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A Severe Form of COVID-19 in an Infant with Underlining Undiagnosed Acute Myeloid Leukemia

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Abstract

The new global pandemic of coronavirus disease 2019 (COVID-19) is caused by the novel coronavirus designated as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was first identified in December 2019, in an outbreak of respiratory illness of unknown in China. The virus spread rapidly all over the world, and on March 11, 2020 the World Health Organization (WHO) declared COVID-19 a global pandemic. Although childhood COVID-19 cases appeared early in the outbreak, the disease burden in children is far less than in adults. The clinical presentation in adults ranges from mild illness to severe pneumonia, acute respiratory distress syndrome, acute cardiac failure, and thromboembolic complications. Children experience critical illness far less than adults with lesser degree of admission to the intensive care unit and mortality. Here is reported the case of an 8-month infant who was admitted for a severe form of COVID-19 and contemporaneously was discovered an underlining, unknown before, myelodysplastic disorder. Concerning a child with severe form of COVID-19, a high index of suspicion should be maintained towards underling diseases which compromise the immune system such as the case of acute myeloid leukemia.

Keywords

COVID-19, Children, Immunity, Severe, Acute Myeloid Leukemia

1. Introduction

Coronavirus disease 2019 (COVID-19), which inflicted the recent global pandemic, is an illness caused by the novel coronavirus designated as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Coronaviruses are a wide

family of viruses in nature, which typically infect animals, but a few of those cause diseases in humans. SARS-CoV-2 seems to be the most recent of them evolved to infect humans, and is supposed to have originated from an animal and seafood market. It was first identified in December 2019, in that time an outbreak of respiratory illness cases of unknown origin took place in Wuhan City in China. The virus spread rapidly all over the world, and on March 11, 2020 the World Health Organization (WHO) declared COVID-19 a global pandemic. By September 2022, over 607 million people were estimated to have been infected worldwide and have resulted in approximately 7 million deaths [1] [2]. Although childhood COVID-19 cases appeared early in the outbreak, the disease burden in children is far less than in adults. However, the exact number of children afflicted by the pandemic is difficult to determine as case definition for screening, testing and disease severity are not universal and a high percentage of them are asymptomatic. The virus is highly infectious and is transmitted through exposure to respiratory droplets or direct contact via hands. It enters the cell by binding to the angiotensin-converting enzyme 2, which is more found in lung cells, alveolar cells, cardiac myocytes, the vascular endothelium and a small subset of immune cells [3] [4]. The time of incubation ranges from 1 to 14 days and median time from exposure to symptoms development is 2 days to 2 weeks. The clinical presentation in adults ranges from mild illness to severe pneumonia, acute respiratory distress syndrome, acute cardiac failure, and thromboembolic complications. Patients with severe disease have evidence of hyper-immune response with persistent fever, elevated inflammatory markers and elevated pro-inflammatory cytokines [5] [6]. Respiratory symptoms as cough, rhinorrhea, nasal congestion, shortness of breath, sore throat, fever are the most common in children, followed by diarrhea, vomiting, abdominal pain, myalgia, fatigue [7] [8] [9]. Children experience critical illness far less than adults with lesser degree of admission to the intensive care unit and mortality.

2. Aim

This case report tends to highlight the underlining medical conditions, that predispose children to severe form of COVID-19, such as the case of acute myeloid leukemia.

3. Case Report

An 8-months old female presented at the University Hospital Center "Mother Teresa" of Tirana, Albania with a history of 5-days high fever, irritability and poor-feeding. On physical examination she appeared ill with high fever 40.5˚C, lethargic, refusing feeding. Respiratory system was in distress with dyspnea, tachypnea respiratory rate was 70 breaths/min, with low blood oxygen saturation 88% in room air, and fine rales on auscultation in both pulmonary fields. Tachycardia 170 beats/min, sinus heart rhythm, without murmurs and weak peripheral pulse were observed on examination. The skin was pale without patho-

logical elements. Abdomen was mildly distended, bowel sounds were present and there were not found increased liver and spleen.

The child had been previously healthy, exclusively breastfeeding, fully vaccinated according to the state calendar of vaccination. Growth parameters were within normal parameters, no signs of malnutrition were observed. She was the second child, given birth from a normal pregnancy and all the family members were healthy. No family contact with COVID-19 positive individuals was reported.

Laboratory investigations on admission revealed a blood cell count WBC 19,400 cells/mm^3 (44.4% neutrophils, 33.9% lymphocytes and monocyte 14.9%), RBC 4,180,000 cells/mm^3, Hemoglobin level 8.4 g/dL, Hematocrit value 28.4%, Platelet count 302,000 cells/mm^3, Erythrocyte sedimentation rate 28 mm/h (<15 mm/h), Aspartat aminotransferase 97 U/L (14 - 35 U/L), Alanin aminotransferase 83 U/L (9 - 24 U/L), Creatin kinase 55 U/L (30 - 200 U/L), Blood urea nitrogen 51.3 mg/dL (15 - 36 mg/dL), Creatinine 0.73 mg/dL (0.44 - 0.64 mg/dL), Serum total protein 5.9 g/dL (6 - 8 g/dL), Albumin 3.1 mg/dL (3.2 - 4.5 mg/dL), C reactive protein 11.95 mg/dL (<0.5 mg/dL), D-dimer 300 mg/dL (<198 mg/dL), Fibrinogen activity 347 mg/dL (160 - 390 mg/dL), Lactate dehydrogenase 280 U/L (120 - 320 U/L), PT quick time 106% (70% - 110%), Prothrombin time/international normalized ratio (INR) 0.96 (0.85 - 1.15), aPTT 28.7 sec (24 - 35 sec). Reverse transcriptase PCR for COVID-19 was negative, IgM and IgG antibodies for COVID-19 were both negative. Blood, urine and cerebrospinal fluid cultures resulted negative.

Abdominal ultrasonography revealed no enlarged liver or spleen or enlarged lymph nodes. Chest radiography revealed bilateral peribronchial thickening.

The diagnosis of sepsis was performed and medications constituted of intra venous broad spectrum antibiotic, penta-globin, perfusions and oxygen-therapy. Fever gradually subsided, abnormal vital parameters as breath rate, heart rate and blood oxygen saturation normalized, liver and renal function restored. The child was active, normally feeding and playful. Inflammatory parameters were lowered considerably except of the anemia which was profound. Then an unexpected deterioration occurred with high persistent fever, white blood cells were rapidly increased (34,900 cells/mm^3), red blood cells, hemoglobin and hematocrit level decreased (RBC 3,100,000 cells/mm^3, Hgb 6.8 g/dl, HCT 23.4%), Reticulocyte resulted 16.0‰ (<20‰), Platelet count decreased (110,000 cells/mm^3), C reactive protein increased (10.65 mg/dL), Lactate dehydrogenase enzyme increased (649 U/L). Serology for COVID-19 detected elevated IgG antibodies (Table 1).

At this point a microscopic examination of peripheral blood smear was performed and revealed abnormal immature, primitive granulocyte and monocyte precursors cells (15%), myelocyte (4%), metamyelocyte (10%), normoblast (100,000/mm^3). Immunophenotyping study revealed an abnormal cell population that comprised 22% of all cells probably myeloblastic. The myeloid markers of the monoclonal antibodies founded were: CD34 (99%), CD117 (99%), CD33 (95%),

Table 1. Clinical outcome of the patient.

Hospitalization time	Day 1	Day 7	Day 10
WBC	19,400 cells/mm^3	8200 cells/mm^3	34,900 cells/mm^3
RBC	4,180,000 cells/mm^3	3,900,000 cells/mm^3	3,100,000 cells/mm^3
Hemoglobin	8.4 g/dl	7.4 g/dl	6.8 g/dl
Hematocrit	28.4%	25.1%	23.4%
Platelet	302,000 cells/mm^3	260,000 cells/mm^3	110,000 cells/mm^3
C reactive protein	11.95 mg/dL	1.12 mg/dL	10.65 mg/dL
Lactate dehydrogenase	280 U/L		649 U/L
Alanin aminotransferase	83 U/L	32 U/L	30 U/L
Aspartat aminotransferase	97 U/L	25 U/L	22 U/L
Blood urea nitrogen	51.3 mg/dL	35 mg/dL	23 mg/dL
Creatinine	0.73 mg/dL	0.49 mg/dL	0.52 mg/dL
D-dimer	300 mg/dL	156 mg/dL	190 mg/dL
IgM SARS CoV-2	Negative		Negative
IgG SARS CoV-2	Negative		Positive

CD13 (80%), CD56 (70%). Ultimately, a bone marrow aspirate biopsy was performed and constituted the diagnosis of acute myeloid leukemia. The child was transferred to the pediatric oncologic hematologic yard, where was initiated appropriate chemotherapy.

4. Discussion

Since COVID-19 emerged in late 2019 and the world entered in a global pandemic, was soon evident that the incidence of pediatric COVID-19 was far lower than the adult one. However this trend changed with the evolving of the pandemic, in late 2021 and in 2022 the number of infected children increased rapidly. So by September 2022 the American Academy of Pediatrics (AAP) reported that the children presented 18.4% of all COVID-19 cases, considering that children are estimated to comprise 22% of the USA population [1]. The new reality was that children were infected with SARS CoV-2 similar to adults but children despite the rapidly increased number of infections still developed less severe disease and far less admissions and mortality to adults. Critical disease and mortality have been rare and occurred mainly in children with underlining medical conditions such as: congenital heart disease, respiratory tract anomaly, low hemoglobin level, severe malnutrition and those with immune deficiency or immunocompromised status [6].

Differences between adult and pediatric are likely the result of changes within

both immune system function and the angiotensin-converting enzyme (ACE)-2 receptor, used by the virus to enter human cells. Children develop a very effective protective mechanism to novel pathogens, due to high levels of innate IgM antibodies with broad reactivity. Mandatary vaccinations in infancy and frequent viral respiratory tract infections in early childhood might help to protect children against SARS CoV-2 [10] [11].

Albania too as other European countries experienced another surge of COVID-19 infections consequently the number of infected children reached the peak since the beginning of the outbreak. To pediatricians now it has become an axiom that in every child with newly onset of fever and/or respiratory tract symptoms, COVID-19 should be considered a possibility.

As the presenting child admitted, she was strongly suspected to have been infected with SARS CoV-2. The findings on physical examination pointed towards a severe form of the disease. Persistent high fever for 5 days, respiratory system suffering considerably with respiratory rate 70 breaths/min, grunting and low levels of blood oxygen 88% in room air, lethargy and poor feeding completed the clinic scenario of a critically ill child. Furthermore abnormalities found on laboratory values (elevated white blood cells, elevated C-reactive protein, low hemoglobin level, elevated liver enzymes, elevated blood urea nitrogen and creatinine) confirmed the severity of the illness. However the results of rhino-pharyngeal swab reverse transcription-polymerase chain reaction (RT-PCR) and serology results (IgM, IgG) for COVID-19 were negative so did not support our suspicions. At this point as the child was critically ill and most of the system and organs were involved, therapy for sepsis was initiated with broad spectrum antibiotics, nasal-oxygen and intravenous pentaglobin. In a few days, clinical conditions ameliorated significantly, inflammatory parameters decreased gradually, fever subsided in sub-febrile degrees and the child was appearing playful and feeding properly. Then when the disease seemed to have gone to an end, a sudden deterioration occurred with high fever, dyspnea and lethargy. Inflammatory parameters elevated rapidly and findings in blood count differentiated from the admission ones. White blood cells increased significantly with lymphocyte predominating the count, hemoglobin level decreased considerably and reticulocyte count did not match with profound anemia, platelet count was slightly decreased. Serology for COVID-19 was performed again and detected elevated levels of IgG antibodies, indicating recent SARS CoV-2 infection which was initially strongly suspected but not confirmed. Peripheral blood smear study detected abnormal cells and further work-up established the diagnosis of Acute Myeloid Leukemia. Ultimately, the path was cleared, the malignant condition pre-existed but not diagnosed till then, was the reason the child had suffered a severe form of COVID-19.

Acute myeloid leukemia (AML) consists in a heterogeneous group of malignant disorders characterized by the replacement of normal bone marrow with abnormal, primitive hematopoietic cells. Although it affects all age groups from

neonatal age to adults, AML has two peaks in occurrence, during early childhood and later in adults. Acute myeloid leukemia accounts for nearly 20% of newly diagnosed cases of leukemia in children each year [12]. It has been reported in children worldwide. Its presentation in children is insidious with fever being the most common symptom. Fever usually is caused by infections which find a suitable environment to grow in a scarcely functioning immune system. So infections of bacterial, fungal, viral origin are a major cause of morbidity and mortality in acute myeloid leukemia [13] [14]. AML as other childhood malignancies is listed in those medical conditions that have a significant association with risk of severe COVID-19 in children.

5. Conclusion

Children are infected with SARS CoV-2 similar to adults, but in contrast to them, children are far less at risk of developing severe disease. Critical disease and mortality have been reported in children too but are rare and occurred mainly in those with other medical conditions. Concerning a child with severe form of COVID-19, a high index of suspicion should be maintained towards underling diseases which compromise the immune system such as the case of acute myeloid leukemia.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper. The publication was performed on consent of the child's parent providing the anonymity.

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