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LETTER TO THE EDITOR

Successful ECMO therapy in a child with COVID-19-associated ARDS and acute lymphoblastic leukemia

To the Editor:

Since the first reports in January 2020, COVID-19 has evolved into a global pandemic and public health challenge. The vast majority of children and adolescents are found to exhibit mild symptoms or remain asymptomatic, even in the context of treatment for a malignant disease.[1]

Most reports of extracorporeal membrane oxygenation (ECMO) therapy for severe SARS-CoV-2-associated pediatric acute respiratory distress syndrome (ARDS) involve immunocompetent older children or adolescents.[2,3] Here, however, we report on successful ECMO therapy in a 2-year-old boy with acute lymphoblastic leukemia (ALL) and therapy-induced neutropenia.

After induction treatment according to the CoALL 08–09 trial,[4] the patient was stratified to the low-risk arm of the trial[4] and received a first consolidation block with intrathecal methotrexate and high-dose cytarabine followed by pegylated asparaginase. On consolidation day 4, the boy presented with fever and tachypnea, but without hypoxemia or signs of upper respiratory tract infection. With a C-reactive protein level of 44.2 mg/L (Figure S1) and impending cytopenia, anti-infectious treatment was initiated immediately. Testing by RT-PCR for SARS-CoV-2 RNA yielded a positive result, and the chest radiograph demonstrated mild infiltrates (Figure 1).

After 2 days of hydroxychloroquine treatment, remdesivir (2.5 mg/kg daily) was initiated as soon as it was available, following the latest available German consensus guidelines.[5] On the sixth day after detection of SARS-CoV-2-RNA (day of infection [DOI] 6), the patient, meanwhile in aplasia, exhibited increased respiratory rates and required oxygen support.

On DOI 9, respiratory symptoms and hypoxemia worsened rapidly, and after short tentative respiratory support via high flow nasal cannula, the patient had to be intubated for mechanical ventilation. Inhalative nitric oxide and inotropic and vasopressor support were initiated for pulmonary hypertension and impaired right ventricular function. After 1 week in aplasia, neutrophil counts rose again above 500/μl on DOI 12.

Required airway pressures continued to rise rapidly, so that the only remaining therapeutic option was veno-venous ECMO therapy on DOI 14 (see Table S1). Therapy with remdesivir was discontinued on DOI 16. Hydrocortisone was initiated the next day based on the latest available German consensus guidelines[5] and our own experience with pediatric ARDS. Today, however, considering meanwhile published evidence, we would choose dexamethasone for anti-inflammatory treatment.[6]

With improving gas exchange, we discontinued ECMO therapy on DOI 32. The patient was extubated on DOI 41, respiratory support via High-Flow nasal cannula was discontinued on DOI 50.

Despite a delay of chemotherapy of 6.5 weeks, neither cerebrospinal fluid nor bone marrow showed any signs of leukemia (minimal residual disease negative[7]). RT-PCR for SARS-CoV-2 was repeatedly negative from DOI 55 onwards. Blood cultures and tracheal samples remained negative by culture and PCR for bacterial agents throughout the entire therapy. However, concerned about possible recurrence of COVID-19, we first installed a 4-week interim phase with intermediate intensity comprising intravenous vincristine, asparaginase, oral 6-mercaptopurine, and intrathecal methotrexate. The patient was discharged from hospital on DOI 82.

On DOI 93, the next chemotherapy block according to protocol was administered at regular dose for consolidation. The patient currently is in first remission of his ALL under maintenance therapy on an outpatient basis, without signs of sequelae of COVID-19.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICS STATEMENT

Written informed consent from the parents has been obtained, specifically including the publication of radiographs.

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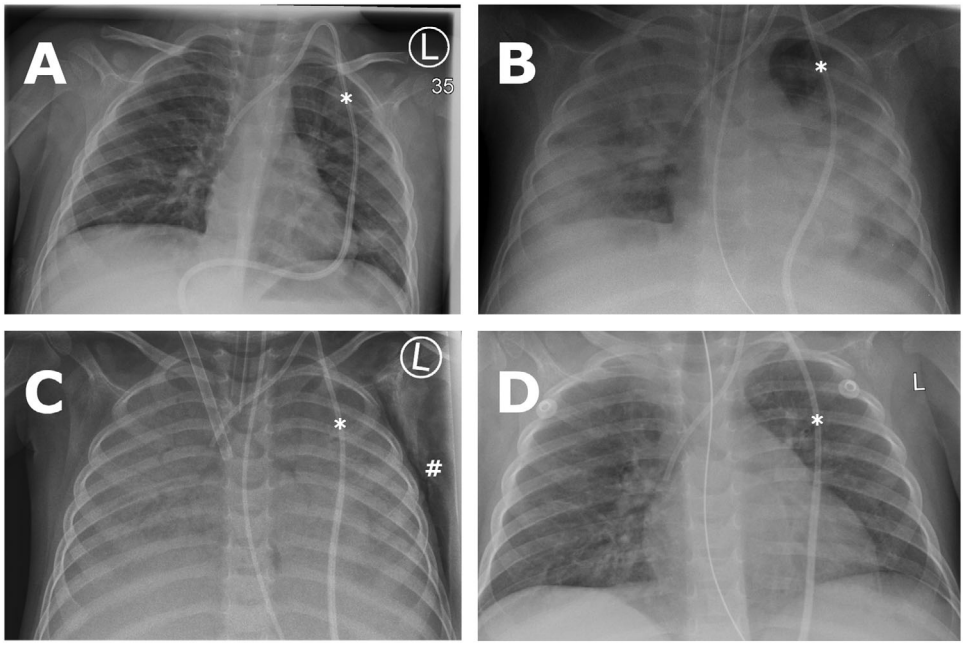

FIGURE 1 Radiographs: (A) at diagnosis of COVID-19 (day 1); (B) after intubation (day 9, endotracheal tube adjusted after radiograph); (C) during ECMO therapy (day 18, # thoracic emphysema); (D) after extubation (day 47), *Broviac catheter

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SUPPORTING INFORMATION

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