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TRANSPLANT INFECTIOUS DISEASE

CLINICAL CORRESPONDENCE

Successful liver transplantation for hepatitis B-related acute liver failure in a patient with active COVID-19

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Abstract

The emergence of coronavirus disease 19 (COVID-19) has significantly disrupted liver transplantation worldwide. Despite significant, collective experience in treating liver transplant recipients with COVID-19, there remains a paucity of data to guide the management of transplant candidates with acute COVID-19 who require urgent transplantation. We present the case of an otherwise well, 39-year-old female presenting for urgent liver transplantation for acute liver failure secondary to hepatitis B, with concomitant acute, mild COVID-19 due to Omicron BA.2. COVID-19 antivirals were not administered pre-transplant as the potential risk of hepatotoxicity precipitating further deterioration of liver function was not felt to outweigh the small, potential benefit of antiviral therapy. No effective SARS-CoV-2 monoclonal antibodies were available; however, the patient was previously vaccinated against SARS-CoV-2 with evidence of anti-spike antibodies at the time of COVID-19. Transplantation surgery and recovery were uncomplicated with no progression of COVID-19 post-transplant, hospital discharge was at day 14. At 30 days post-transplant the patient had recovered, with normal liver function and SARS-CoV-2 was not detectable on nasopharyngeal PCR. While the safety of transplantation of patients with acute COVID-19 cannot be assured by a single case, ours highlights the complex decision-making process undertaken and competing priorities that need to be balanced when assessing patients with acute COVID-19 who require urgent transplantation.

KEYWORDS
acute liver failure, COVID-19, liver transplantation

1 | INTRODUCTION

The emergence of coronavirus disease 19 (COVID-19) caused by severe acute respiratory distress syndrome coronavirus 2 (SARS-CoV-2) has disrupted liver transplantation (LT) worldwide.[1] While our understanding of COVID-19's impact on LT recipients (LTR) has improved over time, there remains a paucity of data regarding the management of patients with active COVID-19 requiring urgent LT. The Transplant Society of Australia and New Zealand recommends deferring LT in those with active COVID-19 for at least 28 days post-symptom resolution and after two negative nasopharyngeal SARS-CoV-2 polymerase chain reaction (PCR) results 24 h apart.[2] We present a case of successful orthotopic LT for hepatitis B virus (HBV)-related acute liver failure (ALF) in a recipient with active COVID-19. This is the first such case reported in Australia.

2 | CASE REPORT

A 39-year-old female with no history of liver disease was transferred to our facility with ALF after presenting with 5 days of nausea and vomiting. On presentation, she had markedly elevated

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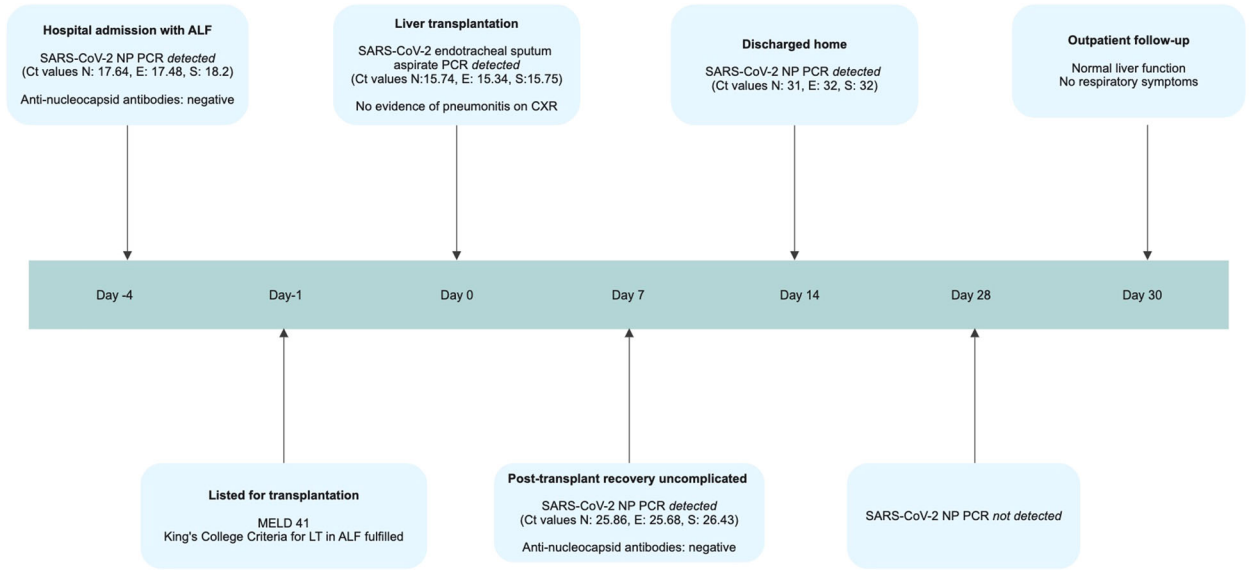

FIGURE 1 Timeline of admission and severe acute respiratory distress syndrome coronavirus 2 (SARS-CoV-2) testing. ALF, acute liver failure; Ct, cycle threshold; LT, liver transplant; MELD, model for end-stage liver disease; NP, nasopharyngeal; PCR, polymerase chain reaction

transaminases (alanine aminotransferase 9152 U/L, aspartate aminotransferase 4770 U/L) and impaired hepatic synthetic function (bilirubin 160 μmol/L, international normalized ratio [INR] > 10). Venous blood gas demonstrated a normal pH of 7.30 with elevated lactate of 8.1 mmol/L. Initially, she was not encephalopathic, had normal renal function and required no inotropic support. SARS-CoV-2 was detected by nasopharyngeal PCR on day 0 of admission with cycle threshold (Ct) values of N gene: 17.64, E gene: 17.48, and S gene: 18.2 (Allplex SARS-CoV-2, Seegene Inc.). Whole-genome sequencing confirmed SARS-CoV-2 Omicron BA.2. Anti-nucleocapsid antibodies were not detected, and quantitative anti-spike antibodies were detected at >2500 U/ml (Roche Elecys). Her latest SARS-CoV-2 vaccination (Spikevax, Moderna) was 1 month before presentation. The clinical picture was consistent with acute COVID-19 in a vaccinated individual. Although she was asymptomatic by the time of transfer, fever, cough, and coryzal symptoms were reported 5 days prior. Chest x-ray on admission demonstrated no pneumonitis.

Further work-up determined the etiology of ALF to be sexually acquired acute HBV infection, evidenced by a positive hepatitis B surface antigen (HBsAg), core immunoglobulin-M (IgM) antibody (HBcAb), and quantitative HBV DNA of 5330 IU/ml (Roche Cobas 4800). The contribution of COVID-19 to ALF was thought unlikely given the absence of other features of severe infection. Despite commencing tenofovir disoproxil fumarate (TDF) plus best supportive care, she developed grade 3/4 encephalopathy requiring intubation and continuous renal replacement therapy. On day 3 of admission, her bilirubin was 262 μmol/L and INR was 6.7 after correction with blood products. Given this deterioration and fulfilment of King's College criteria for LT in ALF, she was urgently listed and transplanted with a donation after brain death allograft on day 4 of admission. On the day of LT, SARS-CoV-2 was detected on routine perioperative endotracheal aspirate PCR with Ct values of N gene: 15.74, E gene: 15.34, and S gene: 15.75. This did not affect proceeding to transplantation given no radiologic pneumonitis. Induction immunosuppression was methylprednisolone and basiliximab to facilitate delay in calcineurin inhibitor initiation because of perioperative renal impairment. She commenced a course of hepatitis B immune globulin, and post-transplant recovery was uncomplicated with no deterioration or pulmonary complications related to COVID-19. No COVID-19 antivirals or monoclonal antibodies were given pre- or post-transplant. Serial SARS-CoV-2 PCR post-transplant demonstrated rising Ct values. The patient was discharged on day 14 post-transplant with maintenance immunosuppression of prednisone and tacrolimus plus TDF. At 30 days post-transplant, the patient recovered with normal liver function tests and a negative SARS-CoV-2 PCR on day 28 post-transplant (Figure 1).

3 | DISCUSSION

This is the third reported case of LT for ALF in a patient with acute COVID-19.[3,4] The decision to proceed with transplantation in this group must balance the urgency of transplantation against potential COVID-19-associated perioperative risks. Our patient presented with ALF meeting King's College Criteria with a model for end-stage liver disease score of 41, predicting poor prognosis and high mortality without LT.[5] Furthermore, ALF due to HBV carries a considerably lower rate of transplant-free survival compared to other etiologies, such as paracetamol overdose.[6] LT per se does not increase the risk of intensive care admission or mortality related to COVID-19 when compared to non-LTR. Instead, the risk of severe COVID-19 in LTR is associated with increasing age and the presence of comorbidities.[7] Given our patient's lack of clinical improvement, young age, and poor prognostic indices, the collaborative decision was made to list her for urgent transplantation by the hepatology, infectious diseases, surgical, and intensive

care teams. Ideally, transplantation would have been deferred until her acute COVID-19 infection had resolved; however, the urgency of transplantation made this unachievable. Data from early in the pandemic demonstrated that postoperative pulmonary complications occurred in half of patients with perioperative COVID-19, and the excess 30-day mortality in patients operated on within 6 weeks of COVID-19 only returned to baseline 7 weeks postinfection.[8,9] Although short-term mortality in patients undergoing surgery with recent COVID-19 is increased, the risk is lower in asymptomatic patients, such as ours, compared to symptomatic patients.[9] Surgical outcomes in patients infected with recent variants, including Omicron, are unclear. Given the high prevalence and transmissibility of Omicron, it is inevitable that patients with acute COVID-19 will present in need of urgent LT. In such cases, multidisciplinary consultation is paramount and must balance the potential risks discussed above. Complicating this decision is the lack of data to guide immunosuppression in LTR with COVID-19, as large trials of COVID-19 treatments excluded transplant recipients. Additional factors in our patient that made a severe COVID-19 outcome less likely were her lack of comorbidities and recent SARS-CoV-2 vaccination with positive spike antibodies, indicating a good vaccine response.

Prior to transplantation, COVID-19-specific therapy was considered. Assuming normal circumstances, COVID-19 antivirals were not indicated in this patient given mild COVID-19 and the absence of risk factors for progression to severe COVID-19. The oral antivirals nirmatrelvir/ritonavir and molnupiravir have demonstrated benefits in preventing progression to severe COVID-19 in at-risk patients (unvaccinated with risk factors for severe COVID-19) but have a lack of safety data in ALF and uncertain advantages in low-risk patients.[10,11] Remdesivir was considered but not given due to the risk of drug-induced liver injury, which may have worsened her liver function.[12,13] Monoclonal antibodies were also contemplated. Sotrovimab was not given, as the circulating variant of SARS-CoV-2 at the time was almost exclusively Omicron BA.2, against which sotrovimab has reduced neutralizing capability.[14] Although tixagevimab and cilgavimab (Evusheld) retain neutralizing activity against Omicron with data to support their role in COVID-19 treatment, they are not currently approved in Australia for treatment.[15] Furthermore, the additive benefit of a neutralizing monoclonal antibody in the setting of an excellent spike antibody response to vaccination, as in our patient, is likely insignificant. Post-transplantation, COVID-19 therapy was not required due to her rapid recovery and lack of COVID-19 progression.

While the safety of transplantation with acute COVID-19 cannot be assured with a single case, ours highlights the complex decision-making process undertaken and competing priorities that need to be balanced. Although the postoperative course in such a patient is unpredictable, the decision to transplant was supported by her young age, lack of comorbidities, mild COVID-19, and high risk of mortality with ALF. Although COVID-19 antivirals or monoclonal antibodies may be considered in other situations, they were not required in this case.

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CONFLICT OF INTEREST

The authors declare they have no conflicts of interest.

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