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A Case of Neutropenia Associated with COVID-19

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Abstract

SARS-CoV2 is a novel respiratory viral illness responsible for a global pandemic that started in the late 2019. Signs and symptoms being non-specific, clinicians relied on a constellation of abnormal results obtained from clinical investigations and imaging to diagnose the illness prior to the availability of widespread, timely testing. One proposed metric was the increased neutrophil to lymphocyte ratio (NLR) observed in patients suffering from COVID-19. Those with higher ratios were generally admitted to the Intensive Care Unit (ICU) with detrimental outcomes. Neutrophilia and lymphocytopenia were common occurrences in COVID-19 cases worldwide, even among those not severe enough to be in ICU. Here, we present a case of a 41-year-old SARS-CoV2 positive male who initially presented with fever, but then developed neutropenia. It is unknown whether his decreased neutrophil count was attributable current medications, an additional underlying infection, or whether it was due to the virus itself. Review of the literature did not yield any similar cases.

Keywords

SARS-CoV2, COVID-19, Neutropenia, Lymphocytopenia

Learning Points

Prior clinical cases have shown that COVID positive patients present with an increased neutrophil to lymphocyte ratio (NLR) where a higher NLR correlates to increased clinical severity; however, our case highlights a case of neutropenia in a covid-19 patient.

Introduction

SARS CoV-2 associated disease COVID-19 was first reported in Wuhan, China in 2019 [1]. Due to its recent discovery, not much is known about the virus. Patients present with non-specific symptoms of fever, cough, nasal congestion, and fatigue, and there are no definitive features that can truly distinguish COVID-19 from other respiratory illnesses [2]. When admitted to the hospital, clinicians typically check a patient's complete blood cell count (CBC) with differentials, complete metabolic panel (CMP), creatine kinase, C-reactive protein (CRP), and ferritin daily in addition to

obtaining a chest x-ray [3]. Recent literature suggests COVID patients show a normal or decreased number of white blood cells in early peripheral blood and a progressive decline in lymphocyte count, which can impact prognosis [4]. In most patients, CRP and serum sedimentation rates increases as well. Chest imaging in the early stages show multiple plaque shadows and interstitial changes, which can lead to the development of multiple ground glass shadows. In severe cases, lung consolidation can occur, presenting as "white lung", with rare pleural effusion and mediastinal lymph node enlargement [5]. Prior clinical cases have shown that COVID positive patients present with an increased neutrophil to lymphocyte ratio (NLR) where a higher NLR correlates to increased clinical severity, however our case provides evidence to suggest neutropenia as a possible complication [6].

Case Presentation

A 41-year-old male patient with past medical history of major depressive disorder, anxiety, schizoaffective disorder, intellectual disability disorder, asthma, and gastroesophageal reflux disease was brought to the emergency department (ED) from a psychiatry facility due to a 1-day history of fever of 102°F. The patient endorsed chills, body aches, dry cough, difficulty swallowing, sore throat, and abdominal pain. As per chart review, he was recently admitted to a psychiatry facility due to a suicide attempt and found to be allergic to Depakote and lithium. His medications included nystatin, fluticasone, pantoprazole, docusate, ferrous sulfate, mirtazapine, carbamazepine, prazosin, clonidine, aripiprazole, and albuterol. Patient endorsed medication compliance. He denied illicit drug, alcohol, or tobacco use. On admission to the ED, the patient was well nourished, comfortable, alert, and oriented. He had a temperature of 99.6°F, heart rate of 92 beats per minute (BPM), respiratory rate of 17/min, blood pressure of 102/74 mmHg, SpO_2 of 96% while breathing ambient air. Head to toe examination did not reveal any abnormal findings. Chest x-ray performed in the ED showed possible subtle infiltrate just above the medial right lung base, but low lung volumes limited assessment as seen in **Fig-1**.

Fig-1: CXR shows possible subtle infiltrate just above the medial right lung base but low lung volumes limited assessment

On laboratory tests, white blood cell (WBC) count was 11.4 (4.8-10.8K/UL), platelet count was 142K/µL (130-400 K/µL), and hemoglobin was within reference range. Absolute lymphocyte count (ALC) was 1200/µL (1.2-3.4 K/UL); INR was 1.1, PT 13.9, and aPTT 30.2 seconds. CMP was unremarkable. CRP 5.2 ng/dL (<1.0 ng/dL), CPK 29 U/L (38- 174 U/L), LDH 153 U/L (98-192 U/L). Symptomatic treatment was initiated while waiting for COVID PCR test results. On hospital days 1-3 the patient continued to be febrile with associated leukocytosis without lymphopenia. He tested positive for SARS- CoV2 and was placed on Hydroxychloroquine 400mg daily and Azithromycin 500mg daily. On hospital days 4-5, the patient developed leukopenia without lymphocytopenia. We also noticed a drop in platelets from 155 to 98 K/µL which we attributed to his psychiatric medications. Carbamazepine was suspended. Around hospital days 6 and 7, the patient developed mild neutropenia (ANC 800/mm^3). Hematology was consulted, and the patient was started on Filgastrim 180 micrograms daily. Within two days his neutrophil count responded. His neutrophil counts were monitored until discharge. The rest of his hospital course was uneventful, and the patient was discharged to a group home with no oxygen requirements.

Discussion

COVID-19 is a novel respiratory disease. Preliminary literature suggests an elevated NLR may be an indicator of clinical severity for COVID-19 patients [4,6,7]. According to Ciccullo *et. al,* when the number of neutrophils is greater than four times the number of lymphocytes, patients were more likely to be transferred to the ICU. Clinical improvement was

predicted by younger age and NLR below three. Lymphocytes are important immune mediators of infection. It is possible that the lymphocyte deficiency seen in COVID-19 is due to the ability of the virus to affect lymphocytes via ACE2 receptor expression or by direct toxicity to the cell [8-10]. Neutrophils, like lymphocytes, are vital cells in fighting off infections, but can be cytotoxic during more severe infections such as pneumonia and coronavirus [11-13]. One of the proposed cytotoxic mechanisms of COVID-19 mortality is the formation of neutrophil extracellular traps (NETs). NETs are web-like structures of DNA and proteins released from neutrophils that grab pathogens. NET formation can trigger inflammatory reactions that can result in severe damage to the heart, kidney, and lungs [10,14,15]. This patient, however, did not have any severe manifestations of SARS-Cov-2 infection. It is possible that the patient's neutropenia mitigated the common thrombotic complications associated with the virus. This patient was on several psychotropic medications that can lead to neutropenia. However, he had not developed this complication in the past despite compliance with a stable regimen for several months. It is therefore possible that neutropenia, in this case, was a sequalae of the viral infection itself.

Data regarding SARS-Cov-2 infection is evolving, however, current literature estimates a case fatality rate of 3.2% and the complications and sequelae from this infection can have long term, hitherto unknown, effects. While research has shown that a high NLR portends a poor prognosis, the prevalence and significance of neutropenia, as seen in this patient, has not been established and should be further researched [7,13].

Conclusions

COVID- 19 has inflicted remarkable damage to countries worldwide with societal and economic implications. Subtle hematologic manifestation may key healthcare providers to the severity of the disease. In other words, the hematologic abnormalities associated with COVID may play a key role in the adverse effects this novel virus has on the body. For example, neutropenia, as discussed in this report, in the setting of novel coronavirus infection could potentially lead to less complications. Understanding the different hematologic manifestations this virus can present with may assist us in formulating a more effective treatment plan.

Informed Consent

Signed consent for publication was obtained.

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None

Conflict of Interest

The authors have read and approved the final version of the manuscript. The authors have no conflicts of interest to declare.

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