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

Maria Lambrou1, Vasiliki Antari1, Georgios Totikidis1, Eleni Papadimitriou2, Emmanuel Roilides3, Evgenia Papakonstantinou1

1Pediatric Oncology Department Ippokratio Hospital, Thessaloniki, Greece.
2Pediatric Infection Unit, Ippokratio Hospital, Thessaloniki, Greece.
3Pediatrics and Infectious Diseases Aristotle University Thessaloniki, Ippokratio Hospital, Thessaloniki, Greece.

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. Hermannii. 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
Hermann 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
coeexisting 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.

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Children’s Hospital Athens.
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