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LETTER TO THE EDITOR

Comment on: Acute lymphoblastic leukemia onset in a 3-year-old child with COVID-19

To the Editor,

We read the letter entitled "Acute lymphoblastic leukemia onset in a 3-year-old child with COVID-19" by Marcia *et al*[1] with interest and we hereby suggest to start chemotherapy within the same timeline as for non-COVID-19 acute lymphoblastic leukemia (ALL) patients, following our experience managing a 3-year-old boy with concomitant diagnoses of precursor B-ALL and COVID-19. The patient was a previously healthy boy who presented to our hospital with a 2-month history of intermittent fevers, night sweats, fatigue, cervical lymphadenopathies, and worsening bone pain. His mother had been tested positive for COVID-19 3 months earlier. At presentation, he had no respiratory symptoms. Physical examination was remarkable for fever, tachycardia, and cervical lymphadenopathies. Blood work revealed pancytopenia and peripheral blasts. Inflammatory markers (ferritin, C-reactive protein, sedimentation rate, fibrinogen, D-dimers) were elevated. Capillary gas, renal function, hepatic function, coagulation studies, cardiac biomarkers, and chest X-ray were normal. COVID-19 testing by nasopharyngeal swab was positive. Bone marrow aspiration revealed 80% precursor B lymphoblasts of hyperdiploid subtype. Patient was admitted to a dedicated COVID-19 ward. Given the absence of SARS-CoV-2 infection's severity criteria, no COVID-19-specific treatment was initiated. Chemotherapy was started promptly, 6 days following the patient's confirmed COVID-19 diagnosis. The patient was treated with a three-drug chemotherapy induction consisting of methylprednisolone, vincristine, and asparaginase, along with routine supportive care measures. The patient's clinical course was favorable; fevers, bone pain, peripheral blasts, and inflammatory markers resolved quickly following the steroid prophase. The first negative COVID-19 test was obtained on day 4 of induction therapy but came back positive 48 h later. The patient was discharged on day 13 of induction therapy. Three consecutive nasopharyngeal swabs were negative on days 21, 23, and 38 following COVID-19 diagnosis (Figure 1).

This case demonstrates the feasibility of treating children with newly diagnosed ALL who tested positive for COVID-19, without chemotherapy delay, nor specific COVID-19 treatments, as done by Marcia et al. The province of Quebec constitutes the COVID-19 epicenter in Canada with half of all Canadian cases; the prevalence of COVID-19-positive cases was 3.3% among children under the age of 10, 5.3% between the age of 10-20 years, and 49.2% for people aged 50 years and above.[2] Importantly, no death has been reported among children in the province of Quebec, while 97.6% of COVID-related deaths were among individuals over the age of 60 years.[2]Children appear to be less affected from COVID-19 infection and exhibit a milder disease course compared to adults, although the impact of COVID-19 infection among pediatric oncology patients remains unknown.[3–5] Current published recommendations in the management of pediatric oncology patients during the COVID-19 pandemic emphasize on the importance of pursuing protocol-prescribed chemotherapy regimens based on the curable nature of most pediatric malignancies and the milder COVID-19 disease course observed in the pediatric population.[5] Management of concomitant COVID-19 infection and newly diagnosed ALL can be challenging. Our patient presented with a multisystem inflammatory syndrome, which made it difficult to discern whether he was symptomatic from the COVID-19 infection versus the leukemia itself. Furthermore, we questioned whether the positive COVID-19 test by PCR amplification in our patient truly reflects active infection since there was a 2-month period between the onset of patient's symptoms and when he was first tested positive. The positive PCR test could result from prolonged viral shedding in an immunocompromised patient affected by his leukemia onset. Alternatively, a positive test does not necessarily indicate the presence of viable virus as Wolfel and colleagues demonstrated that virus could not be grown from samples obtained from hospitalized patients beyond the eighth day of illness.[6] Therefore, the general approach to await a negative result prior to begin chemotherapy might cause significant therapy delay and adversely impact outcomes in newly diagnosed ALL patients during the COVID-19 pandemic. Furthermore, the use of COVID-19-specific antiviral treatment in noncritically ill children is controversial given the lack of efficacy in this population.[7] Nevertheless, the benefit of dexamethasone in COVID-19-positive patients requiring respiratory support in reducing early mortality[8] and the exquisite sensitivity of lymphoblasts to corticosteroids could be an effective early strategy to safely initiate therapy in newly diagnosed ALL patients affected with COVID-19, particularly for those presenting with oncologic emergencies such as hyperleukocytosis or mediastinal mass. As we learn more about the impact of SARS-CoV-2 infection in newly diagnosed cancer patients, an individualized assessment of risks and benefits to initiate or delay cancer therapy will need to be carefully balanced based on patient's clinical symptoms, type of malignancy, and available treatment options for now.

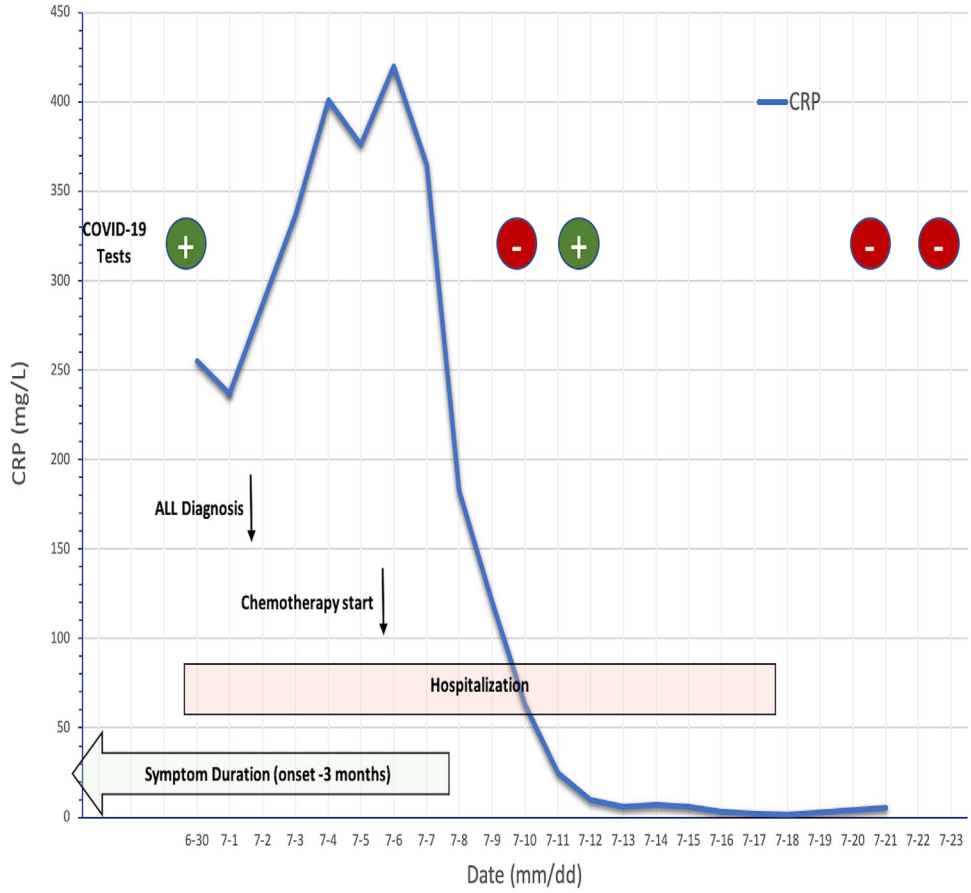

FIGURE 1 Variation of C-reactive protein (CRP) throughout the hospitalization course (blue line). COVID-19 test results are identified in green when positive and red when negative. The day of ALL diagnosis, the day of chemotherapy start (black arrows), the duration of hospitalization (red box), and the duration of symptoms (green box) are indicated. Induction chemotherapy includes methylprednisolone/prednisone (days 1-32), vincristine (days 4, 11, 18, and 25), PEG-asparaginase (day 7), and intrathecal cytarabine (days 1 and 18)

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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