

Covid 19 Pandemic and PNH Patient Management

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Background:

Coronaviruses are enveloped positive-stranded RNA viruses. Since they carry rod-like projections on their surfaces, they are named as coronavirus derived from the word corona which means crown in English. They are important pathogens in animals and human.

In human, the spectrum of the disease caused by coronaviruses ranges from a simple common cold to acute respiratory failure syndrome. Additionally, coronaviruses may also cause enteric, hepatic, renal, and neurologic signs and symptoms.

The first cases caused by novel type corona virus infection were first reported in Wuhan, the capital of Hubei, China in December 2019 as pneumonia cases of unknown etiology. Afterwards, the causative agent was identified. It was a new coronavirus that was not previously detected in humans and it was named as SARS-CoV-2 because of its similarity to SARS CoV.

The name of the disease was reported as Covid -19. All over the world more than two million cases were documented in more than 100 countries. The first documented Covid 19 case in Turkey was reported in 11 March 2020.

The disease progression is more serious and mortality and morbidity rates are higher in patients with comorbidities such as diabetes, coronary artery disease, and hypertension. In the light of the data obtained from influenza outbreaks, immunosuppressive patients also constitute a potential risk group in Covid 19 pandemic. Similarly, PNH patients especially treated with eculizumab therapy are also accepted as immunosuppressive. Therefore, it is predicted that PNH patients constitute a risk group for severe Covid 19 infection and its complications. Since PNH disease is very rare, there is limited data in the literature regarding the follow-up, treatment and management of PNH patients in Covid 19 pandemics.

Under these circumstances, PNH patient management in the era of Covid 19 pandemic depends on expert opinion.

Precautions:

The isolation and social distance rules recommended by the Ministry of Health are also valid for PNH patients. It is recommended staying at home and self –isolation for PNH patients unless it not crucial to go out.

In the case of fever and respiratory symptoms, they should inform the hematology clinics where they are

followed up and come to the health institutions. The recommendations mentioned in the "Infectious Control Measures to Be Taken in Cancer Patient Diagnosis and Treatment Centers" published by the Ministry of Health should also be valid for PNH patients. In the accordance with these measures, when it is necessary, patients and their relatives should come to the health center by wearing a mask. All the patients and relatives should be questioned in terms of Covid 19 infection before entering outpatient chemotherapy units, and clinics. Health workers who are on duty in the follow-up and treatment of PNH patients should not be assigned to Covid services. Healthcare professionals should be questioned every day for COVID-19 symptoms and contact history. If the healthcare providers, who care for the immunosuppressive patients, have any sign or symptom of Covid 19 infection, all necessary precautions should be taken according to Guide of Ministry of Health. By this way, it is aimed to isolate PNH patients from Covid 19 infection as much as possible in health centers.

Treatment of PNH patients:

There are no definitive data or recommendations for unjustifiable preventive withdrawal of chemotherapy, immunotherapy, radiotherapy or immunosuppressive therapies in patients with malignancy and rheumatologic diseases. Although there is very limited data in the literature regarding the follow-up and treatment of PNH patients during Covid 19 pandemic, data obtained from patients with malignancy and rheumatologic diseases can be used for the recommendations in PNH patients. As in all hematological patients, all laboratory tests, number of hospital admissions and duration of hospital stay should also be reduced in PNH patients. All the precautions should be taken to minimize the mobilization of patients in the hospital and their communication with healthcare personnel.

Recommendations:

1. Eculizumab therapy:

a. Patients receiving Eculizumab:

- There is no data in the literature that Eculizumab therapy, which causes inhibition of the complement system, increases the risk of covid 19 infection and / or increases the risk of complications so far.
- Therefore, discontinuation of treatment is not recommended in patients receiving Eculizumab.
- Covid 19 infection may cause pharmacodynamic breakthrough hemolysis. Although the treatment of breakthrough hemolysis is not well documented, modifications such as increase in dose or decrease in the interval between the doses may be considered in case by case basis.

b. Patients not on Eculizumab therapy:

- In patients without indications for treatment, there are no additional recommendations other than protective measures.
- There is no data in the literature regarding the Eculizumab treatment in SARS-CoV-2 infected PNH patients who are not on Eculizumab therapy.
- On the other hand, it is well documented that complement system is activated in infections which may also be seen in Covid 19 infection. Therefore, PNH patients with Covid 19 should followed up closely for hemolysis and thrombosis. In patients with uncontrolled hemolysis and thrombosis, initiation of Eculizumab should be considered.

2. Supportive care:

a. To decrease the hospital admissions:

- Transfusion thresholds for blood and blood components:
 - Hemoglobin < 7 gr/dl
 - Platelet : < 10.000-20.000 / μ l
- G-CSF should be considered in patients with absolute neutropenia (neutrophil <500/ μ l)

b. SARS-CoV-2 infected PNH patients has a high risk of thrombosis due to both covid infection and PNH itself. These patients should be followed up closely for thrombosis. Low molecular weight heparin should be started in all patients unless there is no contraindications.

3. Allogeneic bone marrow transplantation:

In the era of eculizumab therapy, the role of allogeneic bone marrow transplantation is very limited.

During the Covid 19 pandemic, allogeneic bone marrow transplantation should be postponed in all PNH patients except PNH with severe aplastic anemia and patients who need an urgent transplantation. Before transplantation, the donor and the patient should be questioned for the signs and symptoms of Covid 19 infection and procedures for transplantation should be started after documentation of negative results for all required test of infection.

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