COVID-19 in patients with acute leukemia: Two cases with different outcomes

1. Introduction

The novel severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) that causes coronavirus disease 2019 (COVID-19) leads to serious complications in individuals with certain comorbid conditions [1]. There have been only few cases reported specifically looking at the severity and outcomes of COVID-19 in patients with hematologic malignancies [2]. We are presenting 2 patients, one with acute lymphoblastic leukemia (ALL) and the other with acute myelogenous leukemia (AML) who were diagnosed with COVID-19. Both patients were pancytopenic from underlying leukemia and chemotherapy, had similar presentation and were admitted during the same period of time. They received a similar treatment but had different outcomes.

2. Patient 1

On April 8th 2020, a 60-year-old female presented to the emergency room (ER) with one week history of fever. She had a history of B-cell ALL diagnosed a year ago. She failed treatment after 5 cycles of hyper CVAD (3 of part A and 2 of part B), and now was on her 3rd cycle of salvage blinatumomab. Her globulins were in the range of 1.3–2.4 g/dL and her CD4/CD8 ratio was 0.4. She achieved remission as confirmed by recent bone marrow biopsies revealing hypocellular marrow with no evidence of leukemic cells. She did however develop leukopenia for which she received antimicrobial prophylaxis with valacyclovir, fluconazole and levofloxacin. Comorbidities included type II diabetes mellitus. Patient had a history of refractory AML (FLT3 TKD positive), which was diagnosed about 8 months ago. No other significant comorbidities were present. She failed to achieve complete remission with 7 + 3 regimen and was started on single agent gilteritinib for the past 4 months, although was not fully comfortable. She died on day 34 of her admission after she was compassionately extubated.

3. Patient 2

On April 16th 2020, a 63-year-old female presented to the ER with fever, fatigue, dysuria and syncopal episodes for 2 days. She had a history of refractory AML (FLT3 TKD positive), which was diagnosed about 8 months ago. No other significant comorbidities were present. She failed to achieve complete remission with 7 + 3 regimen and was started on single agent gilteritinib for the past 4 months, although was not fully compliant. She had chronic pancytopenia for which she was receiving antimicrobial prophylaxis with levofloxacin, flucloxacilone and acyclovir. She had similar febrile episode 10 days prior to this visit, and during that admission, she tested negative for SARS-CoV-2 virus and was treated for E. Coli urinary tract infection. Patient’s vital signs included temperature of 40 °C, BP of 110/60 mm Hg, heart rate of 114 bpm and SaO2 of 98% on room air. Laboratory data are mentioned in Table 1. Chest X-ray was normal. Blood cultures drawn 2 days prior to presentation grew Staphylococcus hominis in one set and Staphylococcus epidermidis in the other. Patient was started on meropenem and vancomycin. Blood cultures drawn in the ER were negative for bacterial growth but grew Candida parapsilosis from both her peripheral vein as well as central line. Anidulafungin was added and her central line removed. She continued to spike fever and on day 3 of hospital admission a CT scan of chest and abdomen was done and the only finding was scattered minimal ground glass opacities in both her lungs. Although patient denied any exposure history to COVID-19, based on the CT appearance, SARS-CoV-2 (Roche’s Cobas NAA test) nasopharyngeal swab was done which came back positive. She was then placed on airborne isolation precautions and was started on hydroxychloroquine and azithromycin. On day 8, she became hypoxic requiring high flow oxygen at 12 liters per minute (LPM) and was transferred to ICU. She was encouraged to self-prone to improve her oxygenation. Repeat chest CT scan showed diffuse bilateral ground glass opacities (Fig. 1). On day 11, she was intubated and placed on mechanical ventilation, started on norepinephrine for hypotension. She retested positive for COVID-19. She continued to have worsening hypoxemia, requiring 80% FiO2 with a PEEP of 10 cmH2O on the ventilator. Her inflammatory markers were elevated and she received 2 doses of intravenous tocilizumab 400 mg, intravenous solomedrol 80 mg every 6 h for 4 days, then 40 mg every 12 h for total of 12 days. On day 13 of her admission, she also received convalescent plasma. Since her immunoglobulins were low (Table 1), she received a dose of 30 gram of intravenous immunoglobulins. After receiving tocilizumab and steroids, patient remained afebrile until her death. She remained on ventilator for 18 days without improvement and her family decided to make her comfortable. She died on day 34 of her admission after she was compassionately extubated.
infection in the immunocompromised patients. In a cohort study of 128 SARS CoV-2 that came back positive, indicating a silent smoldering to perform CT scans in our patients. While the patients did not have any spectrum antimicrobial therapy. Persistent febrile episodes despite penia, severe lymphopenia, and severe hypogammaglobulinemia.

A New York hospitals system that treated 218 patients with cancer and malignancies is high. In the above cohort study, 8 patients (62%) died [2]. The case fatality of COVID-19 in patients with hematological malignancies [9] . We believe our patient had worse outcome due to persistent severe lymphopenia, low CD4/CD8 ratio and severe hypogammaglobulinemia, and possibly delay in delivering of the anti-inflammatory treatments. On the other hand, our second patient with persistent pancytopenia related to her underlying AML and no comorbidities made full recovery despite persistent leukemia and a lower neutrophil count than our first patient.

Our first patient with B-cell ALL responded well to the second line treatment with blinatumomab, CD19+ B cell ablative therapy, achieving complete remission with negative minimal residual disease. However, the B cell ablation from blinatumomab resulted in persistent pancytopenia, severe lymphopenia, and severe hypogammaglobulinemia. COVID-19 has been reported to be associated with cytokine release syndrome (CRS) and secondary hemophagocytic lymphohistiocytosis (sHLH) which is characterized by unremitting fever, pancytopenia, elevated ferritin and acute respiratory distress syndrome (ARDS) [8]. Interestingly, the filgrastim 300 mcg that was given for two days to treat the persistent fever and neutropenia resulted in worsening of her respiratory symptoms, possibly related to increase in neutrophil activity adding to the CRS seen in COVID-19 patients. The effect of the use of growth factors to alleviate neutropenia in cancer patients with COVID-19 is not known, however, a published case report in which a lung cancer patient was treated for 5 days with granulocyte colony stimulating factor (G-CSF), had full recovery with favorable outcome [9]. We believe our patient had worse outcome due to persistent severe lymphopenia, low CD4/CD8 ratio and severe hypogammaglobulinemia, and possibly delay in delivering of the anti-inflammatory treatments. On the other hand, our second patient with persistent pancytopenia related to her underlying AML and no comorbidities made full recovery despite persistent leukemia and a lower neutrophil count than our first patient. This patient, unlike the first case, had evidence for intact immune system including normal globulins and normal CD4/CD8 ratio. Another favorable difference is that this patient received dexamethasone to prevent differentiation syndrome once she restarted on gilteritinib, which may have suppressed the inflammatory response associated with COVID-19 infection. Although there are few published reports indicating patients with myeloid malignancies and COVID-19 have a higher mortality [10], our patient with active AML and pancytopenia made a full recovery highlighting the need for additional studies to further delineate risk factors contributing to mortality in this subgroup of patients.

According to the presentation of our two cases, it is important to note that the early signs of COVID-19 are usually not apparent on routine chest x-rays and CT imaging may be needed for early detection [11]. Our cases also illustrate the need for high index of suspicion for COVID-19 in actively treated leukemic patients and practice strategies to reduce the risk of infection and increase surveillance for early detection. Furthermore, factors such as lymphopenia, low CD4/CD8 ratio, hypogammaglobulinemia and comorbidities may contribute to worse outcomes of
Fig. 1. Imaging findings A- CT chest on day 3, showing patchy ground glass infiltrates in patient 1. B- On day 8, CT chest showing diffuse bilateral groundglass opacities in patient 1. C- CT chest done on day 2 showing bilateral scattered ground glass opacities in patient 2. D- Chest X-ray done on day 7 showing worsening bilateral airspace opacities in patient 2. E- Normal admission Chest X-ray in patient 1. F- Normal admission Chest X-ray in patient 2.
COVID-19 patients with acute leukemias.

Declaration of Competing Interest

The authors whose names are listed above certify that they have NO affiliations with or involvement in any organization or entity with any financial interest, or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript. The authors have no conflicts of interest to disclose.

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