JCRMHS

Journal of Clinical Case Reports, Medical Images and Health Sciences

Volume 1 Issue 1, 2022

Article Information

Received date: 19/03/2022
Published date: 30/03/2022

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Keywords:
Acute leukemia, COVID19, Escherichia Hermannii, pulmonary embolism

Case Report

Coinfections and pulmonary embolism in a patient with onset of Leukemia concomitantly with COVID19- Case report

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Abstract

The pandemic of COVID19 is ongoing, with the treatment of neoplastic diseases to be challenging. Patients with acute leukemia are vulnerable to many pathogens due to impaired immunity coming from their disease and simultaneous chemotherapy. Although the COVID19 disease evolves milder in children, concomitant treatment for leukemia may be fatal. We present a girl with COVID19 and Escherichia Hermannii infection at diagnosis for Acute Lymphoblastic Leukemia (ALL). This child suffered bilateral pulmonary embolism after initiation of treatment. We discuss the therapeutic challenges about the initiation of chemotherapy in the context of coinfections as well as the role of COVID19 and other predisposing factors to pulmonary embolism. We found that the slight delay in the antineoplastic treatment contributed to the remission of the acute infection and did not negatively impact the initial response to the leukemia treatment. Nevertheless, the resumption of the oncological treatment should remain among our priorities.

Introduction

Given the immunodeficiency due to their disease and chemotherapy, patients with cancer are vulnerable to infections and COVID19 infection is really threatening. We describe a successful management of a girl diagnosed with acute lymphoblastic leukemia (ALL) and COVID19 infection concomitantly with Escherichia Hermannii sepsis. The initiation of chemotherapy was slightly postponed, due to the danger of these severe infections until blood cultures were negative for E. Hermanii. Pulmonary thrombosis was added, as COVID-19 infection predisposes for developing cardiovascular complications, while our patient was under existing predisposing factors for thrombophilia, but with appropriate management had successful outcome.

Case History

A three-year-old girl who presented with a four-day fever, rhinitis, and cough, found positive for COVID19 infection without mutation, as all her family members. She had anemia (Hb: 2.9 g/dL), neutropenia (N: 371/μL), thrombopenia (PLT: 24 K/μL) while tachypnea (RR=31/min), tachycardia (HR=146/min), fever 38.6°C, air oxygen saturation 97%, were found on examination. Empirical antimicrobial treatment with Tazobactam-Piperacillin, Amikacin, Teicoplanin, and Micafungin were given for febrile neutropenia, transfusions (blood, platelets) for myelosuppression, Remdesivir (5 mg/kg) for COVID19. Blood culture yielded Escherichia Hermannii sensitive to receiving antibiotics, but therapy was upscaled to Meropenem due to elevated CRP (109mg/l) and

persistent fever 40.6°C. The antibiotic treatment lasting 14-days ceased after two negative cultures. Baseline chest computed tomography (CT) scan showed small cloudy glass spots, areas of pulmonary thickening, atelectasis. Bone marrow aspiration, with 61% blasts, set the diagnosis of pre-B acute lymphoblastic leukemia (ALL) hyperdiploid, Central Nervous System (CNS) negative. Abdominal ultrasound showed hepatomegaly and splenomegaly. Examinations for thrombophilia revealed heterozygosity for factor V Leiden. Chemotherapy started while positive for COVID according to ALLIC 2009 protocol, standard risk arm, 15 days post diagnosis. Remained in COVID clinic until two negative PCR tests. The ALL re-examination showed good prednisolone response on Day 8, complete remission on Days 15, 33. On Day 40 from the initiation of chemotherapy, she had tachypnea with a value of D-dimer elevated at 2.145 ng/mL. Chest CT revealed subsegmental pulmonary embolism on both lower lobes of the lungs. She had not high oxygen requirements, hemodynamic instability requiring intubation, and was treated with low molecular weight heparin for 3 months. She continued chemotherapy without delays, with regular weekly tests for COVID19 and without reactivations, despite the use of corticosteroids and immunosuppressive therapy.

Discussion

The management of children with haematological malignancies and Sars-Cov 2 infection remains challenging since limited data about the impact of COVID 19 in these children are available. Main goal is to optimize the oncological treatment and avoid severe Sars-Cov2 infection due to immunosuppressive therapy. The Escherichia Hermanni bacteremia1 at diagnosis increased the risk of severe complications and led to slight delay of the chemotherapy initiation. The risk of virus transmission to the immunocompromised children in our department required a structured protocol regarding nursing care and isolation techniques. According to American Society of Hematology guidelines2, (January 2021), treatment for ALL patients is individualized, especially during the induction period. Reducing chemotherapy doses is not recommended since it may alter the expected therapeutic effect on ALL, while the severity of COVID19 does not seem to be affected. According to SFCE3 (French Society Committee for fight children and adolescents' Cancers), the main threat to children with ALL remains the ALL itself, even if life-threatening infections are emerging. We slightly delayed the chemotherapy initiation and prioritized treating the viral and bacterial infection since the type of leukemia of our patient was neither potentially life-threatening nor high risk (WBC<20.000, no HR cytogenetic findings, no CNS involvement). Our concern was that the co infections could be deteriorated if we had started induction chemotherapy and corticosteroids. The limited data available suggest a significant heterogeneity regarding the time till the first negative COVID19 PCR test in oncology patients (from four to 94 days). Bisogno et al. reported 19 patients with a mean time to negative PCR of 22 days and eight patients with 19 days4. Our patient demonstrated negative PCR testing for Sars-Cov2 on the 40th day of chemotherapy. As there is no standard therapy established for paediatric oncology patients with COVID19 yet, many centers follow the treatment strategy as in adults. Bisogno et al. treated nine out of 29 oncological patients suffering from COVID19 with Ritonavir, Hydroxychloroquine, and immune plasma. The Children's Hospital of Philadelphia (CHOP) reported their experience with the plasma administration to critically ill children5. Remdesivir is RNA polymerase inhibitor recommended in children with severe Sars-Cov2 infection and underlying medical conditions, especially in the early course of illness. According to a recent meta-analysis remdesivir has the most promising evidence that improves the time to recovery6. In our patient the seven-day lasting antiviral therapy was well tolerated, without any pathological findings. A challenging clinical problem of our patient was the pulmonary embolism. Sars-Cov2 infection activates platelets, the hyperactive platelets may activate thrombotic and inflammatory cascade in COVID19 positive patients with cancer7. The reported cases of venous thromboembolism may be related to the systemic inflammatory response or a state of hypercoagulability8. Our patient had multiple coexisting risk factors predisposing for thrombophilia, such as administration of Asparaginase, use of a central venous catheter (Hickman), and heterozygous status for the factor V Leiden. In patients with ALL and COVID19, prophylactic administration of anticoagulants may have an impact, but there are not yet standardize recommendations. We need to maintain a high index of suspicion for pulmonary embolism in patients with COVID19 and leukemia and to measure D-dimers regularly. There is need for guidelines for prophylaxis with low molecular weight heparin for pulmonary embolism in patients with COVID-19 and existing risk factors for thromboembolism. The patient was treated successfully with three- month administration of low molecular weight heparin. She continued chemotherapy without delays, with regular weekly tests for COVID19 as some authors have reported reactivations, without reactivations, despite the use of corticosteroids and immunosuppressive therapy.

Acknowledgements

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Citation: Maria Lambrou, Vasiliki Antari, Georgios Totikidis, Eleni Papadimitriou, Emmanuel Roilides, Evgenia Papakonstantinou . Coinfections and pulmonary embolism in a patient with onset of Leukemia concomitantly with COVID19- Case report. Jour of Clin Case rep, Med Imag and Hea Sci 1(1)-2022.