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Case Report

Coronavirus Disease (COVID-19) in a Patient with Chronic HCV-Infection Receiving Direct-Acting Antiviral Agents

AA Yakovlev, SS Suleimanova*, DL Sulima, VN Koryagin, NM Kravchuk and VA Larionov

Department of Infectious Disease, the Pavlov First Saint Petersburg, State Medical University, Russian Federation

***Corresponding Author:** SS Suleimanova, Department of Infectious Disease, the Pavlov First Saint Petersburg, State Medical University, Russian Federation.

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Case report

A female patient Sh. aged 58, was observed in the EXCLUSIVE clinic with a diagnosis

Chronic HCV-infection 1b genotype

- **Replicative option**: Chronic HCV RNA viremia, low viral load 4.3×10^5 IU/ml.
- **Clinical form**: Combined HCV-syndrome:

HCV-associated chronic steatohepatitis (S2/0.50) with moderate necroinflammatory activity (A1/0.35) and minimal fibrosis (F1/0.33).

HCV-associated immunopathological syndrome

- Mixed cryoglobulinemia (cryocrit 3%, RF 30 IU/ml), Meltzer's partial triad.
- Autoimmune thyroiditis, nodal form, euthyroidism;

HCV-associated system low grade inflammation syndrome

- Insulin resistance with hyperinsulinemia and obesity class I (BMI 36.1 kg/m^2).
- Generalized atherosclerosis.
- Chronic periodontitis, sublingual sialoadenitis, xerostomia.

Anti-HCV was first detected in 2001. No antiviral treatment of chronic hepatitis C was received. She has not been infected with the novel coronavirus infection COVID-19, nor has she been vaccinated.

After receiving the survey results before starting the DAAT/1 (direct-acting antiviral therapy first line), a 12-week pangenotypic 2D-regimens VEL/SOF (Velpatasvir/Sofosbuvir) was selected as an optimal treatment option. DAAT/1-therapy started at 23/04/2021. At the beginning of the interferon-free therapy first line, the patient took Metformin (2000 mg/24h) and Diosmin (1000 mg/24h).

After the first week of therapy with VEL/SOF a quick virological response (HCV RNA aviremia) and a quick biochemical response (normalization of ALT, AST and γ-GT activity levels) have been reached. After eight-week treatment, HOMA-IR (insulin resistance index) was optimized, insulin level and laboratory markers of system low grade inflammation syndrome were normalized, including TNF (tumor necrosis factor), IL-6 (interleukin-6), NLR (neutrophil-lymphocyte ratio), PLR (platelet-lymphocyte ratio), MLR (monocyte-lymphocye ratio) and SII (systemic immune-inflamation index).

At the 11th week of DAAT/1-therapy (on 01/07/21), amid complete well-being, a subfebrile fever and weakness appeared. On 02/07/21 a positive SARS-CoV-2 RNA PCR test result was received. Next three days patient's well-being progressively worsened, a febrile fever was registered, a sense of not getting enough air appeared, a blood saturation by breathing with ambient air was at the level of 92%. On 05/07/2021 according to the MSCT results of thoracic organs, bilateral polysegmental pneumonia with the damage volume up to 40% was revealed. Due to the complicated course of COVID-19 and taking into account the presence of an unfavorable premorbid background (metabolic syndrome, dyslipidemia, obesity, generalized atherosclerosis), the patient was hospitalized.

With admission to hospital (05/07/2021), an increased level of acute-phase proteins was revealed: CRP 26.67 mg/l, LDH 267 U/L, fibrinogen 5.56 g/l. At the same time, the level of ferritin remained within the normal range, there was no lymphopenia (WBC 7.79×10^9/l), there was no hypercoagulation (D-dimer 249 ng/ml), levels of activity of hepatic enzymes ALT/AST/γ-GT within the normal range. The patient was assigned to low-flow O_2-therapy, infusion therapy, Dexamethasone, Enoxaparin sodium, Ambroxol. Assigning to the Omeprazole and Esomeprazole was declined due to the potential risk of developing adverse drug interactions between proton pump inhibitors and enzymes inhibitors NS5A (Velpatasvir) and NS5B (Sofosbuvir).

During the entire period of hospital treatment of COVID-19 (from 05/07/2021 to 14/07/2021, a total of 10 days), patient received VEL/SOF inhibitors in a fixed daily dose 90mg/400mg. A publicly available resource https://www.hep-druginteractions.org was used to control drug-drug interactions.

After discharging from the hospital, the patient continued to take Methylprednisolone for 10 days. At the same time, preventive anticoagulant therapy in the postcovid period was not conducted, because of the high risk of developing adverse interactions between inhibitors NS5A (Velpatasvir) and NS5B (Sofosbuvir) and a direct oral inhibitor of the Xa factor (Rivaroxaban).

The SVR (sustained viral response) was evaluated 12 weeks after the end of the 12-week DAAT/1 course. According to results of the checkup, the plasma SVR12 (HCV RNA aviremia), the full biochemical response, the normalization of the values of surrogate markers of subclinical systemic inflammation (NLR, MLR, PLR, SII) and, unfortunately, only a partial immunological response (mixed cryoglobulinemia/polyclonal immunoglobulins with RF activity, cryocrit 2%) were established. Laboratory signs of HCV-induced immuno-mediated pathological reactions in the form of mixed crioglobulinemia reached against the background of the achieved state of SVR12, which required conducting PCR-test of peripheral blood immune cells PBMCs/WBCtf (Peripheral Blood Mononuclear Cells/White Blood Cells total fraction) to find HCV RNA in these cells, but this research was not made due to external factors.

The authors represent this clinical case in order to demonstrate the patient, who started taking the primary non-interferon therapy and got sick with COVID-19 during its conduction. Despite the intermediate severity of the novel coronavirus infection in combination with a burdened premorbid background, during the entire period of hospital treatment, the normal laboratory indicators of values of the hepatocyte membrane permeability (ALT/AST/γ-GT) and the detoxification function of the liver (total bilirubin) remained. It is worth noting that the drug-drug interactions between Dexamethasone and Enoxaparin sodium, which make the basis of pathogenetic therapy to patients with COVID-19, and Velpatasvir and Sofosbuvir inhibitors do not cause problems and their combination is possible.

According to temporary recommendations of the novel coronavirus infection COVID-19 treatment, our patient could be offered antiviral therapy with Favipiravir or Remdesivir, which are also pharmacokinetically compatible with Velpatasvir and Sofosbuvir inhibitors but can induce a direct hepatotoxic effect mixed type. In this regard, using of specific antiviral therapy COVID-19 *ex juvantibus* in such case should be carried out, taking into account the assessment of potential risk and benefits in each particular case.

As the result, the authors did not observe the unfavorable influence of the clinical course of the coronavirus infection COVID-19 on the effectiveness of the direct-acting antivirals Velpatasvir/Sofosbuvir in terms of achieving the target treatment result in the eradication of the HCV virus [1-6].

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