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Case Report

SARS-CoV-2 infection in a pediatric acute leukemia patient on chemotherapy and concurrent sofosbuvir/velpatasvir for HCV

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Abstract: There are new targets identified by experimental and animal research for treatment of SARS-COV-2 (Severe acute respiratory syndrome-Corona Virus-2) infection. Out of many clinical trials registered, there are ongoing human studies highlighting Sofosbuvir's possible role in the treatment of Covid-19 (Coronavirus Disease 2019). Here we present a case of acute leukemia on directly acting antiviral therapy (DAAs) for HCV infection mitigating SARS-COV-2 infection in a patient undergoing chemotherapy. The child was undergoing chemotherapy, along with directly acting antiviral for acute hepatitis C infection. He initially had features of hypoxia and radiological evidence of covid-19. He had an uneventful course and tested negative ten days after onset of illness. With ongoing trials on Sofosbuvir in covid 19 treatment, our finding, albeit coincidental, points to the possible role even in immune-compromised children.

Keywords: Acute leukemia, HCV infection, COVID 19, SOF-VEL, antiviral

Introduction

Recent therapies for emerging pandemic of SARS-CoV-2 are on-going, with many clinical trials. However, role of anti-retroviral agents theoretically has proven efficacy in the CoV-2 infection. We report a case of a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with Acute Hepatitis C virus (HCV) infection in a child with cancer. The child was on directly acting antiviral therapy (DAAs) for HCV and induction chemotherapy for B cell Acute lymphoblastic Leukemia (ALL). He had an uneventful recovery from COVID-19 and completed his induction chemotherapy. Sofosbuvir and Velpatasvir (SOF-VEL) may have helped the child's recovery, which otherwise was severe for clinical parameters [1].

History

The child was evaluated at our center for progressive pallor, easy fatigability, and low-grade fever for three months. He had generalized petechiae for 15 days and haematuria with melena for the last four days. He had received multiple blood transfusions in the previous three months. On examination, the child had pallor, multiple petechiae over face and trunk, non-tender right anterior cervical, and bilateral inguinal lymphadenopathy with massive splenohepatomegaly (smooth, firm, non-tender, with lower edge palpable 9 cm and 7 cm below the costal margin, respectively). Immunophenotyping studies confirmed the diagnosis of B cell ALL with no high-risk cytogenetics or translocations. During the prechemotherapy screening, the child was detected to be HCV IgM positive (performed via chemiluminescent microparticle immunoassay, with a significant 10.11 S/CO units) ratio. Viral load with reverse transcriptase-polymerase chain reaction (RT-PCR) HCV RNA assay was 4,814,219 IU/ml, with log value 6.68 (detection limit 50 IU/ml 1.7 log). HCV genotyping showed it to be type 3.

We initiated treatment for the child with standard four-drug induction regime and oral direct-

acting antiviral (DAA) therapy, sofosbuvir, and velpatasvir. He continued to tolerate chemotherapy well with improvement in general condition.

During the fourth week of induction chemotherapy, the child developed fever, cough, and fast breathing. Respiratory examination revealed tachypnoea with bilateral crepitations. Chest radiography showed bilateral peripheral opacities, consistent with COVID-19. The child tested positive for SARS CoV-2 infection by RTPCR test on a nasopharyngeal and oropharyngeal swab. The child was maintaining saturation of 90-92% on room air and was transferred to COVID dedicated pediatric intensive care facility of our hospital. He was started on broad-spectrum antibiotics and supportive care (oxygen at 2 liters/min). Steroids and DAAs were continued, as per standard guidelines [2]. His white blood cell count (WBC), absolute neutrophil count (ANC), and platelet were 3020, 1330, and 108,000 per mm^3. Liver enzymes serum glutamic-oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT) were 112 and 160 IU/L, respectively, and serum bilirubin was 1.2 mg/dl. His inflammatory markers (C reactive protein (CRP)-6.2 mg/dl, serum ferritin 426 ng/ml, procalcitonin <0.5 ng/ml and IL 6 136 pg/ml) were raised. Coagulation profile and D dimer were within normal range. The child showed clinical improvement on day 5 with defervescence of fever and maintaining saturation on room air. He tested negative for COVID-19 on day 10 of admission to COVID-PICU and was shifted back to ward to complete induction chemotherapy. His inflammatory markers and liver enzymes showed an improving trend. He completed the induction therapy and was in morphological remission. Repeat HCV RNA was undetectable on testing after 4 weeks of DAA intake. He was planned for 12 weeks of antiviral along with chemotherapy.

Discussion

Younger age, underlying pulmonary pathology, and immunocompromising conditions have been associated with more severe COVID-19 infections in children [3]. A flash survey across 25 countries in April 2020 showed that COVID-19 is mild or asymptomatic in children on chemotherapy [4]. This was later, in May 2020, supported by the UK pediatric oncology coronavirus cancer monitoring project [5].

HCV and SARS-CoV-2 are positive-sense single-strand RNA viruses with similar replication mechanism requiring RNA-dependent RNA polymerase (RdRp), which in turn is inhibited by sofosbuvir. Potential inhibitors have been investigated to target various steps in the infectious cycle of coronavirus, including the viral replication machinery [6, 7]. During the initial phase of the COVID-19 pandemic, remdesivir, ribavarin and sofosbuvir were identified as potential drugs against SARS-CoV-2 [8]. Sofosbuvir inhibits SARS-CoV-2 replication in the pulmonary and neuronal cells. Theoretically, the use of sofosbuvir against COVID-19 has been justified [9-11]. It is being used in combination with other DAAs in randomized control trials in Iran, where preliminary outcomes are suggesting it to be beneficial [11, 12]. There are few reports on cell culture and experimental insilico, in-vivo models of sofosbuvir being superior to other HCV antivirals terminating SARS COV-2 infection [13].

The incidence of HCV infection in children is merely 0.4%, and that in children with leukaemia is not well reported [9]. SARS-CoV-2 can infect any system of the body. COVID-19-associated liver injury is defined as any liver damage occurring during disease progression and treatment, with or without pre-existing liver disease. Studies have shown that the outcome of patients with liver injury is satisfactory, alterations of liver enzymes are usually transient and severe liver injury is rare [14]. In March 2020, FDA approved pan-genotypic anti HCV regimen, sofosbuvir/velpatasvir (SOF/VEL), for children >6 years of age or >17 kg body weight [15].

Our patient was already on immunosuppressive therapy which may have aggravated viral replication in early phase of infection, while SOF/VEL may have helped in controlling the viral replication and also in reducing the period of viral shedding. There are conflicting views on whether or not immunocompromised patients have worse outcome with COVID 19 infection [15]. Our patient was on steroids, which is mainstay of most treatment protocols. This may have benefitted the child. The duration of viral shedding in symptomatic patients was reported to be 17 days, which was significantly

less in our patient, this could be attributed to the SOF/VEL anti HCV therapy [16].

Albeit coincidentally, this report highlights the possible utility of sofosbuvir and velpatasvir in COVID-19 patients. Clinical trials initiated in various countries could indicate the efficacy/superiority of the same. Given the safe clinical and pharmacological profile it may serve as an effective anti-SARS COV-2 drug than remdesvir. However, further studies are needed to ascertain the true potential of anti HCV drugs in them.

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Disclosure of conflict of interest

None.

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