DOI: 10.4274/anatoljmed.2023.88155
Anatol J Gen Med Res 2024;34(1):110-6

CASE REPORT / OLGU SUNUMU

ANATOLIAN JOURNAL of GENERAL MEDICAL RESEARCH

Siblings with Severe Neonatal ARDS: Immune Deficiency Versus COVID-19

Neonatal ARDS'li İki Kardeş: COVID-19 ve Şiddetli Kombine İmmün Yetmezlik

Coşkun Armağan[1], Tuğba Üçüncü Egeli[1], Can Akyıldız[1], Serdar Al[2], Suna Asilsoy[2], Funda Erdoğan[1], Nuray Duman[1], Hasan Özkan[1]

[1]Dokuz Eylül University Faculty of Medicine, Department of Neonatology, İzmir, Turkey
[2]Dokuz Eylül University Faculty of Medicine, Department of Child Immunology and Allergic Diseases, İzmir, Turkey

Cite as: Armağan C, Üçüncü Egeli T, Akyıldız C, Al S, Asilsoy S, Erdoğan F, Duman N, Özkan H. Siblings with Severe Neonatal ARDS: Immune Deficiency Versus COVID-19. Anatol J Gen Med Res 2024;34(1):110-6

Abstract

Neonatal acute respiratory distress syndrome (ARDS) is a relatively new diagnosis. Specific treatment, beyond managing the underlying disease, generally relies on lung protective ventilation strategies. Viral infections such as coronavirus-2 are associated with severe ARDS. Dysfunctions in innate immunity contribute to the loss of control over viral replication and inflammatory processes, inevitably leading to a more severe clinical presentation and poor outcomes. In this case report, we present the cases of two siblings diagnosed and managed as N-ARDS with severe combined immune deficiency related to adenosine deaminase deficiency. These cases highlight the challenges of managing neonatal ARDS and the severity of viral infections in patients with immune system disorders, underlining the impact of these conditions on clinical outcomes.

Keywords: Neonatal ARDS, COVID-19, ADA deficiency, SCID

Öz

Neonatal akut solunum sıkıntısı sendromu (ARDS), nispeten yeni bir tanıdır. Altta yatan hastalığın tedavisinden başka, özgül tedavi genellikle akciğer koruyucu ventilasyon stratejilerine dayanır. Şiddetli akut solunum sendromu koronavirüsü-2 gibi viral enfeksiyonlar, şiddetli ARDS ile ilişkilidir. Bağışıklık sisteminin etkilendiği durumlarda, viral replikasyon ve enflamatuvar süreçlerin kontrolü bozulur ve bu durum, kaçınılmaz olarak kötü sonuçlara yol açar. Bu çalışmada, adenosin deaminaz eksikliği ile ilişkili şiddetli kombin immün yetmezliği olan ve farklı viral enfeksiyonlar sebebi ile N-ARDS tanısı alan ve yönetilen iki kardeş olgusu sunulmuştur. Bu olgularda, neonatal ARDS'nin yönetimindeki zorlukları ve özellikle bağışıklık sistemi bozuklukları olan hastalarda viral enfeksiyonların şiddetini ve bu durumun klinik sonuçları üzerindeki etkilerini vurgulamaktadır.

Keywords: Yenidoğan ARDS, COVID-19, ADA eksikliği, SCID

Address for Correspondence/Yazışma Adresi: Coşkun Armağan MD, Dokuz Eylül University Faculty of Medicine, Department of Neonatology, İzmir, Turkey
Phone: +90 555 418 52 03 **E-mail:** drcoko@gmail.com
ORCID ID: orcid.org/0000-0001-9716-130X

Received/Geliş tarihi: 18.12.2022
Accepted/Kabul tarihi: 08.03.2023

Introduction

Acute respiratory distress syndrome (ARDS) was first defined in 1967[1]. After 48 years, the pediatric acute lung injury consensus conference established the first specific definition for pediatric patients[2]. Neonatal ARDS (NARDS), which was first described by de Luca et al.[3], is a relatively new diagnosis compared with other types. Although different drugs and ventilation modalities for the treatment of ARDS have been tried over the years, there is no specific treatment other than the treatment of the underlying disease, and the treatment mostly relies on lung protective ventilation strategies and therapeutic agents to improve gas exchange. Various factors can trigger NARDS, such as pneumonia, sepsis, aspiration, and asphyxia. Viral infections such as severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) are associated with severe ARDS. Innate immunity plays a key role in antiviral responses. Thus, dysfunction of innate immunity may also contribute to the loss of control of viral replication and hence the severity of viral infections[4]. Here we describe 2 siblings diagnosed and managed with NARDS. Further examination for underlying disease revealed adenosine deaminase (ADA) deficiency.

Case Reports

Case 1

A 24-day-old infant was referred to our emergency department with fever for 2 days and cough for a week. This 3150-gram female infant was born at 39 weeks of gestation to a 21-year-old gravida 4, para 2, and abortus 2 mother. The pregnancy was complicated by imminent abortus, and the mother had been using low-molecular-weight heparin (LMWH) since 20 weeks of gestation. Her initial examination revealed no respiratory distress, lymphopenia, slightly elevated C-reactive protein (CRP), and suspected right pericardial pneumonic infiltration on chest X-ray (Figure 1A). Her laboratory findings are summarized in Table 1. The patient was hospitalized and started antibiotic treatment. Her quick nasal swap RSV antigen test was negative. Polymerase chain reaction (PCR) of nasal swap was positive for human parainfluenza type 3 (HPIV-3). Because of the gradual increase in oxygen demand in the first week of her hospitalization and her inability to tolerate oxygen with a simple mask, she was taken to the intensive care unit and non-invasive mechanical ventilation (NIV) was applied. After being followed up on NIV for 1.5 days, the patient was

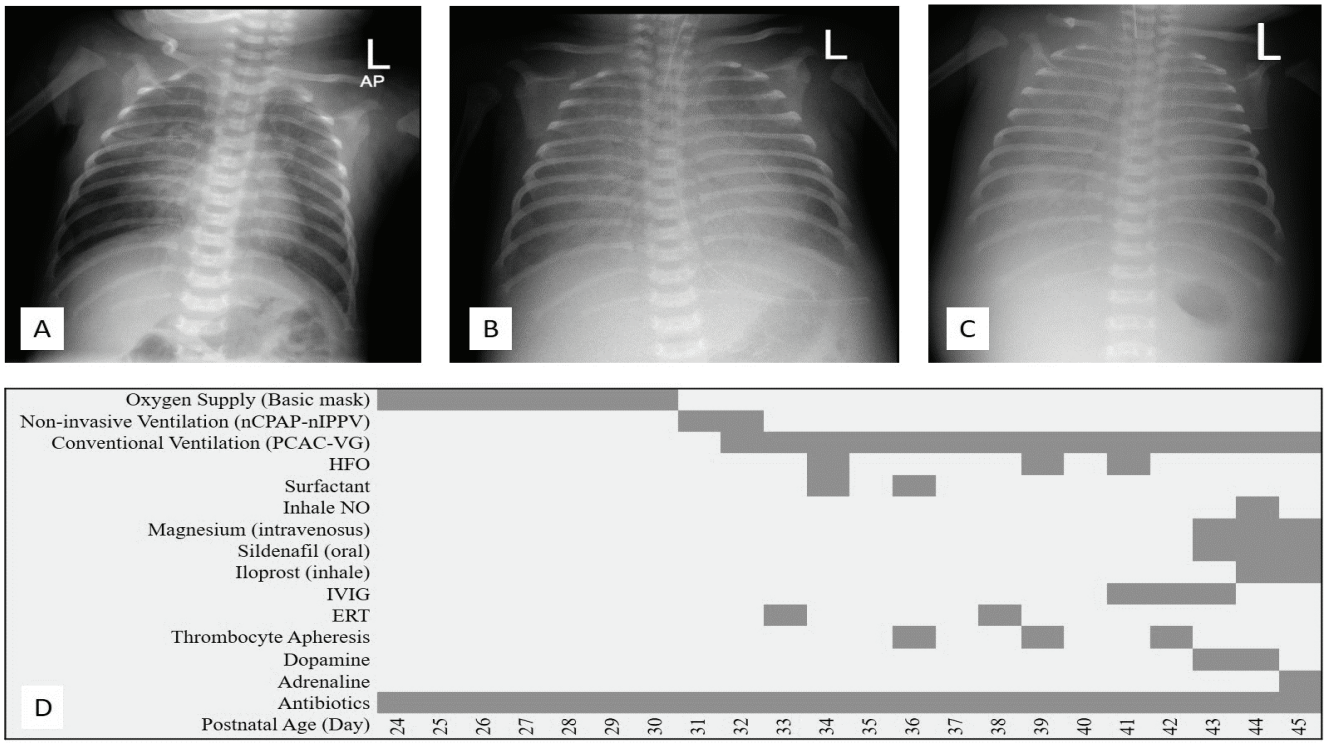

Figure 1. A: Initial chest X-ray of Case 1 (stars: cupping of costochondral junctions); **B:** Chest X-ray of case 1 at the time of NARDS diagnosis; C: Chest X-ray of case 1 on follow-up (arrow: squaring of the inferior scapular angle) **D:** Treatment regimen of case 1

Table 1. Laboratory results of cases 1 and 2

	Case 1			Case 2		
	Initial	At the time of ARDS diagnosis	Follow-up	Initial	At the time of ARDS diagnosis	Follow-up
WBC (10^3/uL)	3400	8800	6100	6300	7800	48900
LYM (10^3/uL)	400	400	100	3000	4500	800
Hb (g/dL)	13	11.3	11.2	13.5	12.1	12.7
PLT (10^3/uL)	258000	52.000	28.000	347.000	52.000	16.000
CRP (mg/L)	13.7	49	98.5	31.4	87.2	59
Cre (mg/dL)	0.18	0.07	0.33	0.17	0.22	1.05
ALT (U/L)	60	49	23	56	41	830
INR	1.1	1.3	1.18	1.2	1.23	3.64
pH/pCO_2/HCO_3 (--mm/Hg- mmol/L)	7.45/44/29	7.30/64/25.7	7.30/69/29	7.44/30.5/22	7.11/110/23.7	7.44/71.8/42.6
Oxygenation index	-	10	24	-	15	28
IgA/IgM/IgG (mg/dL)	32.9/20/328.1			<10/20/1357		
Respiratory tract PCR	Human parainfluenza type 3			SARS-CoV-2		

ARDS: Acute respiratory distress syndrome, WBC: White blood cell, CRP: C-reactive protein, PLT: Platelet count, PCR: Polymerase chain reaction, SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2, Hb: Hemoglobin, ALT: Alanine transaminase, LYM: Lymphocytes, Cre: Creatinine, INR: International normalized ratio

intubated and followed for another 2 weeks. In this process, the patient, who was mostly followed on the pressure control-assist control-volume guarantee (PCAC-VG) mode, was also intermittently tried for high-frequency oscillatory ventilation (HFOV). On the 10th day of her stay (2nd day of intubation), she was diagnosed with ARDS based on clinical and laboratory findings (Figure 2B, C). Her echocardiography revealed only a secundum-type atrial septal defect. Bone marrow aspiration was applied to the patient because of lymphopenia at admission, hepatosplenomegaly, and thrombocytopenia that developed at the time of ARDS. While no hemophagocytic lymphohistiocytosis was observed in bone marrow examination, an increase in myeloid series and a marked decrease in lymphoid precursors were detected. Intravenous immunoglobulin (IVIG) treatment for two days, multiple surfactant treatment, inhaled nitric oxide (iNO), magnesium, sildenafil, inotropes, and iloprost were tried for the management of ARDS and clinical pulmonary hypertension (Figure 2D). During her hospitalization, various cultures obtained from the cerebrospinal fluid, blood, urine, and respiratory tract was negative. Extracorporeal membrane oxygenation (ECMO) was considered, but unfortunately the patient died 22nd day of hospitalization. Due to the declaration of autopsy and further evaluation by the family, the patient's diagnoses were not fulfilled.

Case 2

A 20-day-old infant (sibling of case 1) was referred to our emergency department because of apnea. This 3110-gram female infant was born at 38 weeks of gestation to a 28-year-old gravida 6, para 5, and abortus 2 mother. The patient, whose initial tests for apnea were performed during her observation in the emergency department, was followed up in the intensive care unit because she had recurrent apnea. Other than apnea, her physical examination was normal. Her complete blood count and biochemistry values were in the normal range except for lightly elevated CRP and transaminases (Table 1). Transfontanelle ultrasound and chest X-ray were normal (Figure 2A). Hence, at the time of hospitalization, the Coronavirus disease-2019 (COVID-19) pandemic was started and her nasal swap test was positive. On the 4th day, she needed NIV. Later that day, she developed acute worsening of oxygenation and was intubated, followed by HFOV plus volume guarantee (HFOV-VG). Chest X-ray revealed bilateral irregular diffuse opacity (Figure 2B, C). Echocardiography was normal. The patient met the criteria for neonatal ARDS related to COVID-19, including acute onset hypoxemic respiratory failure, diffuse bilateral lung opacification, absence of pulmonary edema due to cardiogenic disease, and an oxygenation index (OI) exceeding four. According to national/international COVID treatment

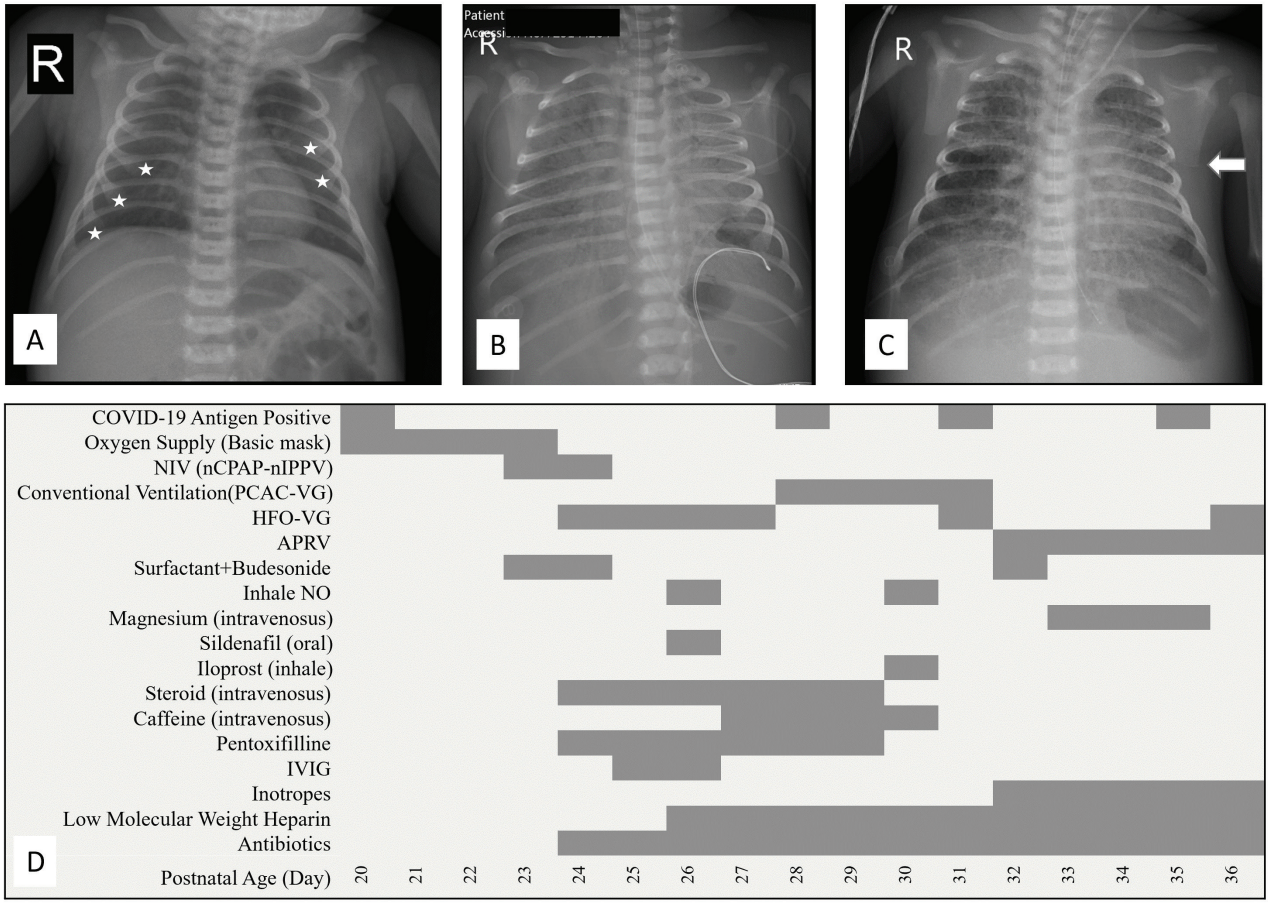

Figure 2. A: Initial chest X-ray of Case 2 (stars: cupping of costochondral junctions); B: Chest X-ray of case 2 at the time of NARDS diagnosis; C: Chest X-ray of case 2 on follow-up (arrow: squaring of the inferior scapular angle); D: Treatment regimen of case 2

COVID-19: Coronavirus disease-2019, IVIG: Intravenous immunoglobulin

regimens and case reports, steroids, low-molecular-weight heparin, antibiotics, budesonide+surfactant combination, caffeine, and pentoxifylline were administered (Figure 2D). With this exacerbation, the family history was questioned in more detail, and we learned that the case had a sibling who had experienced similar things (Case 1). Although lymphopenia was not detected in the complete blood count, the patient's lymphocyte panel could not be studied because of insufficient lymphocytes. The patient was referred to the immunology and hematology departments with a preliminary diagnosis of severe combined immunodeficiency (SCID) considering current information. While the tissue group analyses were sent from the relatives of the patient for bone marrow transplantation, genetic analysis was conducted in terms of immune deficiency from the patient. iNO, sildenafil, and iloprost treatments were tried because oxygenation got worse in HFOV-VG or PCAC-VG between 6th and 12th day. In her last 5 days, she was ventilated on airway pressure-release ventilation (APRV) mode, and blood gas analysis was normalized. After the preparations for ECMO treatment, she developed disseminated intravascular coagulation and multiple organ dysfunction syndrome (MODS) despite all supplementary treatment, and she died on 36th day of life. Her genetic analysis revealed a homozygous "c.956_960delAAGAG (p. E319Gfs*3) mutation in the *ADA* gene that consisted of ADA-deficient SCID.

Discussion

NARDS was first defined by de Luca et al.[3]. According to Montreux standards, five diagnostic criteria must be fulfilled: 1) acute onset of exacerbation; 2) dyspnea (r/o respiratory distress syndrome, transient tachypnea of the newborn, congenital malformations); 3) diffuse, bilateral, and irregular opacities or complete opacification of the lungs; 4) absence

of congenital heart disease explaining the edema; and 5) OI ≥4[3]. In the multicenter cohort study, which evaluated 239 newborns diagnosed with NARDS from 15 different neonatal intensive care units following this study, the prevalence was found to be 1.5%, while the most common etiology was sepsis, aspiration, and pneumonia[5].

In both our cases, all these criteria were met. The first case was diagnosed on the 10th day (50th day of life), and the second was diagnosed on 7th day (26th day of life) of hospitalization. In the first case, the agent that started the process was HPIV-3, whereas in the second case it was SARS-CoV-2. Both cases were previously healthy. Although parainfluenza virus is a much older and known virus than SARS-CoV-2, it usually manifests itself with self-limiting bronchiolitis in young children, but severe infections occur in immune compromised patients[6]. In a study by Roberts et al.[7], viral etiology was detected in 212 of 544 pediatric ARDS patients, and the most frequently detected viruses wererespiratory syncytial virus (RSV), human metapneumovirus (HMPV), adenovirus, and influenza. In a meta-analysis by Lukšić et al.[8] evaluating 56091 severe lower respiratory tract infections under 5 years of age, at least 1 virus was detected in 50.2% of patients aged 0-4 years, while the most common viruses were similar to those found in the study of Roberts et al.[7], parainfluenza was detected in only 2.4% of patients. There are a few cases of parainfluenza-related ARDS, but only two cases have been reported of HPIV-3-related ARDS; one of them is a healthy adult and the other is a 1-year-old patient with transient hypogammaglobulinemia[9,10]. On the other hand, since the beginning of the pandemic, SARS-CoV-2 has caused significant mortality and morbidity because of ARDS all over the world, especially in adults. While severe disease has been observed at very low rates in the childhood age group, in a study of 66 newborns, only 5% of the patients needed mechanical ventilation[11]. Similarly, in the review of Raschetti et al.[12], 176 SARS-CoV-2-positive newborn cases were evaluated, and 70% of them were found to be infected in the postpartum period. ARDS was not detected in any case, although respiratory findings were prominent in 52% of the cases[12]. After these publications, ARDS was reported in 5 neonatal cases, and only one of the patients died[13-17].

The first patient was hospitalized for follow-up with upper respiratory tract symptoms and remained quite stable in the first few days of hospitalization. She was diagnosed with moderate ARDS on the 10th day of hospitalization because of rapid deterioration and inability to provide ventilation and oxygenation despite intubation, high FiO_2 requirement, and an OI of 10. On chest X-ray, there were diffuse opacities and no condition to explain this in the echocardiography (Figure 1B, C). However, her sister, the second case, was diagnosed with moderate-to-severe ARDS on the 6th and 7th day of hospitalization with a more rapid worsening and a more severe clinic, with an OI of 15. Earlier worsening of the patient was considered consistent with the mean clinical worsening time in COVID-19-positive adult and pediatric cases[18,19].

Currently, there is no clear approach for medications and ventilation methods in the management of NARDS. Surfactant therapy is a common treatment for preterm newborns or neonates with secondary surfactant deficiency. Furthermore, the benefits of surfactant administration have been demonstrated even in adults, where SARS-CoV-2 has been shown to reduce surfactant production by damaging type 2 pneumocytes[20,21]. On the other hand, ARDS itself, with its inflammatory cascades, reduces the surfactant. Although recurrent surfactant applications were made with the diagnosis of NARDS in both of our cases, only short-term clinical benefit was achieved, as reported in other studies[13,14]. In our second case, surfactant was administered along with budesonide because cases of N-ARDS had previously benefited from this treatment[22]. Although no signs of pulmonary hypertension were detected in the echocardiographic examination of the patients, iNO treatment was tried once in the first case and twice in the second case as a rescue treatment to correct the ventilation perfusion imbalance; however, the treatment was not continued because of the lack of clinical response similar to other SARS-CoV-2 positive NARDS cases[13,14]. Similarly, magnesium, sildenafil, and iloprost treatments, which were thought to be beneficial, did not provide clinical improvement in patients. With regard to ventilation strategies, lower tidal volumes and higher positive end-expiratory pressure (PEEP) levels have been considered appropriate in ARDS management. In the first case in 2014, HFOV was only used three times for recruitment maneuver, she was mainly followed on PCAC-VG mode, and day after day her PEEP was getting higher starting from 6 to 15 cmH_2O. The second case was followed on HFOV mode; on the 3rd-4th day her PCO_2 levels were getting higher and she needed to be transferred into conventional ventilation (PCAC-VG). While in the HFOV-VG mode, oxygenation was better, ventilation deteriorated, and in the PCAC-VG mode, the opposite was the case. Although intermittent recruitment maneuvers were performed in both modes, there was only temporary well-being. Although the APRV mode has been a frequently preferred mode in

the acute lung injury of adult patients, especially with the COVID-19 pandemic, there are not enough studies on its use in the pediatric age group, especially in newborns[23]. In some animal experiments, neonatal case reports and case series, and pediatric randomized controlled trials, it has been shown that it can be used as a rescue mode for open lung strategy in patients[24-27]. Our patient was followed in the APRV mode for the last 5 days because she could not provide the appropriate conditions for ECMO and ventilation and oxygenation balance could not be achieved despite all other supportive treatments, together with the other two modes. In this process, the patient's blood gasses were observed at more normalized values compared with the other two modes.

Similar to the treatment of ARDS, there are no definite and clear recommendations for the treatment of SARS-CoV-2-infected children. For newborns, recommendations are based on case reports and adult studies. In a systematic review study of patients under the age of 1 with a diagnosis of COVID-19, conducted by Raba et al.[18], approximately half of the patients were treated with interferon, one-third with antibiotics, and only a few with steroids and immunoglobulin. Although the World Health Organization recommends steroid treatment for all COVID-19-infected patients, there is still no definite recommendation for children. Considering various guidelines and treatment protocols, the patient was treated with steroids, LMWH, and IVIG[27-29].

In a study by Peyneau et al.[4], COVID-19-positive patients had adaptive innate immune deficiency, which is associated with disease severity and prognosis because of the loss of control of viral replication. In the second case, lymphopenia was not detected in the first five hemograms of the patient. At the same time, although the patient's peripheral blood smear showed several normoblasts, lymphocytes were considered present. Upon the sudden deterioration in the general condition of the patient, a more detailed anamnesis was performed on the relatives of the patient, and the findings of her deceased sibling were examined in detail. Lymphocyte panel analysis was requested, and lymphopenia was found in the patient. The patient's previous normal lymphocyte values were attributed to the counter counting normoblasts as lymphocytes. The repeated COVID-19 polymerase chain reaction test results were positive in the samples taken intermittently during hospitalization. When the chest radiographs of the patient were evaluated retrospectively, it was seen that there was no thymus shadow and the presence of squaring of the inferior scapular angle and cupping of costochondral junctions (Figure 1 and 2: Arrows and stars) also supported ADA-SCID[30]. Early diagnosis of ADA-SCID and initiation of treatment is essential; otherwise, it is a fatal condition. Therefore, in many countries, unfortunately in our country, SCID is slowly being integrated into the neonatal screening program. ADA-deficient SCID is characterized by severe lymphocytopenia affecting T-and B-lymphocytes and NK cells; however, because of the ubiquitous nature of the enzyme, non-immunological manifestations are also observed, including neurodevelopmental deficits, sensorineural deafness, and skeletal abnormalities[31]. due to severe deterioration of cellular and humoral immunity, ADA deficiency typically manifests early in life with severe infections and failure to thrive, and affected individuals normally die in the first or second year of life without treatment. Early definitive therapy with hematopoietic stem cell transplantation results in a good overall outcome[31].

Conclusion

Neonatal ARDS is a fairly new diagnosis; regardless of the cause, its management is very difficult and there are no definitive guidelines. However, in case of severe clinical manifestation with atypical organisms or unexpected clinical manifestations with known organisms, detailed re-evaluation of the patient and his/her history are of vital importance, especially in countries where immune deficiencies are not screened in the newborn screening program.

Acknowledgments: We would like to express our gratitude to the patient's parents for their understanding and cooperation in this study.

Ethics

Informed Consent: Informed consent was obtained from the parents of the infants included in this report.

Authorship Contributions

Surgical and Medical Practices: C.A., T.Ü.E., Ca.A., F.E., N.D., Design: C.A., Data Collection or Processing: C.A., T.Ü.E., Ca.A., Analysis or Interpretation: C.A., T.Ü.E., Ca.A., F.E., N.D., Literature Search: C.A., S.A., Su.A., H.Ö., Writing: C.A., F.E., N.D., H.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Ashbaugh DG, Bigelow DB, Petty TL, Levine BE. Acute respiratory distress in adults. Lancet 1967;2.
2. Pediatric Acute Lung Injury Consensus Conference Group. Pediatric acute respiratory distress syndrome: consensus recommendations from the Pediatric Acute Lung Injury Consensus Conference. Pediatr Crit Care Med 2015;16:428-39.
3. de Luca D, van Kaam AH, Tingay DG, et al. The Montreux definition of neonatal ARDS: biological and clinical background behind the description of a new entity. Lancet Respir Med 2017;5:657-66.
4. Peyneau M, Granger V, Wicky PH, et al. Innate immune deficiencies are associated with severity and poor prognosis in patients with COVID-19. Sci Rep 2022;12:638.
5. De Luca D, Tingay DG, van Kaam AH, et al. Epidemiology of Neonatal Acute Respiratory Distress Syndrome: Prospective, Multicenter, International Cohort Study. Pediatr Critical Med 2022;23:524-53.
6. Branche AR, Falsey AR. Parainfluenza Virus Infection. Semin Respir Critical Care Med 2016;37:538-54.
7. Roberts AL, Sammons JS, Mourani PM, Thomas NJ, Yehya N. Specific Viral Etiologies Are Associated With Outcomes in Pediatric Acute Respiratory Distress Syndrome. Pediatr Crit Care Med 2019;20:e441-6.
8. Lukšić I, Kearns PK, Scott F, Rudan I, Campbell H, Nair H. Viral etiology of hospitalized acute lower respiratory infections in children under 5 years of age -a systematic review and meta-analysis. Croat Med J 2013;54:122-34.
9. Kakizaki R, Tojo R, Bunya N, Mizuno H, Uemura S, Narimatsu E. A 48-Year-Old Previously Healthy Man Presenting with Acute Respiratory Distress Syndrome (ARDS), Negative Tests for SARS-CoV-2, and Positive Serology for Parainfluenza Virus Type 3 (PIV-3). Am J Case Rep 2022;23:e934362.
10. Cotugno N, Manno EC, Stoppa F, et al. Severe parainfluenza pneumonia in a case of transient hypogammalobulinemia of infancy. BMJ Case Reports 2013:bcr2013009959.
11. Gale C, Quigley MA, Placzek A, et al. Characteristics and outcomes of neonatal SARS-CoV-2 infection in the UK: a prospective national cohort study using active surveillance. Lancet Child Adolesc Health 2021;5:113-21.
12. Raschetti R, Vivanti AJ, Vauloup-Fellous C, Loi B, Benachi A, De Luca D. Synthesis and systematic review of reported neonatal SARS-CoV-2 infections. Nat Commun 2020;11:5164.
13. Trieu C, Poole C, Cron RQ, et al. Severe Neonatal Coronavirus Disease 2019 Presenting as Acute Respiratory Distress Syndrome. Pediatr Infect Dis J 2020;39:e367-9.
14. Correia CR, Marçal M, Vieira F, et al. Congenital SARS-CoV-2 Infection in a Neonate with Severe Acute Respiratory Syndrome. Pediatr Infect Dis J 2020;39:e439-43.
15. Yangin Ergon E, Akbay S, Aytemiz G, et al. A novel case of neonatal acute respiratory distress syndrome with SARS-CoV-2 infection: potential perinatal transmission. Arch Argent Pediatr 2021;119:e531-e5. English, Spanish.
16. Farmer ML. A neonate with vertical transmission of covid-19 and acute respiratory failure. Adv Neonatal Care 2021;21:482-92.
17. Verheijen AC, Janssen EER, van der Putten ME, et al. Management of severe neonatal respiratory distress due to vertical transmission of severe acute respiratory syndrome coronavirus 2: a case report. J Med Case Rep 2022;16:140.
18. Raba AA, Abobaker A, Elgenaidi IS, Daoud A. Novel coronavirus infection (COVID-19) in children younger than one year: A systematic review of symptoms, management and outcomes. Acta Paediatr 2020;109:1948-55.
19. Cevik M, Bamford CGG, Ho A. COVID-19 pandemic—a focused review for clinicians. Clin Microbiol Infect 2020;26:842-7.
20. Raghavendran K, Willson D, Notter RH. Surfactant Therapy for Acute Lung Injury and Acute Respiratory Distress Syndrome. Crit Care Clin 2011;27:525-9.
21. Ghati A, Dam P, Tasdemir D, et al. Exogenous pulmonary surfactant: A review focused on adjunctive therapy for severe acute respiratory syndrome coronavirus 2 including SP-A and SP-D as added clinical marker. Curr Opin Colloid Interface Sci 2021;51:101413.
22. Deliloglu B, Tuzun F, Cengiz MM, Ozkan H, Duman N. Endotracheal Surfactant Combined With Budesonide for Neonatal ARDS. Front Pediatr 2020;8:210.
23. Habashi NM. Other approaches to open-lung ventilation: Airway pressure release ventilation. Crit Care Med 2005;33(3 Suppl):S228-40.
24. Martin LD, Wetzel RC, Bilenki AL. Airway pressure release ventilation in a neonatal lamb model of acute lung injury. Crit Care Med 1991;19:373-8.
25. Gupta S, Joshi V, Joshi P, Monkman S, Vallaincourt K, Choong K. Airway pressure release ventilation: A neonatal case series and review of current pediatric practice. Can Respir J 2013;20:e86-91.
26. Lalgudi Ganesan S, Jayashree M, Chandra Singhi S, Bansal A. Airway pressure release ventilation in pediatric acute respiratory distress syndrome: A randomized controlled trial. Am J Respir Crit Care Med 2018;198:1199-207.
27. Erdeve Ö, Çetinkaya M, Baş AY, et al. The Turkish neonatal society proposal for the management of COVID-19 in the neonatal intensive care unit. Turk Pediatri Ars 2020;55:86-92.
28. WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group; Sterne JAC, Murthy S, et al. Association between Administration of Systemic Corticosteroids and Mortality among Critically Ill Patients with COVID-19: A Meta-analysis. JAMA 2020;324:1330-41.
29. Salvatore CM, Han JY, Acker KP, et al. Neonatal management and outcomes during the COVID-19 pandemic: an observation cohort study. Lancet Child Adolesc Health 2020;4:721-7.
30. Verhagen M, Trevisan V, Adu J, Owens CM, Booth C, Calder A. Chest Radiographs for Distinguishing ADA-SCID from Other Forms of SCID. J Clin Immunol 2020;40:259-66.
31. Flinn AM, Gennery AR. Adenosine deaminase deficiency: a review. Orphanet J Rare Dis 2018;13:65.