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CASE REPORT

A CLINICAL CASE OF A 10-MONTH-OLD CHILD WITH SEVERE COVID-19 WITH MULTISYSTEM INFLAMMATORY SYNDROME ENDED FATALLY

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Abstract. *At the beginning of the COVID-19 pandemic, it was assumed that children were at low risk of infection and that their infection was milder than adults. With an increase in the number of pediatric cases of SARS-CoV-2 infection associated with manifestations of hyperinflammation, the condition of multisystem inflammatory syndrome in children (MIS-C) was defined. We present a clinical case of a 10-month-old male child hospitalized in the Clinic of Infectious Diseases at University Hospital in Stara Zagora, Bulgaria, with a COVID-19. The patient had a number of co-morbidities, including protein-calorie malnutrition, chronic respiratory failure and bronchopulmonary dysplasia. During the hospital stay, he had an active diarrhea syndrome, with evidence of pneumonia and respiratory failure. In the clinical course, a progressive worsening of the condition with signs of multiple organ failure, increase in inflammatory markers and deterioration of coagulation indicators were observed. Placement in the ICU and the inclusion of artificial pulmonary ventilation were required, but after an 18-day hospital stay, the patient died. In conclusion, this was an acute case of COVID-19 in an infant that started with respiratory and gastrointestinal manifestations that progressed to MIS-C with multiple organ failure leading to death. We believe that the reason for this is the compromised immune status in connection with the highly damaged premorbid terrain and young age.*

Key words: *COVID-19, infant, diarrhea syndrome, MIS-C*

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INTRODUCTION

Since emerging in 2019 in Wuhan, China, COVID-19 had become a pandemic process. Although, in the beginning, it was assumed that the main manifestations of the disease are from the respiratory system, after a deeper study and knowledge of this infection, it was already considered more like a multisystem process [1, 2]. Cases in which the gastrointestinal tract is affected are not rare. Nausea, vomiting, diarrhea, and abdominal pain might be the only symptoms in a patient with a positive result for COVID-19 [3, 4]. Patients under the age of 18 are

less likely to require hospitalization or have symptoms such as fever, cough or shortness of breath compared to adults. Childhood mortality linked to COVID-19 remains rare [5]. Subsequent reports from Europe and the US identified cases of children exhibiting a hyperinflammatory syndrome with multisystem involvement - multisystem inflammatory syndrome in children (MIS-C). Many patients had laboratory confirmation of current or previous SARS-CoV-2 infection by reverse transcriptase-polymerase chain reaction (RT-PCR) or serological tests. These new severe clinical manifestations continued to occur [6]. According to recent literature, MIS-C can occur at any time during COVID-19. Previous reports have commented that it usually occurs 2 to 6, on average, 4 weeks after the onset of illness [7]. Children with comorbidities had a higher risk of severe COVID-19 and associated mortality than children without underlying disease [8]. It is estimated that childhood COVID-19 presents with gastrointestinal symptoms in 40% of cases (range: 13.9-62%) [9, 10]. Diarrhea and abdominal pain can occur in both acute COVID-19 and MIS-C [11].

CLINICAL CASE

We present a case of a 10-month-old male child hospitalized in the Infectious Diseases Clinic of University General Hospital for Multiprofile Active Treatment, Stara Zagora, Bulgaria. The patient was born from the third twin pregnancy, delivered by Caesarean section with a weight of 1100 g and a height of 37 cm. Morphological maturity was corresponding to the 28-th week of gestation. He was born with asphyxia and subsequent respiratory failure due to primary surfactant deficiency. Immediately after birth, artificial pulmonary ventilation was required. Respiratory failure continued with intermittent apneas and oxygen dependence. He had a persistent anemic syndrome necessitating periodic hemotransfusions. The patient was placed in a Children‘s Medico-Social Care Home for observation, treatment and intensive care. He had been periodically hospitalized in the Pediatric Clinic due to exacerbation of chronic respiratory failure.

He was admitted to the Infectious Diseases clinic with a history of diarrheal stools more than 10 times daily for the past 3 days. On admission, the rapid test for COVID-19 was positive. A PCR test was then performed, which confirmed the presence of not only SARS-CoV-2 but also respiratory syncytial virus (RSV). The medical team from the Home for Medico-Social Care for Children denied that he had a fever. Upon admission to the Infectious Diseases clinic, the child was afebrile, lethargic and intoxicated with evidence of third degree hypotrophy. At 10 months of age his body weight was 5750 g. He had a dry tongue and pale skin with reduced turgor and elasticity. There was pronounced perioral cyanosis. Tachypnea with respiratory rate up to 50/min and dyspnea were observed. Auscultation revealed diffuse weakened vesicular breathing with single small wet wheezes. The heart rate was 175/min. The abdomen was soft, without an enlarged spleen and liver. Peristalsis was accelerated. No symptoms of meningeal irritation were detected. Diarrhea syndrome was manifested by watery, greenish stools with impurities of mucus. In the beginning, their number reached 10 in 24 hours. Still, by the 5th day, as a result of the applied rehydration and antibacterial therapy, it was reduced to 3 without significant change in consistency. Mixed metabolic-respiratory acidosis persisted, which was difficult to correct. There was a worsening of the anemic syndrome. The values of LDH, CRP and leukocytes are elevated with a neutrophilia (Table 1).

Table 1. Laboratorial investigations of the blood

Indicators	14.10.22	20.10.22	25.10.22	31.10.22	01.11.22
pH	7.27	7,35	7,38	7,24	6,98
BE	-10,3	-5,3	-4,7	-15,4	-18,7
pCO_2	46,5	54,3	58,4	42,2	61,5
pO_2	82,1	85,3	81,2	84,5	84,3
$cHCO_3$	18,2	22,1	32,1	12,3	28,6
SO_2%	97,3	94,2	92,7	86,1	95,7
WBCx10^9/L	4,3	16,8	19,3	28,9	30,0
Gran, %	31	73,4	79.7	75	86
Lym, %	65.6	19,3	18.5	21.6	10.2
RBCx10^{12}/L	4.06	3,41	3.39	2.41	2,31
Hb, g/L	112,1	103,4	99.9	94	66
PLTx109/L	249	298	355	263	212
LDH, IU/L	678	754	923	1074	1221
CRP, nmol/L	16.7	42.3	54,2	68.1	112,2
PT, %	86.3	76,4	--	74,6	64.7
Fibrinogen, g/L	2,1	2,3	1,8	4,5	4,7
D-dimer, ng/mL	0.7	0,58	--	1.29	1,32

X-ray examination showed inhomogeneous inflammatory-infiltrative changes in the lung parenchyma, more pronounced on the left. A minimal pleural effusion was suspected (Figure 1).

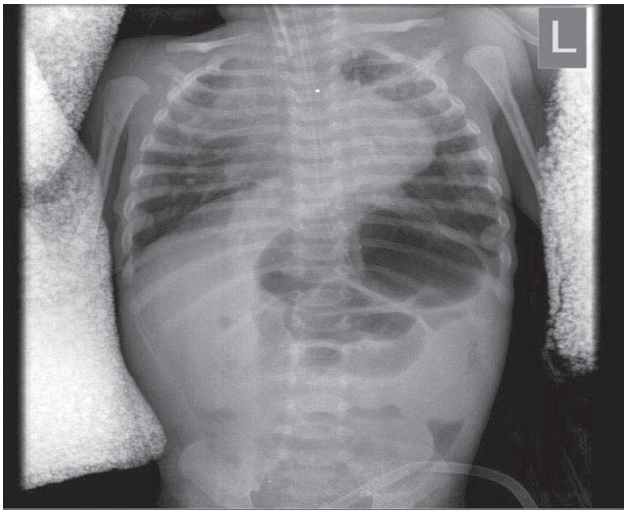

Fig. 1. X-ray of a lung: left-sided pneumonia

In the control imaging study, the described changes were preserved (Figure 2).

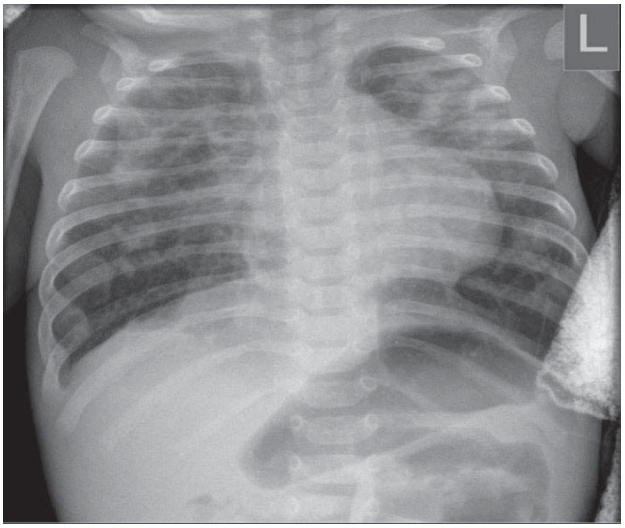

Fig. 2. Control X-ray (14-th day) without changes

Fecal microbiological and serological tests for Salmonella, Shigella, Campylobacter, E.coli, Candida, C. difficile, Norovirus, Astrovirus, Adenovirus and Rotavirus were performed with negative results. The PCR for COVID-19 remained positive throughout the whole patient's hospital stay.

The therapy was carried out with intravenous glucose-salt solutions, antibiotics – ceftriaxone and amikacin, corticosteroids – methylprednisolone, diuretics, antipyretics, vitamins and probiotics. Due to the low saturation, oxygen was started from the beginning. Immunovenin and fresh frozen plasma were also administered. On the 16-th day, a sharp deterioration was registered with signs of severe respiratory and cardiovascular failure – diffuse cyanosis, tachydyspnea and tachycardia. This necessitated his relocation to the intensive care unit and the inclusion of artificial pulmonary ventilation. Despite the active therapeutic and resuscitation measures, the child's condition progressively worsened, and on the 18-th day of hospitalization, a lethal exit occurred.

DISCUSSION

Children under the age of two, especially those with underlying chronic lung disease, have been found to be significantly more likely to develop a severe infection with SARS-CoV-2 [12, 13]. There are a number of reasons for the severe course and fatal outcome in the described clinical case. The our patient's chronic respiratory failure and bronchopulmonary dysplasia, aggravated by pneumonia caused simultaneously by SARS-CoV-2 and RSV, led to respiratory acidosis, unresponsive to medical treatment, oxygen therapy, and subsequently to artificial pulmonary ventilation. As was known, SARS-CoV-2 attacked not only the respiratory but also the intestinal epithelium. The host angiotensin-converting enzyme 2 (ACE-2) receptor is highly expressed in the intestinal epithelium of the ileum and colon, allowing entry and replication of SARS-CoV-2 [14]. In most cases of children with COVID-19 and diarrheal syndrome described in the literature, the disease was mild, often self-limiting. However, there were also more severe cases associated with higher levels of inflammatory markers, suggesting a stronger immune response of the body [9, 15]. In our case, there was a severe diarrheal syndrome and worsening dehydration and metabolic acidosis, despite active therapy – intravenous rehydration and symptomatic antidiarrheal agents. This, together with the underlying anemic syndrome and the existing protein-energy deficiency, determined a more protracted course and the likelihood of a poor outcome [16]. Last but not least is the question of whether the patient may have MIS-C despite the absence of fever. According to the Interim Guidance for Multisystem Inflammatory Syndrome in Children (MIS-C) of the American Academy of Pediatrics, updated February 2023 [17], the criteria for considering a case as MIS-C are age under 21 years, severe course of the disease, elevated CRP values above 30 mg/dL, as well as new onset manifestations of > 2 of the following categories: cardiac, shock, mucocutaneous, gastrointestinal, hematologic. Except for the temperature, MIS-C indicators were present in our patient. The child had a severe infection that

necessitated hospitalization, subsequent admission to intensive care and artificial lung ventilation. There was an increase in CRP 112,2 mg/dL during diarrheal syndrome and bradycardia. A significant decrease in lymphocytes was reported during the course of the disease. In our patient, there was a simultaneous involvement of another virus in the inflammatory process – RSV. Based on this, we had strong grounds to assume that it concerns MIS-C because the patient had gastrointestinal manifestations, pneumonia, and respiratory and cardiovascular failure. In favor of this evaluation were the high levels of markers of inflammatory activity (Leucocytes levels with left shift, CRP, LDH) and disturbances in hemostasis (increased d-dimer, decreased prothrombin index).

CONCLUSION

The described case raised questions about behavior and therapy in children with COVID-19 and comorbidity, especially on the part of the respiratory system. A combination of the severe course of SARS-CoV-2 infection in parallel with RSV, and the progression to MIS-C was cited as the reason for the unfavorable outcome. A poor premorbid background and young age associated with immune immaturity were important, too.

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REFERENCES

1. White-Dzuro G, Gibson LE, Zazzeron L, et al. Multisystem effects of COVID-19: a concise review for practitioners Postgrad Med, 2021;133(1),20-27. doi: 10.1080/00325481.2020.1823094.
2. Coronavirus Resource Center . Available from: https://coronavirus.jhu.edu/
3. Lee IC, Huo TI, Huang YH. Gastrointestinal and liver manifestations in patients with COVID-19. J Chin Med Assoc 2020;83,521–523. doi:10.1097/JCMA.0000000000000319
4. Schultz CM, Burke LA, Kent DA. A Systematic Review and Meta-analysis of the Initial Literature Regarding COVID-19 Symptoms in Children in the United States. J Pediatr Health Care, 2023;37(4),425-437. doi: 10.1016/j.pedhc.2023.02.006.
5. Blatz AM, Randolph AG. Severe COVID-19 and Multisystem Inflammatory Syndrome in Children in Children and Adolescents. Crit Care Clin, 2022;38(3),571-586. doi: 10.1016/j.ccc.2022.01.005.
6. Poeta M, Nunziata F, M Del Bene, et al. Diarrhea Is a Hallmark of Inflammation in Pediatric COVID-19. Viruses. 2022;14(12), 2723. doi: 10.3390/v14122723
7. DeBiasi RL, Harahsheh AS, Srinivasalu H, et al. Multisystem Inflammatory Syndrome of Children: Subphenotypes, Risk Factors, Biomarkers, Cytokine Profiles, and Viral Sequencing. J Pediatr. 2021;237:125-135.e18
8. Tsankov BK, Allaire JM, Irvine MA, et al. Severe COVID-19 Infection and Pediatric Comorbidities: A Systematic Review and Meta-Analysis. Int J Infect Dis. 2021 Feb;103:246-256
9. Assa A, Benninga MA, Borrelli O, et al. Gastrointestinal Committee of ESPGHAN. Gastrointestinal Perspective of Coronavirus Disease 2019 in Children-An Updated Review. J Pediatr Gastroenterol Nutr. 2021;73(3),299-305. doi: 10.1097/MPG.0000000000003204.
10. Lo Vecchio A, Garazzino S, Smarrazzo A, et al. Factors Associated With Severe Gastrointestinal Diagnoses in Children With SARS-CoV-2 Infection or Multisystem Inflammatory Syndrome. JAMA 2021;4(12),e2139974. doi: 10.1001/jamanetworkopen.2021.39974.
11. Rebecca C. Woodruff, PhD, MPH, Risk Factors for Severe COVID-19 in Children, Pediatrics. 2022;149 (1), e2021053418. doi: 10.1542/peds.2021-053418. Epub 2021 Dec 22.
12. Gupta V, Singh A, Ganju S, et al. Severity and mortality associated with COVID-19 among children hospitalised in tertiary care centres in India: a cohort study. Lancet Reg Health Southeast Asia. 2023;13:100203. doi: 10.1016/j.lansea.2023.100203.