



Bilateral Spontaneous Pneumothorax in a Child with Multisystem Inflammatory Syndrome Associated with COVID-19

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Abstract

Introduction: Spontaneous pneumothorax is a rare complication of coronavirus disease 2019 (COVID-19), primarily reported in adults. Pediatric cases with bilateral pneumothorax are much less reported.

Case Presentation: We presented the case of a five-year-old previously healthy boy who developed persistent fever, abdominal pain, generalized maculopapular rash, and dyspnea before admission. His chest computed tomography (CT) showed a viral involvement pattern of pneumonia suggestive of COVID-19. Subsequently, he was confirmed with multisystem inflammatory syndrome in children (MIS-C). While he responded well to the therapies, on the fifth day of admission, he developed respiratory distress again. A chest roentgenogram showed bilateral spontaneous pneumothorax. Bilateral chest tubes were inserted, and his condition improved significantly after five days of admission to the intensive care unit. Two weeks later, he was discharged in good condition.

Conclusions: Children with MIS-C associated with COVID-19 may develop primary spontaneous pneumothorax. Owing to the clinical picture overlapping with MIS-C associated with COVID-19, the timely diagnosis of pneumothorax may be challenging in such patients.

Keywords: COVID-19, Pediatric Multisystem Inflammatory Disease, COVID-19-related, SARS-CoV-2, Spontaneous Pneumothorax, Pediatric

1. Introduction

The coronavirus disease 2019 (COVID-19) pandemic is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is a variant of coronaviruses discovered in late 2019 (1). Children generally account for a small proportion of disease instances and usually present with mild forms of the disease (2). Nonetheless, on April 27, 2020, the Pediatric Intensive Care Society warned about the increasing number of pediatrics with the severe inflammatory syndrome and Kawasaki disease-like features, who mostly were SARS-CoV-2-positive or had COVID-19 exposure (3, 4). Consequently, in mid-May 2020, the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) published sets of case definition criteria for the so-called multisystem inflammatory syndrome in children (MIS-C) for disease surveillance. Causing hyperinflammatory syndrome with multisystem

involvements (above two organs), MIS-C is considered the severe form of COVID-19 in children and an indication for hospitalization (5, 6).

Pneumothorax is divided into spontaneous and traumatic/iatrogenic entities. Spontaneous pneumothorax can occur in people without (primary type) or with (secondary type) a pre-existing chronic lung disease or positive history of trauma (7). Although several cases of spontaneous pneumothorax are reported in COVID-19, mostly elderly male patients with underlying conditions (8, 9); it is even rarer in pediatric COVID-19 patients (10) presented in a few case reports (11-14). Moreover, bilateral spontaneous pneumothorax is reported much less than unilateral cases (11, 14, 15). Herein, we report the case of a five-year-old boy with MIS-C associated with COVID-19 who developed bilateral spontaneous pneumothorax during hospital admission.

2. Case Presentation

2.1. Medical History

A previously healthy Afghan boy, five-year-old, 106-cm tall (25th percentile), and 15 kg weight (third percentile), was referred to a pediatric emergency department with the chief complaints of abdominal pain and fever. The patient was healthy until five days before admission, when he initially developed a fever. Two days later, generalized rashes appeared on his abdomen that extended to his extremities. Consequently, he developed diarrhea, abdominal pain, and abdominal distention. His caregivers did not suspect that he might have had close contact with a positive COVID-19 patient during the last month. He had neither underlying medical conditions nor previous hospital admissions and surgeries. Also, he did not use any medications, had no history of allergic reactions, and was fully vaccinated against COVID-19.

2.2. Presenting Symptoms and Clinical Examination

On physical examination, his vital signs were: a body temperature of 39°C (orally), heart rate of 145 beats/min, respiratory rate of 40 breaths/min, blood pressure of 90/50 mmHg, and arterial oxygen saturation of 90% (breathing the ambient air). On arrival, he presented with red, cracked lips, an erythematous throat, and generalized maculopapular rashes on his abdomen, chest, and extremities. He had suprasternal and subcostal retraction and nasal flaring. Also, wheezing was auscultated. Moreover, he had abdominal distention with mild tenderness but without hepatosplenomegaly. The rectal sphincter tone was normal, and he passed a small amount of yellowish watery stool after rectal examination. No lymphadenopathy was detected.

2.3. Paraclinical Findings

Blood tests showed lymphocytopenia, anemia, thrombocytopenia, increased levels of D-dimer, troponin, interleukin-6, prohormone of brain natriuretic peptide, prothrombin time, partial thromboplastin time, and decreased levels of potassium, magnesium, calcium, and albumin (Table 1).

On admission, a chest roentgenogram (CXR) showed mild diffuse pulmonary infiltration and ground-glass opacities accompanied by faint air bronchograms in both lung fields (Figure 1A). In addition, spiral chest computed tomography (CT) showed diffuse subpleural ground-glass densities associated with multiple subpleural and posterior nodules in lung fields, suggestive of SARS-CoV-2 infection. A mild left-sided pleural effusion was also noted

Table 1. Laboratory Tests Results During Hospitalization

Test	Result	Reference Range
Anti-SARS-CoV-2 serologic immunoassays		≥ 1.1
Immunoglobulin M (IgM)	1.5	
Immunoglobulin G (IgG)	10.5	
Hemoglobin (g/dL)	8.1	11.5 - 14
White blood cell count (cells/μL)	5,500	5,000 - 17,000
Absolute lymphocyte count (cells/μL)	935	1,500 - 9,500
Platelet count ($\times 1000$ cells/μL)	100	150 - 400
Sodium (mEq/L)	135	136 - 145
Potassium (mEq/L)	2.7	3.5 - 5.5
Magnesium (mg/dL)	1.2	1.6 - 2.5
Calcium (mg/dL)	6.8	8.6 - 10.3
Creatinine (mg/dL)	0.66	0.8 - 1.3
Lactate dehydrogenase (U/L)	1,142	< 480
C-reactive protein (mg/L)	150	0.6 - 7.9
Erythrocyte sedimentation rate (mm/h)	88	3 - 13
D-dimer (ng/mL)	> 10,000	< 500
Troponin (ng/L)	107	< 19
Prohormone of brain natriuretic peptide (pg/mL)	82	< 70
Aspartate aminotransferase (U/L)	70	< 37
Alanine aminotransferase (U/L)	65	< 41
Albumin (g/dL)	2.7	3.8 - 4.2
Prothrombin time (s)	17.7	12 - 14
International normalized ratio	1.28	0.9 - 1
Partial thromboplastin time (s)	69	25 - 35
Fibrinogen (mg/dL)	400	200 - 400
Ferritin (ng/mL)	575	7 - 140
Interleukin-6 (pg/mL)	31	< 7

(Figure 1D-G). Abdominopelvic sonography showed a minimal amount of free fluid in the abdominal cavity. Generalized bowel loop dilatation was noted in abdominal CT. Transthoracic echocardiography was normal.

Reverse-transcription polymerase chain reaction (RT-PCR) against SARS-CoV-2 was performed twice via nasopharyngeal swabs, which were negative. However, serological immunoassay showed positive results for immunoglobulin G (IgG) and immunoglobulin M (IgM) against SARS-CoV-2 antigens (Table 1).

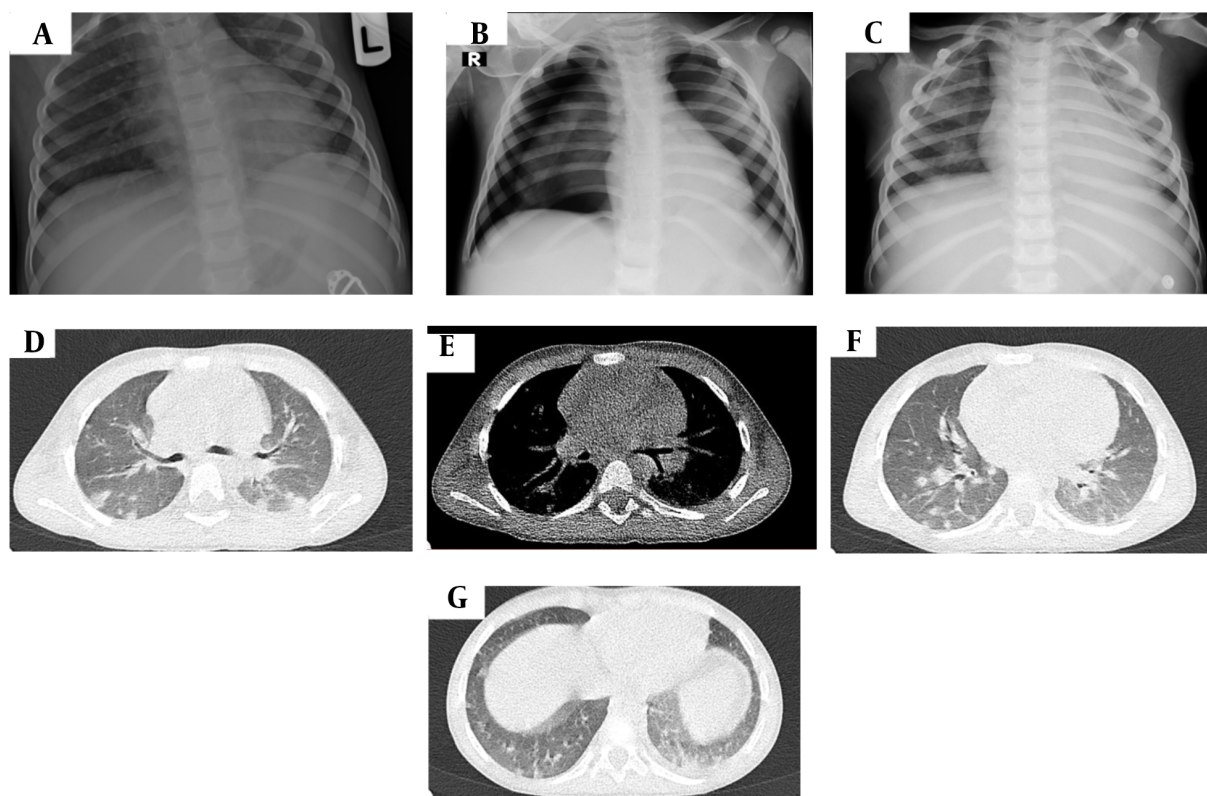


Figure 1. [Top row] Sequential plain posteroanterior (PA) chest X-ray (CXR) images taken on different days of hospital stay. (A) On admission, PA CXR shows mild diffuse pulmonary infiltration and ground-glass opacities accompanied by faint air bronchograms in both lung fields; (B) PA CXR on the fifth day of admission reveals mild left-sided, and moderate right-sided parenchymal lung collapses associated with bilateral air bronchograms, and visible pleural lines consistent with moderate right-sided pneumothorax and mild left-sided pneumothorax; (C) AP CXR after bilateral chest tube insertion on the same day. Chest tubes are properly placed in pleural spaces. Well-expanded lungs with no residual pneumothorax are noted. [Middle and down rows] Spiral chest CT scan cuts in the axial plane, lung window, at different levels of lungs on the first day of admission. (D & E) Below the level of the carina, diffuse subpleural ground-glass densities associated with multiple peripherally located (dominantly subpleural and posterior) pulmonary nodules with peripheral halos are seen in both lung fields. Also, several bilateral reactive hilar lymph nodes are noted on the mediastinal window; (F) At the level of the left ventricle, multiple areas of ground-glass densities associated with peripherally and centrally located pulmonary nodules demonstrating peripheral halos are observed in posterior aspects of the lung fields. Mild left-sided pleural effusion is also noted; (G) At the diaphragm level, multiple areas of subpleural ground-glass densities associated with few pulmonary nodules are seen in the bases of the lungs, prominent on the left. Mild left-sided pleural effusion is demonstrated.

2.4. Therapeutic Focus

The patient was given oxygen with a non-rebreather mask. After consultation with pediatric surgeons, they recommended supportive therapy for his abdominal distention; therefore, nasogastric and rectal tubes were inserted in addition to administering intravenous broad-spectrum antibiotics. During the first hours of hospitalization, he had no urine output. Shock management was performed, along with intravenous (IV) hydration. The fever subsided a few hours after administering 2 g/kg of IV immunoglobulin (IVIG) and 2 mg/kg/day of methylprednisolone. Duolin® inhaler (ipratropium bromide 500 µg + levosalbutamol 1.25 mg per each 2.5-mL of respule) (0.15 mg/kg) was also administered because of the persistent wheezing.

On the second day of the hospital stay, he developed generalized edema. Hence, IV fluids were restricted, and

10 g/day of albumin and 0.5 mg/kg/day of furosemide were infused. After three days, his condition improved; his vital signs turned stable, abdominal distention subsided, he no longer had tachypnea or respiratory distress, and his edema decreased. A liquid diet was initiated, which was well tolerated.

However, on the fifth day of the hospital stay, he developed dyspnea, and his condition worsened. CXR was carried out and revealed mild left-sided and moderate right-sided parenchymal lung collapses associated with bilateral air bronchograms and visible pleural lines consistent with moderate right-sided and mild left-sided pneumothorax (Figure 1B). Hence, bilateral chest tubes were inserted, and his condition was returned to stable (Figure 1C).

Five days later, the chest tubes were removed, and he was discharged one week after. Follow-up echocardiography was performed two weeks later, which showed nor-

mal cardiac function and coronary artery dimensions. Two months later, he was in good health on the second appointment.

3. Discussion

Spontaneous pneumothorax is rarely reported in pediatric COVID-19 patients (8, 10). A systematic review of 37 articles on CT features in pediatric COVID-19 patients found only two cases of pneumothorax and one case of bullae, none of which was bilateral (10). Hashemi et al. (12) described a two-year-old boy with hyper IgM syndrome and COVID-19 infection who developed unilateral spontaneous pneumothorax during the hospital stay. Also, Montgomery and Finck (13) described a 17-year-old boy with COVID-19 infection who presented with unilateral hemopneumothorax, which was exacerbated during the hospital stay. Furthermore, Dixit et al. (14) reported a three-month-old boy with COVID-19 infection who presented with a massive bilateral pneumomediastinum and subcutaneous emphysema. Our case is the second report of MIS-C associated with COVID-19 who had multisystem involvement, including cardiovascular, respiratory, gastrointestinal, hematological, and dermatological systems, and developed bilateral primary spontaneous pneumothorax. To the best of our knowledge, there is only one report about MIS-C complicated with spontaneous bilateral pneumothorax (11). Laaribi et al. (11) described two boys with COVID-19 (nine-month-old and 18-month-old) who developed bilateral spontaneous pneumothorax. They did not mention MIS-C associated with COVID-19 in their two cases; however, by definition (6), MIS-C is evident. In addition, contrary to our case, pneumothorax was developed before admission in those two cases.

We could not find the definite cause of bilateral spontaneous pneumothorax in our patient. Barotrauma associated with positive pressure mechanical ventilation can lead to pneumothorax (16). In Zantah et al. analysis of 902 COVID-19 patients, all six patients who developed pneumothorax had a unilateral pathology, four of whom were associated with mechanical ventilation (17). Our case did not receive any ventilation supports before pneumothorax diagnosis, reflecting that barotrauma could not be the cause of pneumothorax. Interestingly, in all similar cases (11-14), barotrauma was also ruled out. One plausible explanation might be excessive coughing, which is common in COVID-19 patients. It can increase intra-thoracic and alveolar pressure. In addition, COVID-19 pneumonia can cause alveolar damage directly (18). Furthermore, hyperinflammatory status is linked to more severe lung injuries (i.e., adults with severe COVID-19 who developed pneumothorax) (19, 20). Interestingly, our case had multisystem in-

volvements and laboratory evidence of hyperinflammatory status. Overall, bilateral primary spontaneous pneumothorax in our patient might be attributed to the inflammatory reactions secondary to COVID-19.

3.1. Conclusions

In conclusion, children with MIS-C associated with COVID-19 may develop spontaneous pneumothorax during the hospital stay, without barotrauma or previous underlying medical conditions. Owing to the clinical picture overlapping with MIS-C associated with COVID-19, the timely diagnosis of pneumothorax may be challenging in such patients.

Footnotes

Authors' Contribution: AS conceptualized and led the study, managed the clinical aspects of the patient, and critically revised the manuscript. FZ drafted the manuscript and critically revised it. MHB collected the relevant data and drafted the manuscript. FR provided the images and critically revised the manuscript. SR critically revised the manuscript. All authors approved the final version of the manuscript and are accountable for all aspects of the work.

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Data Reproducibility: The corresponding author will share data upon reasonable request.

Ethical Approval: The protocol and patient informed consent form were reviewed and approved by the Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.MED.REC.1400.342). The parents of the studied patient signed informed consent and agreed to participate in the study and publish the data.

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References

- Habibzadeh P, Stoneman EK. The Novel Coronavirus: A Bird's Eye View. *Int J Occup Environ Med*. 2020;**11**(2):65-71. [PubMed ID: 32020915]. [PubMed Central ID: PMC7205509]. <https://doi.org/10.15171/ijoom.2020.1921>.
- Zimmermann P, Curtis N. COVID-19 in Children, Pregnancy and Neonates: A Review of Epidemiologic and Clinical Features. *Pediatr Infect Dis J*. 2020;**39**(6):469-77. [PubMed ID: 32398569]. [PubMed Central ID: PMC7363381]. <https://doi.org/10.1097/INF.0000000000002700>.
- Greene AG, Saleh M, Roseman E, Sinert R. Toxic shock-like syndrome and COVID-19: Multisystem inflammatory syndrome in children (MIS-C). *Am J Emerg Med*. 2020;**38**(11):2492 e5-6. [PubMed ID: 32532619]. [PubMed Central ID: PMC7274960]. <https://doi.org/10.1016/j.ajem.2020.05.117>.
- Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. *Lancet*. 2020;**395**(10237):1607-8. [PubMed ID: 32386565]. [PubMed Central ID: PMC7204765]. [https://doi.org/10.1016/S0140-6736\(20\)31094-1](https://doi.org/10.1016/S0140-6736(20)31094-1).
- Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19. World Health Organization; 2020, [cited 5/15/2020]. Available from: <https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19>.
- Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with Coronavirus Disease 2019 (COVID-19). Centers for Disease Control and Prevention; 2020. Available from: <https://emergency.cdc.gov/han/2020/han00432.asp>.
- Özalp A, Sevdı MS, Demırgan S, Gümüş Özcan F, Win M, Erkalp K, et al. Pneumothorax in the ICU: Retrospective Analysis of Two Years' Experience. *Bagcilar Med Bull*. 2020;**5**(1):7-12. <https://doi.org/10.4274/BMB.galenos.2019.12.028>.
- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*. 2020;**323**(11):1061-9. [PubMed ID: 32031570]. [PubMed Central ID: PMC7042881]. <https://doi.org/10.1001/jama.2020.1585>.
- Mohammadi A, Boroofeh B, Mohebbi A, Mirza-Aghazadeh-Attari M. Expanding spontaneous pneumothorax in COVID-19 pneumonia: Case report and review of literature. *J Cardiovasc Thorac Res*. 2021;**13**(3):258-62. [PubMed ID: 34630976]. [PubMed Central ID: PMC8493232]. <https://doi.org/10.34172/jcvtr.2021.16>.
- Wang JG, Mo YF, Su YH, Wang LC, Liu GB, Li M, et al. Computed tomography features of COVID-19 in children: A systematic review and meta-analysis. *Medicine (Baltimore)*. 2021;**100**(38):e22571. [PubMed ID: 34559092]. [PubMed Central ID: PMC8462638]. <https://doi.org/10.1097/MD.00000000000022571>.
- Laaribi I, Mimouni H, Bouayed Z, El Aidouni G, Berrichi S, Bahouh C, et al. Bilateral spontaneous pneumothorax in critically-ill COVID-19 infants: About two cases. *Ann Med Surg (Lond)*. 2022;**73**:103172. [PubMed ID: 34904055]. [PubMed Central ID: PMC8648378]. <https://doi.org/10.1016/j.amsu.2021.103172>.
- Hashemi SM, Esfahanian N, Ahmadizadeh SN, Behzad A, Alemzadeh M, Shirvani F, et al. Spontaneous Pneumothorax in a Child with COVID-19. *Arch Pediatr Infect Dis*. 2021;**10**(Suppl). <https://doi.org/10.5812/pedinfect.114691>.
- Montgomery AB, Finck C. Spontaneous hemopneumothorax in an adolescent with COVID-19. *J Pediatr Surg Case Rep*. 2021;**69**:101852. [PubMed ID: 33828949]. [PubMed Central ID: PMC8016539]. <https://doi.org/10.1016/j.epsc.2021.101852>.
- Dixit A, Uvaise M, Canet-Tarres A, Lillie J. Spontaneous Massive Pneumomediastinum in a Previously Well Infant With COVID-19. *Pediatrics*. 2021;**148**(6). [PubMed ID: 34851418]. <https://doi.org/10.1542/peds.2021-051904>.
- Coraplı G, Tekin V. An extremely rare case of COVID-19: bilateral spontaneous pneumothorax. *Eur Rev Med Pharmacol Sci*. 2022;**26**(7):2569-71. [PubMed ID: 35442471]. https://doi.org/10.26355/eurrev_202204_28493.
- Zhou C, Gao C, Xie Y, Xu M. COVID-19 with spontaneous pneumomediastinum. *Lancet Infect Dis*. 2020;**20**(4):510. [PubMed ID: 32164830]. [PubMed Central ID: PMC7128610]. [https://doi.org/10.1016/S1473-3099\(20\)30156-0](https://doi.org/10.1016/S1473-3099(20)30156-0).
- Zantah M, Dominguez Castillo E, Townsend R, Dikengil F, Criner GJ. Pneumothorax in COVID-19 disease- incidence and clinical characteristics. *Respir Res*. 2020;**21**(1):236. [PubMed ID: 32938445]. [PubMed Central ID: PMC7492794]. <https://doi.org/10.1186/s12931-020-01504-y>.
- Aydin S, Öz G, Dumanlı A, Balci A, Gencer A. A Case of Spontaneous Pneumothorax in Covid-19 Pneumonia. *J Surg Res*. 2020;**3**(2):96-101. <https://doi.org/10.26502/jsr.10020060>.
- Ye Q, Wang B, Mao J. The pathogenesis and treatment of the 'Cytokine Storm' in COVID-19. *J Infect*. 2020;**80**(6):607-13. [PubMed ID: 32283152]. [PubMed Central ID: PMC7194613]. <https://doi.org/10.1016/j.jinf.2020.03.037>.
- Hameed M, Jamal W, Yousaf M, Thomas M, Haq IU, Ahmed S, et al. Pneumothorax In Covid-19 Pneumonia: A case series. *Respir Med Case Rep*. 2020;**31**:101265. [PubMed ID: 33101895]. [PubMed Central ID: PMC7576439]. <https://doi.org/10.1016/j.rmcr.2020.101265>.