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Letter to the Editor

Intravenous Immunoglobulin and Favipiravir treatment for A Kidney Transplant Patient with Severe Covid-19 Pneumonia

To The Editor;

The kidney transplant patients are at serious risk in this outbreak due to their immunocompromised status. However, there is insufficient knowledge and experience in the management of COVID-19 in this patient group. Intravenous immunoglobulin (IVIg) is frequently used in kidney transplant practice both in the treatment of rejection and Polioma (BK) nephropathy. Considering its effectiveness particularly in Ebola virus disease patients with medium to high viremia, Favipiravir [1]; an RNA polymerase inhibitor against RNA viruses, received approval for clinical trials against COVID-19 [1,2]. Until today, there are no data in terms of the use and effectiveness of these two drugs in COVID-19 disease of kidney transplant patients.

Here, a 66-year-old female kidney transplant patient who presented with respiratory failure and treated with IVIg and Favipiravir after the diagnosis of severe COVID-19 pneumonia was presented.

The patient whose primary kidney disease was chronic glomerulonephritis, received a six antigen-matched kidney from a 50-year-old male cadaveric donor 7 years ago. She had negative panel reactive antibody tests before the operation and did not have any problems in the early and late post-transplant periods. Basal serum creatinine value was 1.0 mg / dL. As maintenance immunosuppressive therapy, She received prednisolone (5 mg / day), mycophenolate sodium (180 mg / bid) and tacrolimus (1.5 mg / day). The final tacrolimus blood level was as 4.3 ng / mL. At admission; his body temperature was 38.3 °C, partial oxygen pressure in arterial blood gas analysis was 55 mmHg and oxygen saturation was 88%. Chest tomography demonstrated bilateral widespread ground glass opacities accompanied by paving stone pattern, more prominent on the right. The inflammatory involvement rate in lung parenchyma was 25-50%. Chest tomography findings at admission and on days 5-10 and 14 are shown in Fig. 1. The patient's SARS-CoV-2 test was negative by nucleic acid-based polymerase chain reaction (PCR) in two throat swabs. However, both serological antibody detection by COVID-19 IgG/IgM Rapid Test was positive. She was evaluated as COVID-19 pneumonia.

Of the kidney function parameters, serum urea was 41 mg / dL, uric acid 7.2 mg / dL and creatinine 1.0 mg / dL. Inflammatory markers were as follows: CRP 121 mg / L, LDH 286 U/L, procalcitonin 0.14 ng / mL, leucocyte count 5800 / mm3, lymphocyte count 850 / mm3, hemoglobin 12.8 g / L and platelet 144.000 / mm3. PT, aPTT was normal but D-Dimer was 565 ng / mL. hs-Troponin and CK- MB were normal. NT-pro-BNP was 2970 ng / L (negative value < 125). Laboratory values during the follow-up period are given in Fig. 2.

The patient's maintenance immunosuppressive drugs were discontinued, except for methylprednisolone 20 mg / day IV. Initial treatment started with oseltamavir p.o 150 mg / day, a loading dose of hydroxychloroquine 800 mg / day followed by 400 mg / d maintenance dose, moxifloxacin p.o 400 mg / day and meropenem IV 2 grams / day. However, there was no response to treatment in the first three days. Upon the increase of respiratory failure and the development of lymphopenia on the hemogram, IVIg (400 mg/kg/ day) was added to the treatment for five days. During the five-day follow-up, the patient's clinical course was stable, SpO2 by pulse oximeter with (5 lt/min via t-piece) and without oxygen was 80-85% and 95%, respectively, and CRP levels were between 80-120 mg/L. As the lung parenchymal involvement rate was progressed to 50-75% in control CT on the fifth day of treatment (Fig. 1); Favipiravir (a loading dose 2 x 1200 mg / d and maintenance dose 2 x 600 mg / d for four days) and subcutaneous enoxaparin 2 x 40 mg/d were added to the treatment. Side effects of drugs were not observed.

On the 9th day of hospitalization, the oxygen requirement of the patient and CRP values decreased and on the 11th day the oxygen treatment was stopped. On the 10th day, chest CT revealed significant regression in parenchymal inflammation of both lungs (< 25%) (Fig. 1). The patient's antibiotherapy was completed on the 14th day, the maintenance immunosuppressive drugs arranged as prednisolone 10 mg/d with tacrolimus 3 mg/d and was discharged with an outpatient appointment for two weeks later.

IVIG and Favipiravir therapy may be a treatment option in patients with kidney transplantation and severe COVID-19 pneumonia. In a recent study, post-mortem pathological examination of COVID-19 pneumonia was associated with pulmonary edema and hyaline membrane formation, suggestive of early-phase ARDS and interstitial inflammation dominated by T-lymphocytes [3]. Also, CD4 and CD8 + T-cell hyperactivation is evident in peripheral blood analysis [3]. All IVIg preparations contain variable amounts of CD4 and CD8 molecules which interfere with antigen recognition by the T cells [4] In addition to its anti-inflammatory effects, IVIg neutralizes T-cells and down-regulates T-cell mediated cytokine production. Because of these established features, IVIg has been applied to clinical practice for many years [5,6]. IVIg can also improve to secondary immune deficiency in transplant patients. Due to the above-mentioned features, IVIg administration may be useful in the treatment of these cases. Also, in a case series of three patients with COVID-19, the administration of high-dose IVIg (25gm/d, for five days) have successfully ameliorated the clinical course, laboratory indicators and chest CT-scan findings [7]. However, there is not enough data for kidney transplant patients. Besides, as stated in a study, we think that administration of reasonable dose corticosteroids in COVID-19 pneumonia will be beneficial in the process leading to ARDS. Favipiravir, a purine nucleic acid analog, is an antiviral drug developed against RNA viruses [1,2]. Favipiravir is also considered to be effective against COVID-19 in some clinical studies [2]. However, There is no study on this issue regarding kidney transplantion. We provided effective treatment with favipiravir in this patient and we did not see any side effects.

There is currently no proven drug against COVID-19. Therefore, the

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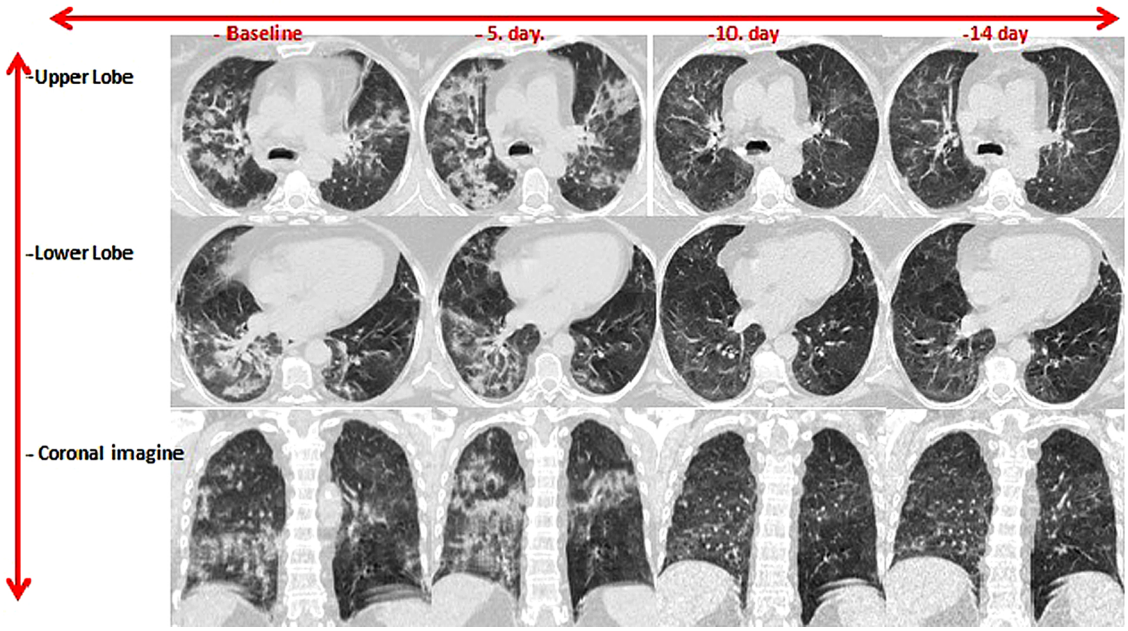

Fig. 1. Thorax CT During The Follow-up of The Case

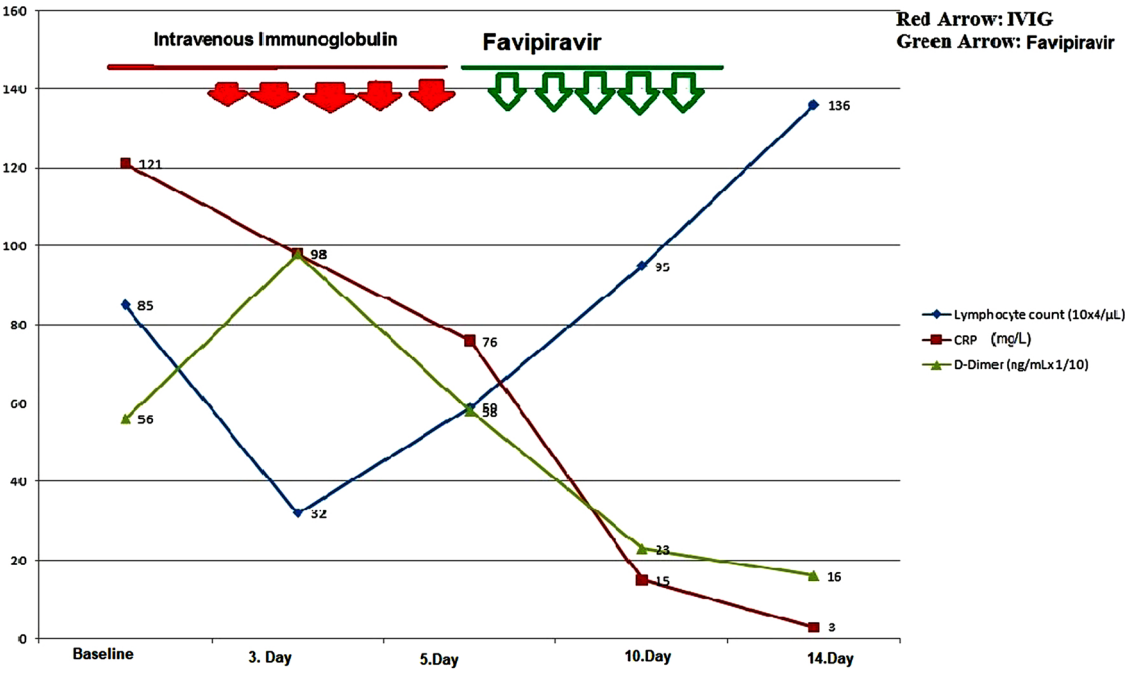

Fig. 2. Treatment Protocol and Laboratuvar Results During The Follow-up of The Case

majority of the treatment recommendations are speculative. While developing a treatment method, we should adhere to the pathophysiological mechanisms elucidated from autopsy studies in patients with COVID-19 pneumonia. Therefore IVIg can be an important treatment option especially in cases of kidney transplantation considering immune deficiency. Besides, we may use Favipiravir that has shown efficacy in previous corona virus epidemics. Large-scale studies are needed for this subject.

Declaration of Competing Interest

No conflict of interest was declared.

Author Contributions

Erhan Tatar: manuscript preparation, literature search and manuscript write and management of the patient, Murat Karatas: the patient's doctor, manuscript preparation and literature search. Ilter bozacı: Data collection and interpretation, Alpay Ari: management for antiviral treatment protocol of the patient, Turker Acar: Radiological evaluation, Cenk Simsek: management for treatment protocol of the patient, Ali Murat Yildirim: the patient's doctor and Data collection, Ozden Yildirim: Data collection and interpretation, Adam Uslu: manuscript preparation, literature search and manuscript write.

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Informed consent

The patient gave consent to the use of all data of her disease in order to be used for scientific purposes.

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