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OLGU SUNUMU

COVİD-19 hastasında tocilizumab ilişkili ventriküler taşikardi vakası

Tocilizumab-Associated ventricular tachycardia case in a COVID-19 patient

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ABSTRACT

To present the cardiac side effects of the drug called tocilizumab used during treatment in a patient diagnosed with COVID-19 and without a previous history of cardiovascular disease. Our article is an observational study and is a case report. A 68-year-old male patient with a history of hypertension was being followed in the COVID-19 intensive care unit due to severe pneumonia. The patient's pulse and electrocardiography were normal at admission. Due to the development of cytokine storm in the follow-up, tocilizumab treatment was given. After the infusion, a complication of ventricular tachycardia was observed in the patient. Especially, cytokine storm that develops due to hyperinflammation may be responsible for heart damage. Therefore, patients infected with COVID-19 should be evaluated for myocardial damage during their hospital stay, even if they do not have cardiovascular disease.

Keywords: COVID-19; Tocilizumab; Pneumonia.

ÖZ

COVID-19 tanısı alan, daha önce kardiyovasküler hastalık öyküsü olmayan bir hastada, tedavi esnasında kullanılan tocilizumab adlı ilacın kardiyak yan etkisini sunmaktır. Gereç ve Yöntemler: Makalemiz gözlemsel bir çalışma olup olgu sunumudur. Bulgular: 68 yaşında bilinen hipertansiyon öyküsü olan erkek hasta COVID-19 yoğun bakımda ağır pnomoni nedeniyle takip edilmekteydi. Hastanın yatışında nabzı ve elektrokardiyografisi normaldi. Takiplerinde sitokin fırtınası gelişmesi üzerine tocilizumab tedavisi verildi. İnfüzyon sonrası hastada ventriküler taşikardi komplikasyonu gözlendi. Sonuç: Özellikle hiperinflamasyona bağlı olarak gelişen sitokin fırtınası kalp hasarından sorumlu olabilir. Bu nedenle, COVID-19 ile enfekte olan hastalar, kardiyovasküler hastalığı olmasa bile hastanede kaldıkları süre boyunca, mutlaka miyokardiyal hasar açısından değerlendirilmelidir.

Anahtar Kelimeler: COVID-19; Tocilizumab; Pnomoni.

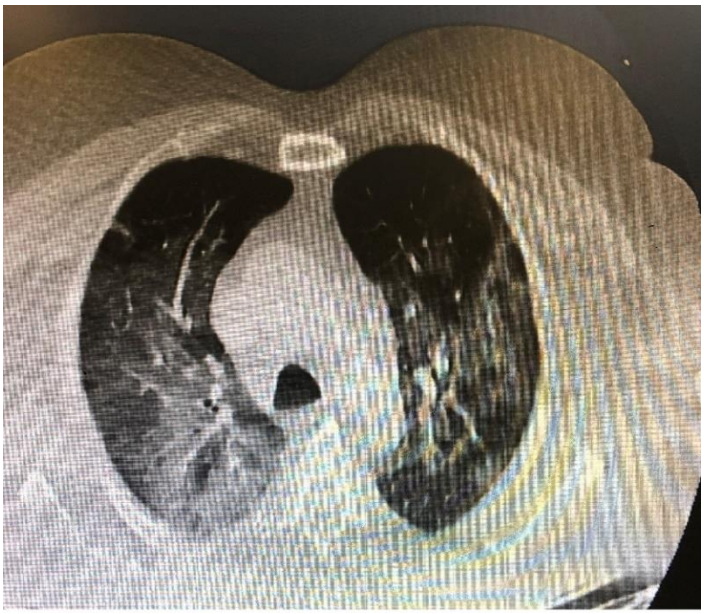
INTRODUCTION

The virus named Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) that causes COVID-19 disease (Coronavirus disease 2019) emerged in Wuhan, China in December 2019 and resulted in a pandemic after spreading all over the world, including our country (1). Cough, fever, fatigue, shortness of breath, muscle and joint pain, diarrhea and loss of taste and smell are among the symptoms of the disease (2). COVID-19 has significant impacts on digestive system, hematopoietic system and cardiovascular system as well as resulting in viral pneumonia (3). In light of the researches conducted from outbreak of the pandemic, it was found out that the group which is affected most by COVID-19 and has the highest mortality rate constitute the individuals with cardiovascular disease and old aged people (4). Stimulation of sympathetic system, cytokine storm, endothelial cell injury, direct infusion of myocardial cells, respiratory failure-associated hypoxia and side effects of the drugs used in COVID-19 treatment are listed as the causes of cardiac clinical pictures who had COVID-19. COVID-19 infects the host cells via angiotensin converting enzyme-2 (ACE-2) receptors. ACE-2 is found in epithelial cells, epithelial cells of smaller bowel, arterial and venous endothelial and smooth muscle cells. The cardiac complications frequently seen in COVID-19 are cardiac injury (high troponin I and creatine kinase), arrhythmias (atrial fibrillation, ventricular tachycardia and ventricular fibrillation), heart failure and acute myocardial infarction (1).

CASE REPORT

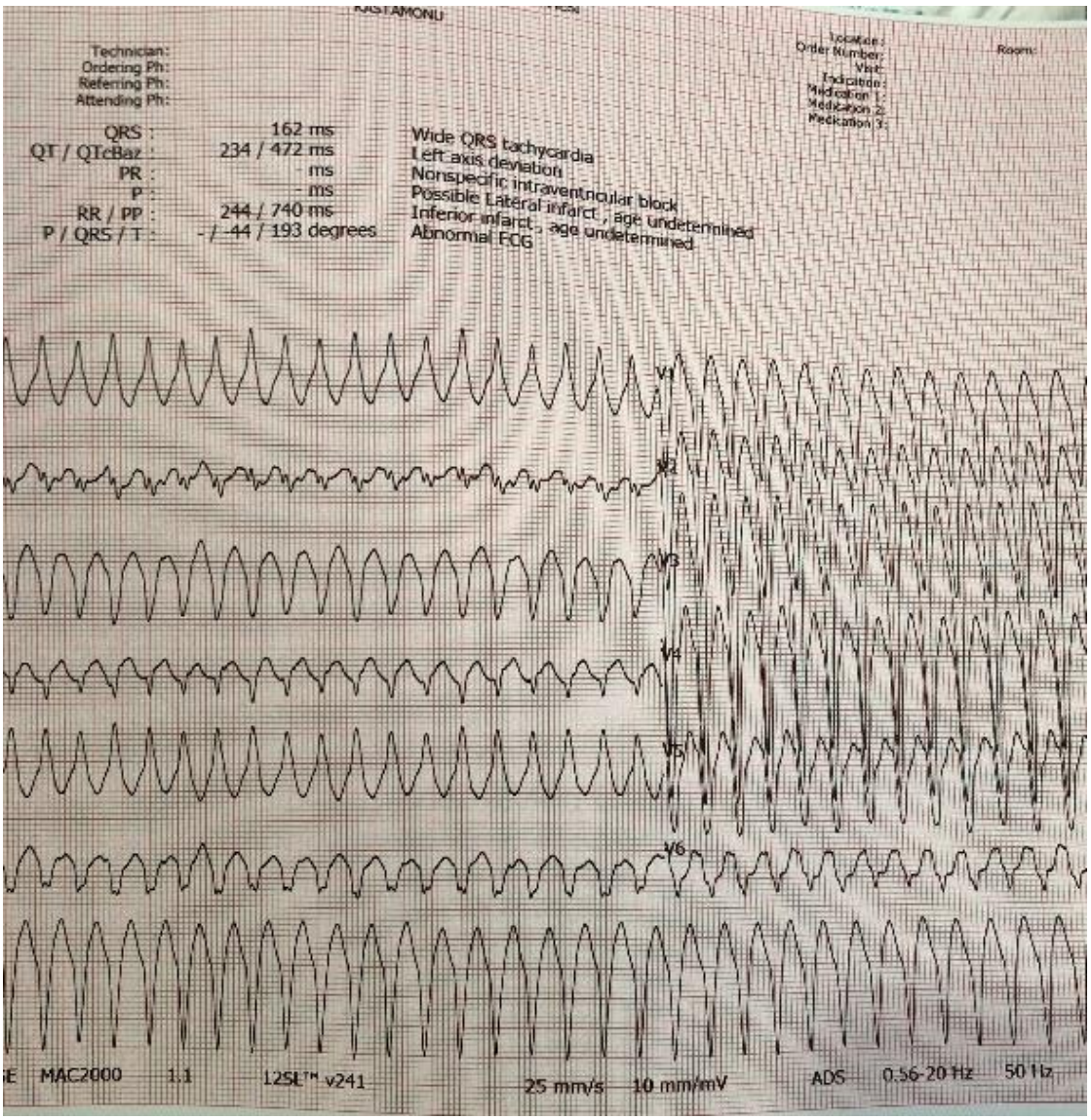
A 68-year-old male patient was diagnosed with COVID-19 related viral pneumonia. He was being followed up in COVID-19 intensive care unit under intubation due to his worsening general state. Besides, he was diagnosed with hypertension eight years ago. The patient was using candesartan+hydrochlorothiazide 1x1 tablet. He began to have dry cough, fatigue and joint pain five days before his application to hospital. The patient started to receive medication of faviprevir in tablet form after getting a positive result from COVID-19 PCR test. Chills, shivering and shortness of breathing were added to his complaints at the end of five days, so he applied to emergency department of our hospital. In his first physical examination, it was seen that the patient with obesity problem was conscious oriented-cooperative and dyspneic, he had fever (36.9°C), his respiratory rate 42/min, oxygen saturation 57 and blood pressure corresponded to and 145/90 mmhg, respectively and he had a pulse of 100/min measured with pulse oximetry. Decreased breathing sounds and bilateral

crepitant rale were heard. The patient had bilateral pulses. On the other hand, any additional sound and murmur were not detected. His abdominal examination was smooth. He was taken to COVID-19 intensive care unit as intubated. The below results were obtained according to the examination performed: WBC 8.580 $10e^3$/uL, lymphocyte 690 $10e^3$/uL, PLT 71 $10e^3$/uL, Hgb 16.2 g/dL, d-dimer 4.73 mg/L, urea 85 mg/dL, creatinine 0.94 mg/dL, AST 27 U/L, ALT 22 U/L, Glucose 112 mg/dL, CRP 84 mg/L, ferritin 70 ng/mL, LDH 388 U/L, PH 7.25, HCO3 24 mmhg and pCO2 72 mmhg. Based on the unenhanced ct scan of the chest, bilateral consolidation, glass appearance and CORADS-5 were reported. (Picture.1)



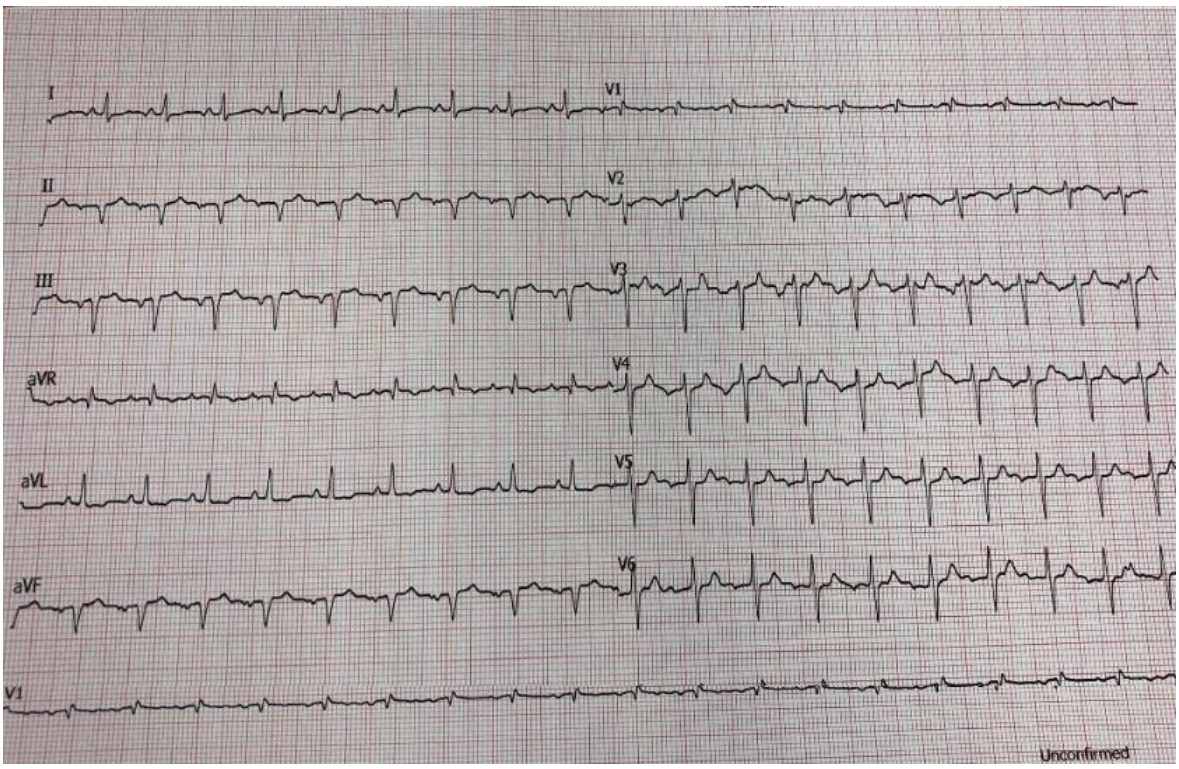
Picture.1. Image of unenhanced CT scan of the chest

The patient continued to receive faviprevir in tablet form. Moreover, treatment of Piperacillin-Tazobactam, N-acetylcysteine, low molecular weight heparin and high dose corticosteroids started. Between 48th and 72nd hours of the intensive care follow-ups, LDH, ferritin and CRP values of the patient increased and his temperature exceeded 39°C repetitively. For this reason, tocilizumab treatment was initiated, considering macrophage activation syndrome. Tocilizumab dose of 8 mg/kg would be given every 48 hours. Rhythm disorder was seen 10 min after the patient took the first tocilizumab dose in 60 min intravenously. (Picture.2)



Picture.2. Ventricular tachycardia, the first ECG (Electrocardiogram) of the patient after tocilizumab

Cardiopulmonary resuscitation was started, intravenous (IV) lidocaine was administered and electrical cardioversion was applied after no result was received in pulse and blood pressure measuring. IV amiodoron and noradrenaline infusion was started upon the detection of pulses. Cardiac rhythm improved after the intervention. Any elevation in the cardiac enzymes (CK-MB, Troponin I) administered was not seen. (Picture.3)



Picture.3. ECG after Treatment

Cardiology consultation was requested. Transthoracic echocardiography was performed. Wall motion disorder was not observed. Ejection fraction was reported as 60%. Sinus rhythm was detected in ECG which the patient had in the beginning of the hospitalization. According to chest x-ray applied to the patient in supine position, pathologic fracture, pleural fluid and pneumothorax were not observed. Instead, bilateral consolidation was seen. Different agents were included in his treatment. Any pathological state did not emerge during the follow-ups of cardiac enzymes and ECG.

DISCUSSION

Clinical characteristics of COVID-19, including 38% neutrophilia, 35% lymphopenia, 52% increased IL-6 levels and 84% high CRP were identified in the first study performed in China (5). Another study conducted for 85 dead patients involved 11.8% leucopenia, 77.6% lymphopenia, 41.2% thrombopenia, 48.2% anemia, 22.4% hypofibrinogenemia and 78.8% hypoalbuminemia (6). Increased chemokine rates and TNF-α were seen in several studies (7). The conclusion drawn from here presents a critical inflammation setting. One of the mechanisms which determine mortality and morbidity in COVID-19 cases is that increased

expression of type-1 IFN, IL-1β, IL-6 and TNF-α activate immune system of the patient (8). The first agent administered to such patients in treatment is corticosteroids. It was thought that targeted anticytokine treatments can be beneficial in cases of cytokine storm and macrophage activation syndrome (MAS) which does not react to corticosteroids. Tocilizumab came to the forefront among these treatments and was included in treatment guide of numerous countries. Tocilizumab is specific for tocilizumab IL-6 which is a recombinant human monoclonal antibody (9). Today, there is not any randomized controlled study about the activity and reliability of tocilizumab in COVID-19 patients. Arrhythmia risks rose because of the metabolic derangements seen in the progress of COVID-19. Our patient did not have rhythm disorder and electrolyte abnormality before the administration of tocilizumab. He was monitorized for follow-up and his vital findings were stable during the practice. Ventricular tachycardia developed at the end of 1-hour infusion of tocilizumab.

CONCLUSION

We evaluated in light of the literature that COVID-19 disease may affect the other systems as well respiratory system. Cytokine storm emerges in severe cases. To eliminate this setting, the options such as corticosteroids and interleukin-1-6 inhibitors are applied. Tocilizumab which is interleukin-6 inhibitor is one of the agents most frequently used in our country in case of cytokine storm caused by COVID-19. It is known that it leads to QT prolongation in ECG, so the said drug should be avoided for the patients with history of cardiac disease. In our case, tocilizumab treatment was considered appropriate for a patient who was in a cytokine storm setting resulted by COVID-19 disease even though he had no cardiac problem in his medical history. From our point of view, it should be considered that tocilizumab may cause ventricular arrhythmia among the patients without cardiac problem.

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Conflict of Interest: None

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