CASE REPORT

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Coexistence of Severe Acute Respiratory Syndrome-Coronavirus-2 and Human Metapneumovirus in a Child with Severe Pneumonia

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ABSTRACT Coronavirus disease-2019 (COVID-19) is a respiratory system disease caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2). In cases with COVID-19 pneumonia, other respiratory viral agents may be simultaneously present. An 11-month-old male patient diagnosed with hydrocephalus, epilepsy and mental-motor retardation was referred to our hospital with fever, cough, and vomiting. The nasopharyngeal swab sample was positive for SARS-CoV-2 and human metapneumovirus. The patient's respiratory distress increased on the third day of the follow-up, and hydroxychloroquine sulfate was added to his treatment. On day 11 of follow-up, based on the deteriorating general condition of the patient and increased acute phase reactants, sepsis secondary to nosocomial infection was considered. Acinetobacter baumannii growth was seen in the blood culture. After antibiotic treatment, the patient's clinical condition improved. Our findings support the idea that COVID-19 can be severe in young children when it coexists with viruses that cause other respiratory tract infections.

Keywords: Bacteremia; child; COVID-19; metapneumovirus; pneumonia

Coronavirus disease-2019 (COVID-19) is a respiratory system disease caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), which emerged in Wuhan, China in December 2019.[1,2] The clinical manifestation of the disease ranges from asymptomatic nature to very severe cases of pneumonia.[3]

In 5% of the cases, at least one additional virus is detected in nasopharyngeal swab samples, and these patients may require intensive care.[4] Human metapneumovirus (hMPV) was first detected in 2001 in pediatric patients.[5] The hMPV infection is more severe in those with underlying chronic diseases, the elderly, and young children.[5,6]

This paper discusses our clinical observations in a pediatric patient with a comorbid condition, who presented with SARS-CoV-2 and hMPV positivity in the nasal swab sample and severe pneumonia, and also developed a hospital-acquired infection during the follow-up.

CASE REPORT

An 11-month-old male patient, who was being followed up with the diagnosis of hydrocephalus, epilepsy, and motor retardation, was referred to our hospital with fever, cough, and vomiting. On physical examination, he was conscious, his oropharynx was hyperemic, respiratory sounds were bilaterally coarse, and breathing indicated mild tachypnea. His heart rate was 143 beats/min, respiratory rate was 43/min, blood pressure was 92/65 mmHg, oxygen saturation was 88%, and body temperature was

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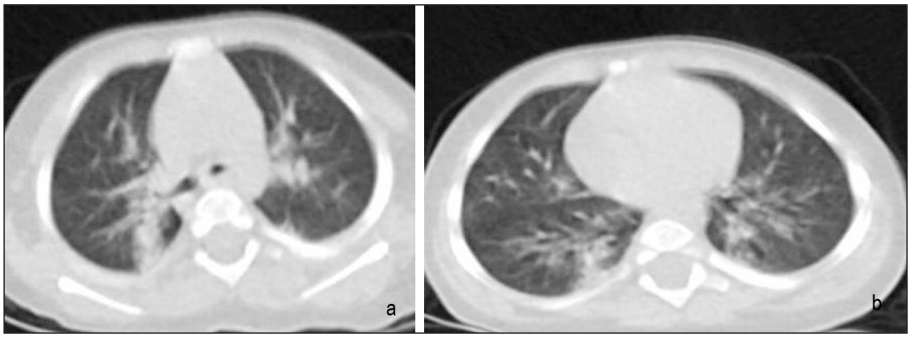

FIGURE 1: A, B) Chest computed tomography images at presentation, showing bilateral sporadic ground-glass opacities and consolidated areas in the right lung.

38.4˚C. In blood tests, the white blood cell count was determined as $15.1\times10^3/\mu L$, procalcitonin (PCT) 3.85, D-dimer 785 ng/mL, and C-reactive protein (CRP) 61 mg/L. In venous blood gas, pH was 7.3, PCO_2 47.4, HCO_3 19.3, lactate 4.4, and mixed acidosis was present.

Bilateral ground-glass opacity was detected on chest computed tomography (CT) (Figure 1A, Figure 1B). There were no family members with suspected or diagnosed COVID-19; however, the clinical, laboratory findings and chest CT findings were indicative of this disease. The nasopharyngeal swab sample taken for COVID-19 was positive for SARS-CoV-2, which was examined with the reverse transcriptase polymerase chain reaction (RT-PCR) test, and hMPV studied with the PCR test.

His respiratory distress and oxygen need increased and nutrition deteriorated, and therefore he was transferred to the second-level pediatric intensive care unit, where high-flow oxygen therapy was started. The venous blood gas measurements were as follows: pH 7.28, PCO_2 68.9, lactate 3.3, CRP 22.7 mg/L, and PCT 0.21 ng/mL, and D-dimer increased to 1,082. A control chest CT was performed. Compared to the CT performed three days earlier, there was an increase in ground-glass appearance in both lungs, which was evaluated as radiological progression (Figure 2A, Figure 2B).

The patient's treatment was revised as piperacillin-tazobactam, teicoplanin, azithromycin, and hydroxychloroquine sulphate. Electrocardiography monitoring was undertaken to monitor possible side effects of the drugs. Echocardiography of the patient was normal. Azithromycin was terminated on the fifth day. During his follow-up, D-dimer increased to 1,792 and white blood cell count decreased to $3,700\times10^3/\mu L$. The CRP and PCT levels did not remain high during the severe clinical state (Table 1). Hydroxychloroquine sulfate treatment was completed in five days. COVID-19 immunoglobulin (Ig) M and IgG in venous blood were negative.

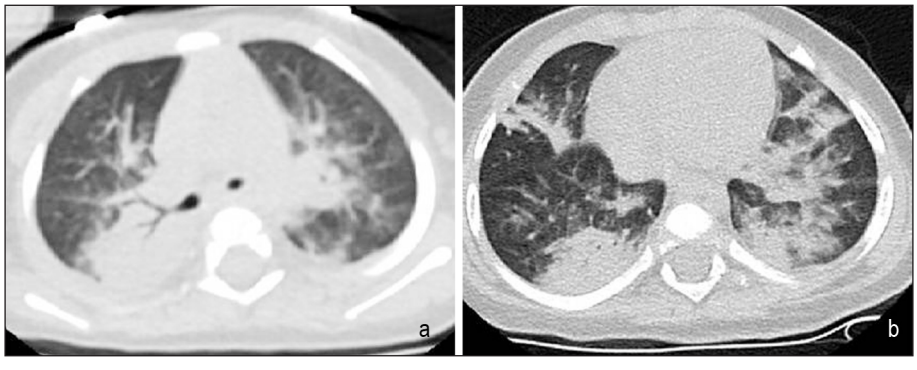

FIGURE 2a, b: Chest computed tomography images on the third day of admission, showing complete-incomplete consolidated areas and ground-glass opacities in the basal segments and perihilar region, more prominent in the middle and lower zones of the bilateral lung parenchyma, and sporadic atelectatic changes.

TABLE 1: Blood test results during the COVID-19 pneumonia period and at the onset of *hospital-acquired infection.

Test (normal range)	Day 1	Day 2	Day 3	Day 5	Day 6	*Day 11
White blood cell (3.9-10.8×10³ µL)	15.1	5.5	3.7	4.4	7.2	9.8
Lymphocyte count (1.1-3.6×10³ µL)	3,400	4,600	2,800	3,600	4,900	4,300
Procalcitonin (0.5-2 ng/ml)	3.85	0.33	0.21	0.06	0.05	37.5
D-dimer (0-500 ng/mL)	785	1,082	1,792	1,266	559	1,072
C-reactive protein (0-5 mg/L)	61	18.1	22.7	7.8	0.99	103
Albumin (3.5-5.6 g/dL)	3.34	3.17	3.14	3.11	3.28	2.77
Alanine aminotransferase (10-40 U/L)	47	66	94	65	38	44
Lactate dehydrogenase (0-248 U/L)	374	-	1,103	687	494	387

The patient developed a vascular access problem on the ninth day of antibiotic treatment, upon which a central venous catheter was inserted. On the 11th day of his admission, the patient's general condition deteriorated again and he had a fever of 39 °C, CRP elevated to 10^3 mg/L, and PCT to 37.5 ng/mL (Table 1). There was no abnormal auscultation finding and no need for oxygen. As a result, sepsis secondary to a hospital-acquired infection was primarily considered. Since the patient's general condition deteriorated under the treatment of piperacillin-tazobactam, and teicoplanin, these treatments were stopped, and meropenem and amikacin were initiated. His body temperature returned to normal after 48 hours. *Acinetobacter baumannii* grown in blood culture was susceptible to meropenem and amikacin. The central venous catheter could not be removed due to his vascular access problem. Meropenem and amikacin treatment was completed on the 14th day. There was no growth in control blood cultures. The central venous catheter was removed. The patient did not have any further complaints and his vital signs are stable. On the 26th day of admission, he was discharged with full recovery.

The parents of the patient provided written informed consent for publication of this case report.

DISCUSSION

SARS-CoV-2 is a new human coronavirus belonging to the same family of coronaviruses associated with Middle East respiratory syndrome-CoV (MERS-CoV) and SARS-CoV.[7]

The vast majority of COVID-19 patients are adults.[8] It has been reported that the clinical findings of children diagnosed with COVID-19 younger than one-year-old, may be more severe. It has also been shown that pre-existing medical conditions in children are associated with the need for intensive care.[4] Our case supports these two suggestions.

Götzinger et al. reported that 5% of COVID-19 cases had at least one additional virus detected in their samples and that the symptoms and signs of upper and lower respiratory tract infections were more severe in these patients.[4]

hMPV, a member of the paramyxovirus family (pneumovirinae subfamily), is a respiratory viral pathogen that causes a spectrum of illnesses that range from asymptomatic infection to severe bronchiolitis and pneumonia in children.[9] In a study by van den Hoogen et al., the vast majority of 28 cases with hMPV were children under the age of five years (0-12 months=13, under 5 years=27).[5] In another study evaluating a total of 72 children and adults who were detected to be SARS-CoV-2-positive and died, it was reported that no sample of adult patients was hMPV-positive, while the coexistence of SARS-CoV-2 and hMPV was seen in three pediatric cases.[10] Our patient had serious comorbidities. So, in our case, the coexistence of hMPV with COVID-19, may have contributed to the rapid deterioration of lung findings.

It has been reported that chest radiography is insufficient to show lung lesions in detail in children suspected to have COVID-19, and chest CT should be used in the diagnosis and follow-up of these patients.[11] In our patient, the chest CT findings on admission were indicative of COVID-19 infection, but as a result of the progression of the disease, the findings became more typical in repeated CT (Figure 1, Figure 2).

In a study by Henry et al. evaluating pediatric COVID-19 cases, CRP and procalcitonin (PCT) increased in 13.6% and 10.6% of the patients, respectively.[2] In the same study, it was emphasized that a viral lower respiratory tract infection accompanied by high PCT should strongly suggest the presence of a coexisting bacterial infection in children. In another study, PCT was found to be 80% higher in adults with COVID-19, regardless of the presence of a coexisting bacterial infection.[11] In our case, CRP and PCT were initially only moderately elevated and rapidly regressed to normal levels. However, during the period when nosocomial infection developed, CRP and PCT were observed to significantly increase. This finding suggests that acute phase reactants may behave differently in children than in adults.

Currently, in children diagnosed with COVID-19, antiviral treatment should be evaluated separately for each patient and planned in severe cases. Turkish Ministry of Health offers hydroxychloroquine sulfate, lopinavir/ritonavir and favipiravir (in children >15 years) for the treatment of COVID-19 infection in the last guideline.[12] In our patient, hydroxychloroquine sulfate treatment was initiated due to the rapid deterioration of respiratory function and clinical deterioration as a result of severe pneumonia, and clinical response was seen.

In conclusion, our findings support the idea that COVID-19 may progress severely in young children if it coexists with other viruses that cause other respiratory tract infections. Also these patients should be followed closely in terms of secondary bacterial infections.

Ethical Approval

The study was conducted after obtaining permission from the Republic of Turkey Ministry of Health (dated 12.6.2020) and approval from the Clinical Research Ethics Committee of Atatürk University Faculty of Medicine (dated 6.26.2020, meeting number: 07, decision number: 27).

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Muhammet Akif Güler;* ***Design:*** *Muhammet Akif Güler, Naci Ceviz;* ***Control/Supervision:*** *Naci Ceviz;* ***Data Collection and/or Processing:*** *Muhammet Akif Güler, Fuat Laloğlu;* ***Analysis and/or Interpretation:*** *Muhammet Akif Güler, Fuat Laloğlu, Naci Ceviz;* ***Literature Review:*** *Muhammet Akif Güler, Fuat Laloğlu;* ***Writing the Article:*** *Muhammet Akif Güler, Fuat Laloğlu, Naci Ceviz;* ***Critical Review:*** *Muhammet Akif Güler, Naci Ceviz.*

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