-19 infection. Using our experience as an example, orthotopic liver transplantation in patients that have recovered from COVID-19 may be safe.

INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) that causes coronavirus disease 2019 (COVID-19) was first reported in Wuhan, China, in December 2019 and spread rapidly to cause a worldwide pandemic. In the United States alone, there have been 14.6 million confirmed cases and more than 281,000 deaths attributed to COVID-19.[1,2] Limited hospital resources have led to a steep decline in the number of liver transplants.[3] In addition, the safety of liver transplantation in patients previously infected with COVID-19 infection is not understood. We present an orthotopic liver transplantation (OLT) case in a patient recently infected with COVID-19.

CASE REPORT

A 46-year-old woman with alcohol-related cirrhosis presented with shortness of breath, dry cough, malaise, fatigue, and worsening jaundice for 1 week. She denied fever, abdominal pain, hematemesis, or melena. Initial vital signs were stable with a saturation of 96% on room air. Physical examination showed jaundice, bibasilar crackles, and lower extremity edema. Laboratory results showed sodium of 130 mq/L, creatinine of 2.20 mg/dL, total bilirubin of 20.1 mg/dL, alkaline phosphatase of 120 IU/L, aspartate aminotransferase of 282 U/L, alanine aminotransferase of 62 U/L, international normalized ratio of 1.9, and fibrinogen of 140 mg/dL. The blood ethanol level was negative. Her initial model for end-stage liver disease with sodium (MELD-Na) was 34. Thoracic x-ray showed ground-glass opacities with left perihilar infiltrates (Figure 1). A thoracic computed tomography without contrast showed scattered ground-glass opacities in both lungs, with an asymmetric ground-glass opacity in the left perihilar region extending to the left mid and upper lung field (Figure 2). Abdominal ultrasound showed slightly coarse hepatic parenchymal echotexture, mild splenomegaly, and a trace of ascites. She was treated with antibiotics for bacterial pneumonia. A paracentesis was negative for spontaneous bacterial peritonitis. Diuretics were discontinued, IV albumin was given for her abnormal renal function, and lactulose was given to treat encephalopathy. After 2 weeks of hospitalization, given a persistently elevated MELD-Na score of 34, she was transferred to our hospital for liver transplant evaluation.

On arrival, she was screened for COVID-19 with Abbott real-time polymerase chain reaction (PCR) testing and was positive. By this time, the patient with respiratory symptoms had resolved. OLT evaluation was postponed, and supportive management was

ACG Case Rep J 2021;8:e00634. doi:10.14309/crj.0000000000000634. Published online: July 9, 2021

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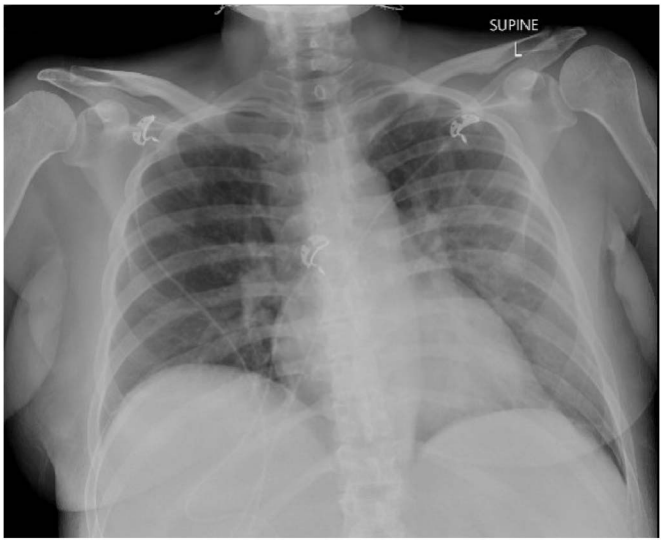

Figure 1. Anterior-posterior thoracic x-ray on admission showing a left perihilar ground-glass infiltrate.

continued. After 1 week, testing for COVID-19 was repeated and was negative. A second COVID-19 test, using the PCR test developed by the Robert J Tomsich Pathology and Laboratory Medical Institute, remained negative 2 weeks after admission. At this point, OLT evaluation was initiated, and the patient was listed for transplantation with a MELD-Na of 35. At the time of listing, she was hemodynamically stable, saturating 100% on room air, and without respiratory symptoms. Five days after being listed, an organ from a COVID-19 negative donor became available and the patient again retested negative (using the PCR Pathology and Laboratory Medical Institute test) for COVID-19 the day of surgery. She underwent OLT 21 days after her positive COVID-19 test (Figure 3). Intraoperatively, after reperfusion, the patient developed a right atrial thrombus requiring intravenous tissue plasminogen activator (tPA) infusion with resolution of the thrombus. Of note, a thromboelastography on the morning of the transplantation was normal (Table 1). Postoperative day 2, she was taken to the operating room for abdominal washout because of a drop in hemoglobin. No source of bleeding was identified, and the bleeding was considered secondary to medical anticoagulation given during transplantation. Subsequently, she remained stable and was extubated on the third postoperative day. Her liver graft function was good on the standard immunosuppression protocol with steroid taper, mycophenolate, and tacrolimus. Three months postoperatively, the patient has continued to do well.

DISCUSSION

Available data on COVID-19 infection occurring in patients after liver transplantation suggest that mortality may not be higher in this population.[4] However, data on liver transplantation in patients with resolved COVID-19 infection are scarce.[5–7] We present one of the first cases of OLT in a patient previously infected with COVID-19.

In July 2020, Martini et al published the first report of liver transplantation in a 39-year-old woman who had cirrhosis secondary to autoimmune hepatitis, was listed with a MELD of 36, and had mild COVID-19 infection that was diagnosed 9 days before transplantation.[5] They ensured 2 negative consecutive COVID-19 tests before transplantation. Dhand et al published another report of an OLT in a 42-year-old man with alcoholic hepatitis (MELD 33) 71 days after his initial mild COVID-19 diagnosis; they also confirmed several negative consecutive COVID-19 tests before transplantation.[6] Tabrizian et al published a report of liver transplantation in a 57-year-old woman with decompensated hepatitis C cirrhosis, hepatocellular carcinoma, and human immunodeficiency virus who had recovered from mild COVID-19 infection initially diagnosed 63 days earlier; the resolution of infection was confirmed with 2 consecutive COVID-19 tests.

Similar to previously published case reports, our patient was young, had a high MELD (34), had mild COVID-19 infection, and did not have any serious cardiopulmonary or thromboembolic consequences before her liver transplantation. This made her an acceptable candidate for OLT, despite

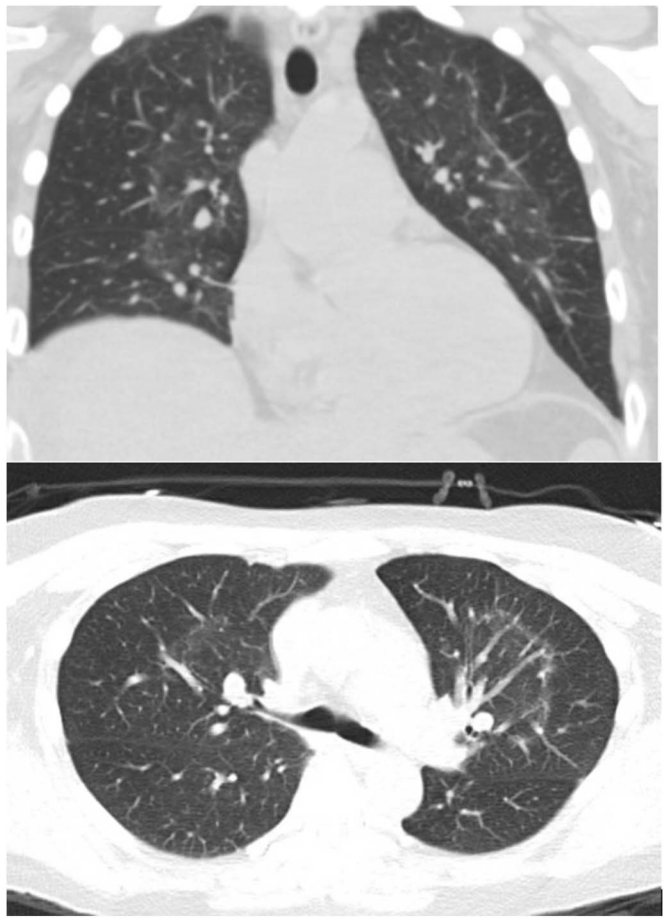

Figure 2. Thoracic computed tomography without contrast showing scattered ground-glass opacities in both lungs. Asymmetric ground-glass opacity in the left perihilar region extending into the left mid and upper lung field involving predominantly the anterior and lingular segments of left upper lobe.

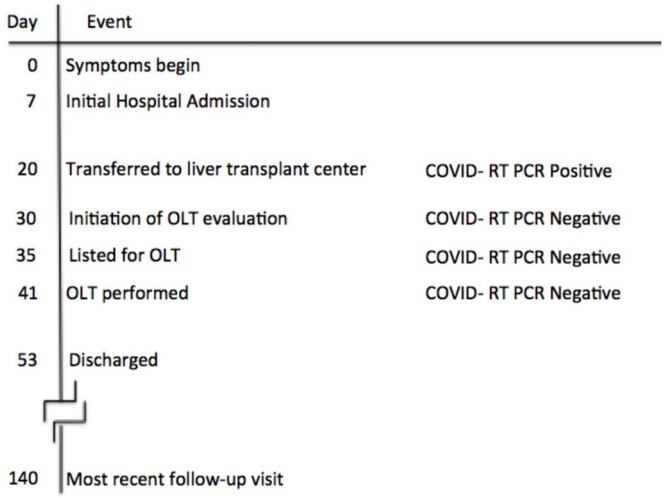

Figure 3. Timeline of events from the onset of symptoms.

unprecedented circumstances and uncertain outcomes. Importantly, it seems that all authors were meticulous in having at least 2 negative COVID-19 tests before proceeding with liver transplantation. The duration from initial COVID-19 diagnosis to time of transplantation varied from 9 to 71 days. COVID-19 has affected the healthcare system in multiple aspects. Elective procedures have been delayed. However, liver transplantation in sick patients is not considered an elective procedure. Delay in liver transplantation in patients with high MELD may lead to higher mortality. The issue is that there is uncertainty regarding the timing, prognosis, and outcomes of OLT in patients previously infected with COVID-19 with high MELD scores. Our decision for this sick patient was to wait for 10 days after resolution of symptoms and 2 consecutive negative COVID-19 tests.

Overall, our patient did well after OLT. She was found to have a right atrial thrombus seen developing on an intraoperative echocardiogram that required intravenous tPA. Thromboembolic events may be present in 25%–30% of patients with COVID-19 because of excessive inflammation, platelet activation, endothelial dysfunction, and stasis.[8,9] Our patient was on prophylactic dose subcutaneous heparin throughout admission, per guidelines.[10] It is unclear whether the hypercoagulability caused by COVID-19 contributed to this case. Reperfusion of the liver graft, which may overwhelm anticoagulant mechanisms, may have led to these thrombi (11), which promptly respond to IV tPA, as in this case.

A concern in liver transplant recipients is the use of immunosuppression and its risk of new, severe, or recurrent infection. In a case series by Bhoori et al, immunosuppression in long-term liver transplant recipients did not seem to increase the severity of COVID-19. Instead, the presence of metabolic-related comorbidities seemed to be associated with an increased risk of severe COVID-19.[4] Overall, preliminary data seem to indicate that post-OLT immunosuppression does not impart a significant increase in infection frequency, severity, or recurrence. Our patient was placed on our center's standard post-transplantation protocol, including steroid taper, mycophenolate, and tacrolimus. She was placed on prophylaxis with fluconazole, trimethoprim-sulfamethazole, and valganciclovir. It is important to recognize the importance of a multidisciplinary approach to liver transplantation, especially during this COVID-19 pandemic.

Table 1. Thromboelastography obtained on the day of surgery

Test	Value	Range
Split point initial fibrin formation	4.8	N/A
R value	5.2	5–10 min
K value	1.6	1–3 min
Degree angle	68.2	53–72 degrees
Maximum amplitude	58.6	50–70 mm
Clot strength	7.1	4.5–11.0 kdynes/cm^2
Estimated percent to lysis	0.0	0–15%
Lysis time 30	0.0	0–8%
D dimer	6,310	<500 ng/mL

In conclusion, OLT in patients that recovered from COVID-19 seems to be safe. The long-term outcome is yet to be determined. The ideal timing for liver transplantation after resolution of COVID-19 infection is not known. The risks and benefits of OLT should be considered. Patients with high MELD scores do not have the luxury of waiting for a transplant. Our approach for this sick patient was to wait for the resolution of symptoms and 2 consecutive negative COVID-19 tests. More studies are needed to investigate further the safest time for transplantation in this patient population.

DISCLOSURES

Author contributions: A. Gonzalez, D. Castaneda, and K. Tandon wrote the manuscript, reviewed the literature, and approved the final manuscript. X. Zervos, K. Al Khalloufi, and A. Pinna wrote and edited the manuscript and approved the final manuscript. C. McWilliams and C. Donato edited the manuscript, reviewed the literature, and approved the final manuscript. D. Reino and S. Ebaid edited the manuscript and approved the final manuscript. K. Al Khalloufi is the article guarantor.

Acknowledgments: The authors would like to acknowledge Dr. Francis Tardy, radiologist of the Cleveland Clinic, Weston, Florida.

Financial disclosure: None to report.

Informed consent was obtained for this case report.

Received September 23, 2020; Accepted March 30, 2021

REFERENCES

1. Zhu N, Zhang D, Wang W, et al; China Novel Coronavirus Investigating and Research Team. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med.* 2020;382(8):727–33.

2. *Cases in the U.S.* (https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html) (2020). Accessed December 8, 2020.
3. Loupy A, Aubert O, Reeese PP, Bastien O, Bayer F, Jacquelinet C. Organ procurement and transplantation during the COVID-19 pandemic. *Lancet*. 2020;395(10237):E95–E96.
4. Bhoori S, Rossi RE, Citterio D, Mazzaferro V. COVID-19 in long-term liver transplant patients: Preliminary experience from an Italian transplant centre in lombardy. *Lancet*. 2020;5(6):532–3.
5. Martini S, Patrono D, Pittaluga F, et al. Urgent liver transplantation soon after recovery from COVID-19 in a patient with decompensated liver cirrhosis. *Hepatol Commun.* 2020;5(1):144–5.
6. Dhand A, Bodin R, Wolf DC, et al. Successful liver transplantation in a patient recovered from COVID-19. *Transpl Infect Dis.* 2020;23(2):e13492.
7. Tabrizian P, Pourmand K, Florman S. Liver transplantation in a patient with human immunodeficiency virus and COVID-19. *Liver Transpl.* 2020 [Epub ahead of print May 31, 2021].
8. Bikdeli B, Madhavan MV, Jimenez D, et al. COVID-19 and thrombotic or thromboembolic disease: Implications for prevention, antithrombotic therapy, and follow-up. *J Am Coll Cardiol.* 2020;75(23):2950–73.
9. Klok FA, Kruip MJ, van der Meer NJM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thromb Res.* 2020;191:145–7.
10. Tang N, Bai H, Chen X, Gong J, Li D, Sun Z. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. *J Thromb Haemost.* 2020;18:1094–9.
11. Gologorsky E, De Wolf AM, Scott V, Aggarwal S, Dishart M, Kang Y. Intracardiac thrombus formation and pulmonary thromboembolism immediately after graft reperfusion in 7 patients undergoing liver transplantation. *Liver Transpl.* 2001;7(9):783–9.