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COVID-19 in Liver Transplant Recipients - A Case Report

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Abstract

The severe acute respiratory syndrome corona virus-2 pandemic had a great impact on public life in general as well as on populations with preexisting disease and co-morbidities. Liver transplant and immunosuppressant medication predisposes to more severe disease and is often associated with poor outcome. The clinical features, disease course, treatment and process of modulating the immunosuppression is challenging. The immunosuppression minimization or withdrawal was done based upon the clinical severity. Consideration of tocilizumab and convalescent plasma as well as antivirals like remdesvir done in severe cases. The routine practice of prophylactic anticoagulation, consideration of repurposed drugs (teicoplanin and doxycycline), and watchful monitoring of asymptomatic recipients helped to achieve an uneventful recovery.

Keywords: COVID-19, Liver transplant, Remdesivir, Immunosupression

Introduction

Coronavirus disease 2019 (COVID-19) is a serious respiratory illness caused by the SARS-CoV-2 virus [1]. The majority of cases often present with mild symptoms, like fever, cough and shortness of breath; however, the severity of symptoms increases with presence of co-morbidities and pre-existing diseases, such as the presence of chronic liver disease [2]. The data on immunosuppression therapy, post-transplant status and impact of SARS-CoV-2 infection on a liver graft as well as the overall survival in liver graft recipients is largely inadequate. A similar lack of information is present regarding the treatment, drug interaction and overall outcome with solid organ transplant and corona virus disease 2019 (COVID-19). So, here we present a case report of COVID-19 infection in post liver transplant (LT) recipient. Written informed consent was obtained from the patient.

Case Report

A 63 year-old-male patient, 7 years post liver transplant for decompensated ethanol-related cirrhosis with diabetes and hypertension presented with 5 days history of fever and difficulty in breathing. At presentation, he was febrile with a temperature of 101^{0}F, Oxygen saturation of 88% on 10 Lts of oxygen on face mask, respiratory rate of 32 breaths/min, blood pressure of 140/90 mmhg, pulse rate of 94/min. Chest X-ray showed bilateral middle and lower lobe infiltrates . Chest computed tomography (CT) revealed Patchy ground glass opacities and consolidation in bilateral lung fields with lower lobe and subpleural predominance with a CT severity score of 15/25. The initial labs showed an increase in neutrophil count with increased inflammatory markers. The patient was admitted to the Intensive care unit (ICU) and was started on Non-invasive mechanical ventilation with pressure support of 12 and PEEP of 8 with a fiO_2 of 80%, keeping in view his general condition and PaO_2 of 50 mmhg on 10 Lts of oxygen on face mask. He was started on loading dose of Remdesvir 200 mg on day of admission followed by 100mg for the next 4 days. Convalescent plasma was given on the day 2 of admission and second session was given on day 4 of admission. Antibiotic Meropenem and Tiecoplanin was started from the day of admission to counteract superadded bacterial infections that were tested blood culture positive for gram negative cocci. Paracetemol was given thrice daily as an anti-pyretic, Prophylactic Enoxaparin was given subcutaneously from day 1 till discharge, Nebulisation with Budesonide and Levosalbutamol was done every 8th hour. The previous immunosuppression regimen (i.e mycophenolate 500 mg) was stopped and the patient was maintained on Tablet methylprednisolone 16 mg twice daily. Chest & Limb physiotherapy with incentive spirometry were given from day of admission. Gradually FiO_2 requirement was reduced to 60% by day 3 with a PaO_2 of 92 mmhg, From day 4 onwards patient was afebrile and put on a face mask with flow of 6-8 liters/min . On day 8 of disease the X-ray had improved considerably and patient was shifted on room air and was maintaining adequate oxygen saturation. Repeat RT-PCR was done on day 9 which was Negative and the patient was subsequently discharged.

Discussion

The SARS-CoV-2 infection and outcome among solid organ transplant recipients is variable. Whether immunosuppression therapy is a risk is largely unknown, but the severity of disease and outcome has been generally poorer than observed in others. Similar to non-transplant COVID-19 patients, Becchetti et al., observed fever (79%), cough (55%) and gastrointestinal symptoms (33%) in the majority of LT recipients. ARDS developed in 19% with a case

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fatality rate of 17% Allograft function showed mildly elevated liver enzymes in 14.7% patients and severe graft dysfunction were observed in 2.7% patients [3]. Like all immunosuppressive regimens, corticosteroids may lead to a reactivation of previously acquired infections. Specific concerns have been raised regarding HBV reactivation in the context of COVID-19, and several lines of evidence suggest that occult HBV infection (defined as the presence of HBV DNA in serum or liver of HBsAg- negative patients) might be reactivated in patients undergoing corticosteroid therapy [4]. Therefore, attention must be paid to HBV reactivation following corticosteroid therapy, especially during the administration of high doses after considerable time and whenever other immunosuppressants are co-administrated. In our case HBV infection or reactivation was ruled out by testing HBsAg negative.

Although immunosuppression in Liver transplant may attenuate the initial inflammatory response, it may increase virologic injury, resulting in higher rates of severe COVID-19 morbidity and mortality. Solid organ transplant (SOT) recipients are generally at increased risk of viral, bacterial, and fungal infections, and infection remains an important cause of post-SOT morbidity and mortality [4]. Management of immunosuppression in SOT patients with COVID-19 remains uncertain. Most of the recommendations have been for minimization or temporary withdrawal and balance of risk for rejection. However, this modification is individualized but mostly agrees for stopping the antiproliferative drug, reducing or stopping calcineurin inhibitor nephrotoxicity drugs and maintaining on a low dose of steroid [6]. The same course was followed in this case and the patient was started back on his immunossupression regimen post discharge.

The recovery trial recommend the use of 6 mg dexamethasone in patients SARS-CoV-2 infection requiring oxygen support's [7]. In our case we have used methylprednisolone 16 mg twice daily which served dual role of immunosuppression and to aid recovery from COVID.

Remdesivir is a nucleotide analogue with demonstrated activity against SARS-CoV-2 in human cell lines.. No mortality benefit has been demonstrated, but remdesivir shortens duration of illness and hospitalization and appears to be most effective when given to patients on supplemental oxygen within 10 days of symptom onset.In a study by Grein et al on compassionate use of remdesivir in 61 covid-19 patients, of the four patients who discontinued remdesivir only two of them had transaminitis as the cause [8]. As COVID-19 illness also can cause liver injury, to distinguish the cause of transaminitis due to remdesivir or COVID-19 virus may become challenging at times. In our recipient bilirubin and aminotransferase levels during remdesivir administration did not show an increase. Remdesivir may be offered for a 5-day duration to hospitalized patients with liver disease or liver transplant recipients hospitalized with COVID-19 and requiring supplemental oxygen [9].

Convalescent plasma action occurs through binding of the transfused antibodies to the pathogen, resulting in cellular cytotoxicity, phagocytosis, or direct neutralization of the pathogen. One large study showed that early administration of antibodies led to an optimal clinical effect, as compared to later administration [10]. In this case Convalescent plasma was used early on presentation as the patient was not vaccinated and had no prior history of SARS-CoV-2 infection showed good results in or patient, However, the data on transplant recipients need to be studied in larger cohorts to determine a routine recommendation.

COVID-19 disease in LT recipients can range from mild to severe disease but generally a majority of the patients require hospital admission, the mainstay of management of COVID in these subset patients include modification of the immunosupreesive Antivirals like Remidesvir may be used early in the disease in absence of liver dysfunction. Supportive care, prevention of infection and its treatment maintenance of acid-base balance, close monitoring in an ICU setup with adequate support for failing organs remains the mainstay of medical management of COVID-19 in Liver transplant recipients.

Glossary of Terms: COVID-19 = coronavirus disease 2019, SARS-CoV-2 virus = Severe acute respiratory syndrome coronavirus 2, LT = Liver transplant, Lts = Liters, Mmhg = milimeters of mercury, PaO_2 = partial pressure of oxygen, FiO_2 = fraction of inspired oxygen, LDH = lactate dehydrogenase.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the Journal. The patient understands that his name and initials will not be published, and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

Conflict of interest: Nil; **Source of support:** None

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