Transient severe neutropenia in a pediatric patient associated with acute COVID-19 infection

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Abstract

Although severe acute respiratory syndrome coronavirus 2 is primarily known for its significant and potentially fatal pulmonary manifestations, case reports and literature review have linked the infection to multiple organ systems, including hematological manifestations. Scattered among these reports are cases of lymphopenia and neutropenia as well as evidence of children presenting in hypercoagulable states related to COVID-19. We present a case describing a pediatric patient who presented with leukopenia, thrombocytopenia, and severe neutropenia: a unique combination based on the current literature.

Introduction

Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been reported to cause a myriad of manifestations and complications in both children and adults. One of the less reported phenomena relates to its effect on the bone marrow. There are several documented cases of idiopathic thrombocytopenic purpura (ITP) as well as autoimmune hemolytic anemia (AIHA) secondary to SARS-CoV-2 infection. However, limited evidence exists for transient severe neutropenia in the setting of an acute diagnosis of COVID-19 infection in pediatric patients.[1,2] Xu et al[3] described the mechanism of thrombocytopenia related to COVID-19 as multifactorial including lung injury resulting in increased platelet consumption, direct infection of bone marrow stromal cells, and cytokine storm resulting in destruction of bone marrow progenitor cells. Likewise, there are documented cases of lymphopenia secondary to proposed lymphocyte apoptosis during inflammatory storms.[4]Additionally, two cases of severe neutropenia in neonates have been reported by Venturini et al[5] in association with mild COVID-19. We present a case of a 17-year-old female diagnosed with laboratory confirmed SARS-CoV-2 infection with leukopenia, thrombocytopenia, and severe neutropenia who was cared for at our academic community-based tertiary center.

Case Description

A 17-year-old female with a history of trisomy 21, aortic insufficiency, celiac disease, and obesity was admitted to our institution as a transfer from an outside emergency department with dehydration, fever, diarrhea, and a recent, known household member positive for SARS-CoV-2. Prior to admission, the patient experienced five days of fever, lethargy, mucopurulent nasal secretions, decreased oral intake, and decreased urine output. The patient's vital signs were normal at time of admission. Laboratory evaluation revealed leukopenia (900/uL), thrombocytopenia (98,000/uL), and severe neutropenia (0.351 X 10^9/L neutrophils). No morphological abnormalities were observed on the peripheral blood smear. Chest radiography revealed findings compatible with bilateral pneumonia visualized in the lower lung fields. The patient was placed on empiric antibiotics secondary to severe neutropenia.

Over the course of the next 24 hours, the patient's nasopharyngeal swab was reported positive for COVID-19. She developed hypoxemia requiring escalation of care to our pediatric intensive care unit and high flow oxygen therapy was initiated. The patient was treated with corticosteroids and an antiviral (remdesivir) given

worsening clinical status according to institutional guidelines and in consultation with pediatric infectious disease. The patient underwent further laboratory evaluation for multisystem inflammatory syndrome (MIS-C), with findings of mildly elevated D-Dimer level (0.87 mcg/mL) and hypoalbuminemia (2.7 mg/dL). Otherwise, no additional laboratory abnormalities were noted.

Throughout the course of her hospital stay, the patient's hematological manifestations improved with uptrend of her white blood count (1400/uL), platelet count (132,000/uL), and absolute neutrophil count (0.798 $X10^9$/L neutrophils) without clinical complications. The patient was transferred to the general pediatrics floor on day five of hospitalization, weaning off oxygen support. She was subsequently discharged on day six of hospitalization after tolerating room air without further hypoxemia. The patient followed up with her pediatrician one month later and repeat laboratory evaluation revealed normal white blood count, platelet count, and absolute neutrophil count.

Discussion

Previous cases of bone marrow suppression related to SARS-CoV-2 infection described in literature included a 33-year-old female patient who underwent extensive evaluation for myelodysplasias including bone marrow biopsy and ultimately received granulocyte colony-stimulating factor (G-CSF) for severe neutropenia 11 days following acute COVID-19 infection.[6] Additionally, a 5-month-old was noted to have severe neutropenia treated with G-CSF following recent SARS-CoV-2 infection. The child was diagnosed with MIS-C in the setting of 36-hour history of persistent fever, perineal cellulitis, and lip ulceration with a negative SARS-CoV-2 PCR but positive IgG and IgM antibodies. No previous clinical symptoms occurred for which an acute COVID-19 infection was suspected.[7] Lastly, a 23-day-old and a 39-day-old neonate with mild COVID-19 infection were noted to have severe neutropenia that resolved without intervention, thought to be related to postinfectious transient neutropenia associated with viral infections in infancy.[1] Of note, our patient did not undergo further evaluation with a bone marrow biopsy due to the rapid recovery of her cell lines. The true extent of viral induced bone marrow failure is not completely understood, especially as it relates to SARS-CoV-2. For example, the influenza virus and the hepatitis virus families are thought to induce thrombocytopenia by the uptake of platelets by viral particles facilitating hepatic clearance.[8, 9] Enterovirus infections have been described as profoundly altering the relative proportions of different cell populations in the bone marrow, depleting hematopoietic progenitor cells, and markedly reducing the restorative capacity of specific subsets of progenitor cells in the bone marrow.[10]Ebstein-Barr virus, cytomegalovirus, and human herpesvirus 6 can cause neutropenia through increased neutrophil adherence to the endothelium, enhanced neutrophil utilization, and anti-neutrophil antibody formation.[11] Overall, bone marrow suppression secondary to infections by well-known viruses could explain the hematological manifestations of SARS-CoV-2; however, the presence of leukopenia, thrombocytopenia, and severe neutropenia remain novel findings. Our patient's laboratory abnormalities in the setting of COVID-19 are noteworthy as rapid bone marrow response occurred without therapeutic intervention or clinical complications. Bone marrow biopsy may not be indicated in patients with COVID-19 infection and pancytopenia given the transient nature of hematological manifestations even in patients with trisomy 21.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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