

Fluctuating Leukocyte Count and Use of G-CSF in a Kidney Transplant Patient with Diagnosis of COVID-19

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97

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Lymphocyte depletion is a common finding in COVID-19 patients; it is regarded as an unfavorable prognostic finding, although it can also be observed in mild cases. Some explanations for the pathogenesis of lymphopenia have been proposed; however, exact causes are unknown (1, 2).

There are limited data on the use of G-CSF in COVID-19 patients. It has been claimed that the use of G-CSF in COVID-19 cancer patients can have negative effects on the prognosis (3). To the best of our knowledge, there is no report on the use of G-CSF in kidney transplant patients diagnosed with COVID-19.

We would like to share our experience with a kidney transplant recipient diagnosed with COVID-19. For this patient, we used G-CSF for neutropenia, and her c-reactive protein (CRP) and white blood cell (WBC) count fluctuated over the follow up-period, irrelevant to her symptoms.

A 47-year-old female patient with functional renal allograft was admitted because of mild fever (at maximum 37.3°C), myalgia, and mild chronic non-productive cough. Dyspnea was absent and oxygen saturation by pulse oximetry was above 95% at all occasions. Her maximum body temperature was 37.5 during the entire follow-up. One of her family members was diagnosed with COVID-19, based on presence of compatible symptoms and polymerase chain reaction (PCR) detection of

viral nucleic acid in nasopharyngeal swab. Her diagnosis of COVID-19 was confirmed by compatible clinical findings, computerized tomography of the lung, and her close contact with a COVID-19 patient. Later, her COVID PCR test was reported to be positive. During the follow-up, she had diarrhea and intractable nausea lasting a few days.

She had undergone a kidney transplantation 11 years ago from a cadaveric donor. She had vesicoureteral reflux and frequent urinary tract infection. During her visit four months ago, her creatinine was 1.8 mg/dL, and she did not have urinary tract infection since the last visit. Her medications included tacrolimus 1.5 mg bid, mycophenolic acid 360 mg bid, prednisolone 2.5 mg per day, levothyroxine 100 mg, calcitriol 0.5 microgram, ramipril 5 mg, and allopurinol.

After admission to the ward, administration of mycophenolic acid and allopurinol were stopped immediately. A combination of hydroxychloroquine and favipiravir was given. Enoxaparin, moxifloxacin, meropenem, and metronidazole were used during the course of the disease for brief periods. For delayed resolution of leucopenia, myalgia, and nausea, methylprednisolone 32 mg/day was used for four days. Her symptoms completely resolved until the day 8, but the total WBC count, lymphocyte count, and CRP levels fluctuated over the course of the disease, regardless of the symptoms of the patient. On the 3rd day, a single dose of granulocyte



Table 1. Clinical and laboratory data of the patient+

	Day 1	Day 3	Day 4	Day 6	Day 8	Day 10	Day 14	Day 16
WBC ($\times 10^3/\text{mm}^3$)	3.86	1.43	10.4	3.73	4.09	3.37	6.17	2.87
Lymphocyte($\times 10^3/\text{mm}^3$)	0.38	0.51	0.73	0.52	0.39	0.27	1.33	0.71
PLT ($\times 10^3/\text{mm}^3$)	119	70.8	77.4	85.1	101	102	186	157
CRP (mg/L)	6.3		2.4		4.8	20	1.8	7.9
		↑ G-CSF 48 mU			↑ complete symptom resolution			
COVID-19 PCR	positive on three occasions until the day 19. The sample was negative on the day 22							
Tacrolimus	aimed to be kept around 6 ng/mL (mean 6.5, minimum 2.7, and maximum 12.8)							
Creatinine	fluctuated between 1.54 mg/dL and 2.72 mg/dL. Our impression was that creatinine fluctuation was not linked to COVID 19, rather it might be due to hypovolemia, angiotensinogen converting enzyme inhibitors, tacrolimus level, or urological problems							
QTc time	was between 416 and 449 msec, assessed several times by a cardiologist							

colony-stimulating factor (G-CSF) was used due to decreased WBC and the high perceived risk of additional infections, and a brisk response followed (Table 1). Her Ferritin level was over 2000 ng/mL (normal 13-135) and lactate dehydrogenase level was between 150 and 250 (normal 135-225 U/L) throughout the follow-up. She recovered completely; her COVID-19 PCR test became negative, and in the visit one month after the appearance of symptoms, her WBC, lymphocyte, platelet counts and CRP levels were $7830/\text{mm}^3$, $2800/\text{mm}^3$, $231000/\text{mm}^3$, and 2.3 mg/L, respectively. In contrast to the previous report, our patient did not experience any worsening in oxygenation and other vital signs, and the course was benign (3). We speculate that G-CSF could be used in COVID-19 patients with severe leukopenia, where perceived risk of infection is high; fluctuation of acute phase markers might be due to the fluctuating activity of the virus and the virus-triggered release of cytokines.

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