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LETTER TO THE EDITOR

SARS-CoV-2 At diagnosis of acute lymphoblastic leukemia—Case series. To worry about COVID or leukemia? A developing country's perspective

To the Editor:

The current published recommendations for management of pediatric cancer patients during coronavirus infection disease (COVID) pandemic emphasize protocol-based cancer therapy regimens. Milder disease of COVID-19 observed in pediatric population in relation to other age groups and potential curable nature of most pediatric malignancies formed the basis for these recommendations.[1] However, during the initial phase of pandemic, when the impact of COVID-19 infection among pediatric oncology patients was unknown, the management of concomitant COVID-19 infection in newly diagnosed acute lymphoblastic leukemia (ALL) was challenging. We report the management of three cases of newly diagnosed B-cell ALL who were found to be COVID positive at the time of diagnosis.

Case 1:

A 6-year-old girl was admitted with fever for 20 days with generalized lymphadenopathy and hepato splenomegaly. Blood tests showed hemoglobin 4.6 g/dl, WBC 4.2×10^9/L, and platelets 0.46×10^9/L. Peripheral smear showed 69% lymphoblasts. Renal function tests, liver function tests, and tumor lysis workup was normal. Diagnosis was confirmed by peripheral blood flow cytometry, which showed blast cells, compatible with B-cell ALL. During routine screening at admission, nasopharyngeal swab was positive for SARS-CoV-2.

Case 2:

A 5-year-old female child was admitted with complaints of multiple joint pain and swelling with generalized lymphadenopathy. Blood tests showed hemoglobin of 7.5 g/dl, total leukocyte count 6.1×10^9/L, and platelets 0.35×10^9/L. Peripheral smear showed 4% atypical lymphocytes. Diagnosis of B-cell ALL was confirmed by bone marrow flow cytometry. Nasopharyngeal swab for routine screening of SARS-CoV-2 turned positive

Case 3:

A 4-year-old male child was hospitalized with complaints of pain in multiple joints for 6 months and difficulty in walking for 2 weeks. On examination, there was swelling of bilateral knee joints and small joints of hand with mild tenderness but no lymphadenopathy or organomegaly. Blood tests revealed hemoglobin of 8.4 g/dl, total leukocyte count of 5.1×10^9/L, and platelets 1.76×10^9/L. Peripheral smear showed 3% atypical lymphocytes. Bone marrow aspirate flow cytometry confirmed diagnosis of B-cell ALL. Nasopharyngeal swab for SARS-CoV-2 was positive on day 1 of admission.

All the three children were managed in isolation ward by pediatric and infectious disease team, with inputs from the primary pediatric oncology team. The patients were commenced on hyper-hydration and allopurinol, and serial tumor lysis workup was uneventful. They were asymptomatic in COVID infection point of view and inflammatory markers—ferritin, C reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, D-dimers, coagulation profile—were normal. CT chest showed no lung pathology. Steroids were started on day 2 of diagnosis. They had an uneventful steroid prophase, and repeat nasopharyngeal swabs for COVID-19 were negative on days 7 and 14. They also had good prednisolone response, and were commenced on induction phase with three-drug regimen on day 8 and MRD at the end of induction phase was <0.01%. None of them received COVID-directed therapy. The three children have completed intensive phase and are currently in maintenance phase without any significant events.

At the time of start of the SARS COV-2 pandemic, pediatric oncologists were facing hardships due to lack of standard guidelines to manage COVID-19 in newly diagnosed children with malignancies. With passage of time, we realized that children appeared to be less affected and children with malignancies were not at an increased risk as suspected initially.[2] But management of concomitant COVID positivity in a newly diagnosed acute leukemia was still challenging during the initial phase of the pandemic. The routinely practiced cautious approach of waiting to get a negative report before starting chemotherapy is not advisable in newly diagnosed acute leukemias, as delays in initiating induction phase could have an adverse effect on the outcome. Starting antiviral therapy in asymptomatic/noncritical cases is not recommended due to lack of proven efficacy and potential harmful effects in pediatric population on such therapy.[3]

There are very few reports of concomitant COVID positivity in newly diagnosed leukemias.

Colaiacovo et al. have recommended starting chemotherapy within the timeline as non-COVID ALL.[4] Marcia et al. reported a case of 3-year-old boy who had COVID positivity at the time

of diagnosis of B-cell ALL. The child received antiviral therapy and was started on steroids after his repeat COVID test became negative.[5]

The risk versus benefits of initiating or delaying chemotherapy in newly diagnosed cancer children should be based on the severity of clinical features and type of malignancy and should be individualized on case-to-case basis.

We recommend that induction therapy should be started without any delay and no COVID-19-directed specific therapy should be administered in children who are asymptomatic with normal inflammatory markers and CT chest.

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