ISSN: 2543-0343 Volume 7 Issue 2 April - June 2023

Pediatric Respirology and Critical Care Medicine

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- Cilia
- Periciliary fluid
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- Cellular inflammation

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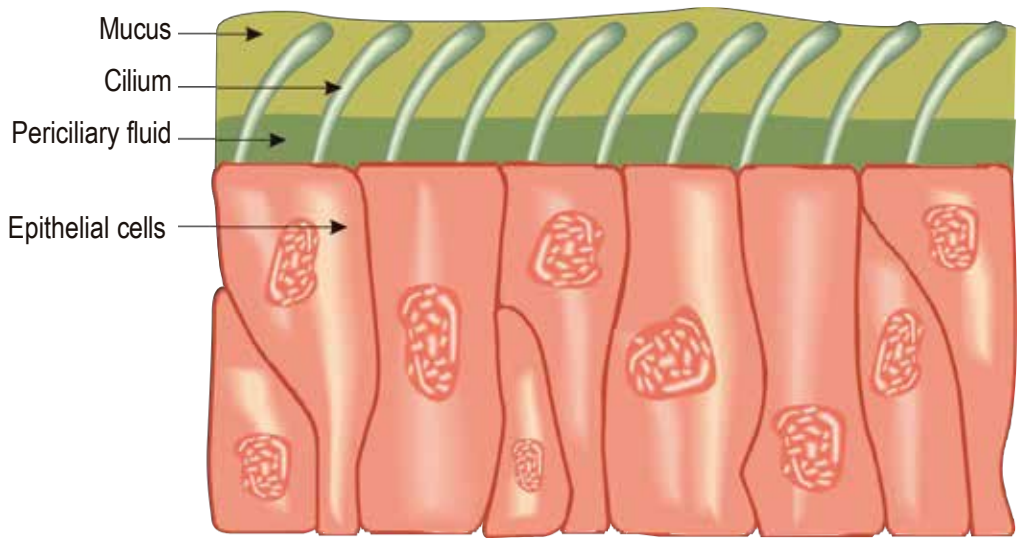

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Print ISSN: 2543-0343, E-ISSN: 2543-0351

Pediatric Respirology and Critical Care Medicine

Official Journal of Asian Paediatric Pulmonology Society, Hong Kong Society of Paediatric Respirology and Allergy, and Taiwan Society of Pediatric Pulmonology and Critical Care Medicine

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General Information

The journal

Pediatric Respirology and Critical Care Medicine is a journal for pediatricians to discuss the latest clinical practice and research in pediatrics and child health. It is the official Journal of Asian Paediatric Pulmonology Society, Hong Kong Society of Paediatric Respirology and Allergy, and Taiwan Society of Pediatric Pulmonology and Critical Care Medicine. The journal's full text is available online at http://www.prccm.org. The journal allows free access (Open Access) to its contents and permits authors to self-archive final accepted version of the articles on any OAI-compliant institutional/subject-based repository.

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Published by
Wolters Kluwer India Private Limited
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Village Marol, Andheri (East), Mumbai - 400 059, India.
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Pediatric Respirology and Critical Care Medicine

Volume 7 ¦ Issue 2 ¦ April-June 2023

Contents

The Asian Pediatric Respirology Medicine: A Vibrant Field

The current issue of the journal saw publications from different parts of Asia. It is this exchange of knowledge that allows progress in this field. Wang *et al*.[1] compared the data of community-acquired pneumonia (CAP) with the hospital-acquired pneumonia and found CRP to be an independent risk factor for mortality in CAP. This is in line with the report from Israel by Barak-Corren *et al*.[2] who reported that CRP was a useful prognostic marker for children with suspected bacterial pneumonia. This serves as a timely reminder of the need for quantification of inflammatory markers in children admitted for pneumonia. Lai and Liao[3] reported the interesting observation of pneumomediastinum after the BioNTech COVID-19 vaccine. This adverse effect was reported before also from Taiwan[4] and it is important to conduct further study to see if this observation is causally related to BioNTech COVID-19 vaccine or not.

Finally, Samra *et al*.[5] reported a very challenging case of COVID-positive patient with a compromised upper airway that could not be intubated. Fortunately, the patient could be ventilated and successfully tracheostomized. This emphasizes the need to train pediatricians and anesthetists in the skill of infraglottic airway placement, which is undoubtedly not common in most centers.[6] I trust this case should form part of simulation training for all pediatricians and anesthetists to avoid future mortality or even perhaps successful intubation in the future patients.

I would like to take this opportunity to wish all readers a happy summer and look forward to meeting you at our coming annual meeting in Indonesia in October.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Submitted: 31-05-2023 **Accepted:** 31-05-2023 **Published:** 21-06-2023

Access this article online

Quick Response Code:

Website: www.prccm.org

DOI: 10.4103/prcm.prcm_14_23

How to cite this article: Ng DK. The Asian pediatric respirology medicine: A vibrant field. Pediatr Respirol Crit Care Med 2023;7:27.

Epidemiology and Risk Factors of Pediatric Pneumonia in a Tertiary Center in Taiwan

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Abstract

Background: Pneumonia is a common disease in children, and causes a substantial burden both on patients and health care systems. Comparison between community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP) and the prognosticator of hospitalized pneumonia patients in Taiwan is unclear. **Materials and Methods:** In this retrospective study, data from hospitalized children aged <18 years with a diagnosis of pneumonia from 2012 to 2013 in our institutional database were investigated. Demographic characteristics, laboratory data, identified pathogens, and treatment course was recorded for analysis. A value of $P < 0.05$ was considered statistically significant. **Results:** A total of 548 patients with 598 episodes of pneumonia (male/female ratio = 1.08) were enrolled in the database. Underlying diseases are more common in patients with HAP than those with CAP. Patients with HAP had a higher mortality and length of hospital and intensive care unit (ICU) stay than that of those with CAP. C-reactive protein (CRP) and band form plus segment neutrophil percentage were higher in patients with CAP. In multivariate analysis of CAP group, underlying disease, CRP, and band form plus segment neutrophil percentage were independent prognosticators of admission to ICU. Underlying disease and CRP were independent prognosticators of mortality. The most common pathogens were respiratory syncytial virus, *Streptococcus pneumoniae*, and influenza virus. **Conclusions:** Patients with HAP had significantly higher mortality rates and longer lengths of hospital and ICU stay than those with CAP. CRP was an independent prognosticator of admission to ICU and mortality in patients with CAP, and also served as a prognosticator of mortality in patients with HAP.

Keywords: Children, C-reactive protein, pneumonia

Introduction

Pneumonia is a common disease in the pediatric population and is associated with high morbidity and mortality rates in some countries.[1] About four million children die each year from pneumonia-related acute respiratory distress syndrome and respiratory failure. A retrospective study[2] conducted on children hospitalized with pneumonia between 2010 and 2013 in Taiwan showed that the average annual population-based incidence of hospitalization for pneumonia was 69.5 episodes per 100,000 children aged <18 years. The mortality rate was 2.5 per 100,000 child-years, even though the vaccine coverage for respiratory disease had increased.[3] Children with a good prognosis could not be distinguished from those who develop severe respiratory failure or acute respiratory distress syndrome. With advances in medical care, the management of severe pneumonia remains supportive of lung-protective ventilation strategies.[4,5] Various biomarkers were studied and thought to be prognosticators of pneumonia.[6-10] Accurate estimation of disease severity and patient risk of death is of significant importance for predicting prognosis and improving resource utilization.

In this study, we compared the epidemiology and search for risk factors of community-acquired pneumonia (CAP) or hospital-acquired pneumonia (HAP).

Access this article online

Quick Response Code:

Website: www.prccm.org

DOI: 10.4103/prcm.prcm_7_23

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Submitted: 26-10-2022 **Revised:** 03-03-2023
Accepted: 04-03-2023 **Published:** 21-06-2023

How to cite this article: Wang P-Y, Tseng W-C, Wu E-T, Lu FL, Wang C-C. Epidemiology and risk factors of pediatric pneumonia in a tertiary center in Taiwan. Pediatr Respirol Crit Care Med 2023;7:28-32.

Materials and Methods

Patients with pneumonia were reviewed from the medical records in the database of this institution from 2012 to 2013. The inclusion criteria were as follows:

(1)Age at diagnosis <18 years
(2)Patients diagnosed with pneumonia
(3)Patients who did not have chronic lung disease or other congenital airway anomalies

The following parameters were collected and analyzed: age, sex, weight, underlying diseases, initial laboratory data including complete blood count, differential count and C-reactive protein (CRP), pediatric intensive care unit (PICU) stay, and 28-day mortality.

The study protocol adhered to the ethical guidelines of the 1975 Declaration of Helsinki. This study was approved by the Research Ethics Committee of National Taiwan University Hospital (number: 201403063RINB).

Statistics

Variables are summarized as mean ± standard deviation, median and interquartile range, or numbers and percentages, as appropriate. The values were analyzed using Student's *t* test, chi-square test, and analysis of variance for repeated measures when appropriate. To explore the factors related to the outcomes, univariate correlates with $P < 0.2$ in the logistic regression analysis were selected for the multivariate regression model. Statistical analyses were conducted using SAS University Edition and SPSS (version 20.0 for Windows, SPSS Inc., Chicago, IL, USA). Statistical significance was set at $P < 0.05$.

Results

Reviewing medical records from the database of our institution from 2012 to 2013, we identified 548 patients with 598 episodes of pneumonia (310 men and 288 women), who were admitted to our hospital. The mean age at admission were 59.6 ± 1.95 months, and the average lengths of stay were 11.4 ± 0.70 days. Five hundred and thirty episodes were identified as CAP and the remaining 68 episodes were determined to be HAP. Patients with CAP had a significantly shorter length of stay than those with HAP (8.2 days vs. 36.5 days, $P < 0.001$, Table 1). Most patients with CAP do not have any underlying disease. The most common comorbidities in patients with CAP were neurological disease and atopic history (57 and 50 episodes, respectively). Seventeen percent of patients experienced ICU treatment. However, in patients with HAP, 26 episodes (29/68 = 42.6%) experienced ICU admission during the treatment course. Cardiovascular disease was the most common comorbidity (16 episodes). Hemato-oncology and neurological diseases were the second most common (13 episodes each). The most commonly identified pneumonia sites were bilateral pneumonia and right-sided pneumonia in both the CAP and HAP groups. White blood cell counts were similar between the two groups, but band form plus neutrophil percentage and CRP were higher in the CAP group. There was no significant difference in extracorporeal membrane oxygenation machine use or video-assisted thoracoscopic surgery performance in either group. The overall mortality rate was 0.037, and the mortality rate was significantly higher in the HAP group ($P < 0.001$).

In the CAP group, 90 episodes were admitted to the ICU during the hospital stay. The length of ICU stay ranged

Table 1: Demographic characteristics of all patients and comparison between CAP and HAP in the years 2012–2013

	All patients ($N = 598$)	CAP ($N = 530$)	HAP ($N = 68$)	*P* value
Age (month)	61 ± 48	58 ± 44	66 ± 67	0.224
Weight (kg)	19.7 ± 14.7	16.7 ± 3.7	13 ± 6.5	0.858
Male/female ratio	0.9	0.9	0.7	NS
Presence of underlying disease*, *n* (%)*	273 (45.7%)	218 (41.1%)	55 (80.9%)	<0.001
Number of underlying diseases	1.6 ± 2	1.5 ± 2	2.6 ± 2	<.001
Pneumonia site	Right and bilateral	Right and bilateral	Right and bilateral	NS
White blood cell count (per μL)	11942 ± 7204	11853 ± 6783	12702 ± 10145	0.52
Band + segment percentage	61.7 ± 20.5	62.4 ± 20.2	56.0 ± 22.6	0.035
C-reactive protein (mg/dL)	5.5 ± 7.8	5.8 ± 8.0	3.1 ± 5.3	0.001
Admission to ICU, *n* (%)	119 (19.9%)	90 (17.0%)	29 (42.6%)	<0.001
ECMO use (days)	0.01 ± 0.09	0.01 ± 0.09	0.01 ± 0.12	0.542
VATS, *n* (%)	20 (3.3)	19 (3.6)	1(1.5)	0.362
Length of ICU stay (days)	2.9 ± 9.2	2.0 ± 6.9	10.1 ± 18.0	<0.001
Length of hospital stay (days)	11.4 ± 17.1	8.2 ± 10.5	36.5 ± 31.5	<0.001
Mortality, *n* (%)	22 (3.7)	12 (2.3)	10 (14.7)	<0.001

Data are presented as mean ± standard deviation

CAP = community-acquired pneumonia, ECMO = extracorporeal membrane oxygenation, HAP = hospital-acquired pneumonia, ICU = intensive care unit, NS = not significant, VATS = video-assisted thoracoscopic surgery

* Underlying diseases included heart disease, hemato-oncology, allergy, gastrointestinal, neurological, and others

from 1 to 68 days. Patients who needed ICU care had a significantly longer length of hospital stay than those who did not (22.5 vs. 5.3 days, $P < 0.001$). Although most patients had no underlying diseases, the underlying diseases were significantly different between those who required ICU admission and those who did not. Neurological diseases were the most common comorbidity in those who needed ICU admission (23 episodes), and atopic diseases were the most common comorbidity in those who needed only general care (49 episodes).

In the univariate regression analysis, age, presence of underlying disease, CRP and band form plus neutrophil count were significant predictors of admission to ICU among patients with CAP. In the multivariate regression model, only the presence of underlying disease, and CRP were independent predictors of admission to ICU [Table 2]. Age, presence of underlying disease, CRP, and band form plus neutrophil count predicted mortality in univariate regression analysis of patients with CAP, but only the presence of underlying disease and CRP remained in multivariate regression [Table 3]. For patients with HAP, no predictor was found for admission to ICU. CRP was the only factor which could predict mortality in both univariate and multivariate regression analyses.

In the pathogen analysis, pathogens were identified in 223 (37.3%) pneumonia events. Respiratory syncytial virus (15.7%), *Staphylococcus aureus* (15.7%), influenza virus (13.1%) and *Pseudomonas aeruginosa* (12.0%) were the leading pathogens [Figure 1].

Discussion

We found that patients with HAP had significantly longer lengths of hospital and PICU stays than those with CAP. A higher mortality rate was noted in the HAP group [Table 1]. Additionally, high CRP and presence of underlying disease were risk factors of complications in patients with CAP. High CRP could only predict mortality in patients with HAP.

The retrospective study results showed that pneumonia developing in the hospital in children caused longer hospital and PICU stays, which was compatible with a previous study in adults.[11] This may be explained by the medical advances in recent years, which shortened the treatment duration of uncomplicated CAP cases.

In this study, 17% of patients with CAP experienced ICU treatment. Commonly evaluated risk factors which predicted worse outcomes are important for treating children from communities. We found that the presence of underlying disease, CRP elevation and higher band form mature neutrophils are independent risk factors of ICU admission in multivariate analysis. In a large-scale study in China,[12] younger ages of less than one year, congenital heart disease, prematurity, respiratory distress symptoms, abnormal WBC, and CRP results were risk factors for ICU treatment. The results were similar to our results. In addition, CRP and the presence of underlying disease were risk factors for mortality in our study. CRP is an inflammatory biomarker, which would rise in many bacterial infections.[13] In a recent study,[14] CRP is

Table 2: Odds ratios from univariate and multivariate logistic regression model of risk factors of patients with community-acquired pneumonia for admission to intensive care unit

	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Age	1.755	1.191–2.585	**0.004**			0.419
Female			0.164			
Underlying disease	2.138	1.351–3.384	**0.001**	2.882	1.725–4.816	**<0.001**
C-reactive protein	1.065	1.039–1.092	**<0.001**	1.073	1.045–1.103	**<0.001**
White blood cell count			0.119			
Band + segment	1.021	1.008–1.035	**0.001**	1.014	1.001–1.028	**0.036**

CI = confidence interval, OR = odds ratio, bold value means significant

Table 3: Odds ratios from univariate and multivariate logistic regression model of risk factors of patients with community-acquired pneumonia for mortality

	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Age	0.429	0.205–0.898	**0.025**			0.917
Female			0.937			
Underlying disease	7.452	1.616–34.356	**0.010**	10.524	2.147–51.597	**0.004**
C-reactive protein	1.064	1.017–1.113	**0.007**	1.082	1.031–1.135	**0.001**
White blood cell count			0.069			
Band + segment	0.975	0.951–0.999	**0.044**			0.08

CI = confidence interval; OR = odds ratio, bold value means significant

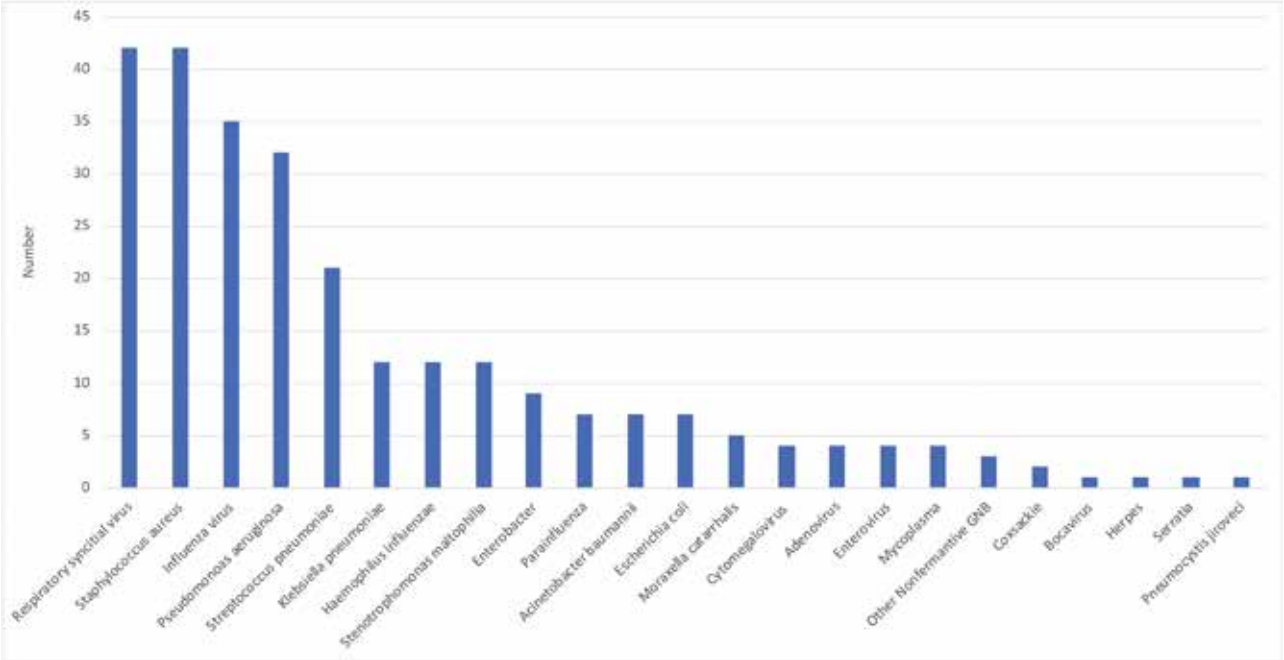

Figure 1: Pathogen distribution of hospitalized children with pneumonia

significantly associated with several pediatric pneumonia complications, including hospitalization, admission to ICU, and parapneumonic effusion. A multi-center study in Taiwan also had a similar finding.[2] Thus, CRP is a useful clinical marker in treating children with pneumonia.[15]

Patients with HAP had more complicated courses including more admissions to ICU, longer length of stay and higher mortality than those with CAP. A recent Spanish study reported similar findings.[16] We could not find a significant risk factor for admission to ICU, while CRP was still a risk factor for mortality. Patients having HAP often had underlying diseases which were being treated in hospital, and HAP was a complication during the treatment course. Thus, the prognosis was mainly affected by the underlying diseases.

In Taiwan, the most common etiologic agents of CAP in children included respiratory syncytial virus, mycoplasma, and *S. pneumoniae.*[17] In a recent multi-center study,[2] *S. pneumoniae* and *Mycoplasma pneumoniae* are the two most common pathogens, and adenovirus is the most common virus. Respiratory syncytial virus is strongly associated with children under 2 years of age. In this study, respiratory syncytial virus and *S. pneumoniae* were also common, but mycoplasma was not the leading pathogen, instead, *S. aureus* and *P. aeruginosa* were quite common. Pathogen identification was not routinely performed in mild cases; on the other hand, it was crucial in more severe pneumonia. Thus, the pathogen identified in this study might be affected by the severity of the disease. Nevertheless, it reflected the pathogens which our institution commonly encountered and treated.

Our study has some limitations. First, it was a retrospective study conducted in a single tertiary center in a metropolitan city, so the data may not reflect the whole picture of Taiwan. Second, we recruited only hospitalized patients, so the pathogen distribution may be skewed by the severity. Studies which enroll not only hospitalized patients but also cases from out-patient clinic are needed to clarify the epidemiology of pneumonia pathogens.

Conclusion

In this study, we found that patients with HAP had significantly longer lengths of hospital and PICU stays than those with CAP. CRP and the presence of underlying diseases were independent risk factors of admission to ICU and mortality in patients with CAP; however, no significant risk factor was found for admission to ICU in patients with HAP. Respiratory syncytial virus, *S. aureus,* and influenza virus were the most commonly identified pathogens.

Financial support and sponsorship

This study was supported by grants from National Taiwan University Hospital, grant number: NTUH.104-N2924.

Conflicts of interest

There are no conflicts of interest.

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Original Article

Pneumomediastinum Following Immunization of BioNTech COVID-19 Vaccine: a Coincidence?

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Abstract

Background: To build immunity against the pandemic severe acute respiratory syndrome coronavirus-2 infection in adolescents, wide-ranging immunization with BioNTech (BNT) vaccine was initiated in September 2021 in Taiwan. Some adverse events are, therefore, reported after vaccination. Herein, we stated a case series with uncommon pneumomediastinum after BNT vaccination. **Materials and Methods:** This study retrospectively enrolled adolescents, who being diagnosed to have pneumomediastinum, during the 3-month period (between September 22, 2021, and December 22, 2021). Clinical information, such as clinical symptoms, radiographic characteristics, and clinical outcomes, were further analyzed. **Results:** A total of eight adolescents developed pneumomediastinum during the 3-month period after BNT vaccination. The time interval between pneumomediastinum and vaccination showed bimodal peak (around 10 and 60 days after BNT vaccination). Significant Macklin effect can be sketched in radiographic images of six patients. **Conclusion:** Several cases of pneumomediastinum were found in adolescents after BNT vaccination. The precise association is needed for further investigation.

Keyword: BNT vaccine, COVID-19, pneumomediastinum, SARS-CoV-2

Introduction

Pneumomediastinum is a situation of free air found in the soft tissue space of mediastinum. According to the etiology, it can be divided into two categories: spontaneous and secondary. Secondary pneumomediastinum usually resulted from the aerodigestive tract injury after trauma, surgical or medical procedure.[1] However, spontaneous pneumomediastinum (SPM) is defined by the occurrence of pneumomediastinum without any preceding injury as being described above. Pervious literature review showed that the incidence of pediatric SPM revealed a bimodal peak. The highest peak was found between 6 months and 3 years of age, and the lower peak was located at the age of adolescence.[2] Valsalva maneuver, that being triggered by bronchospasm, cough, vomiting, foreign body aspiration, or physical exercise, was considered to result in the Macklin effect in children with SPM.[2] The pathophysiological mechanism of Macklin effect was described by Macklin *et al*.[3] in 1944. It demonstrated a radiological characteristic that showed the air-collection dissects around bronchovascular sheath toward hilum and into mediastinum.

A novel coronavirus which later designed severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) occurred in China at the end of 2019, significant morbidity and mortality then ensued after the global coronavirus disease 2019 (COVID-19) pandemic. Thanks to the measures of Central Epidemic Command Center (CECC) that including extensive case detection, detailed contact tracing, strict immigration control, and mandated self-quarantine, Taiwan keeps among the lowest test-positivity and mortality rates globally.[4] Since September 2021,

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Submitted: 02-03-2023 **Accepted:** 29-03-2023
Published: 21-06-2023

Access this article online

Quick Response Code:

Website: www.prccm.org

DOI: 10.4103/prcm.prcm_6_23

How to cite this article: Lai S-H, Liao S-L. Pneumomediastinum following immunization of BioNTech COVID-19 vaccine: A coincidence? Pediatr Respirol Crit Care Med 2023;7:33-6.

CECC approved BioNTech (BNT) COVID-19 vaccine for adolescents elder than 12 years old and later initiated the first shoot of BNT vaccine for this population on September 22, 2021.[5] However, some adverse events were then reported after this wide-ranging vaccination. Herein, we demonstrated a case series with uncommon SPM event after BNT vaccination.

Materials and Methods

This retrospective study was performed after the approval of institutional review board of Chang Gung Memorial Hospital at Linkou (IRB No. 202200806B0). During the 3-month period (between September 22, 2021, and December 22, 2021), inpatient and outpatient adolescents, between 12 and 18 years old, were included for chart review. Those, who being diagnosed to have pneumomediastinum, were enrolled in this case-series study. The demographic data, symptoms, radiographic characteristic, and clinical outcomes (including treatment and length of hospital stay) were further analyzed.

Pneumomediastinum was confirmed by air collection in mediastinal, prevertebral, and subcutaneous space in computed tomography (CT) or radiography. SPM was further diagnosed by the excluded other secondary etiology by history-taking, bronchoscopy, or barium esophagography.

Patient characteristics were recorded as means and standard deviations. Histogram and all analyses were performed using Prism 8 for macOS version 8.2.1 (San Diego, California).

Results

There were eight patients who developed pneumomediastinum during the 3-month period after the first dose of BNT vaccine. As shown in Table 1, there were seven boys and one girl, with a mean age of 14.8 years (12–16.7 years in range). Their body weight and body height were also disclosed in Table 1. The mean body mass index is 18.6 (15–23.9 in range). The presenting symptoms of these patients were shown in Table 2. Chest pain (6/8) and swallowing discomfort (5/8) are among the commonest clinical presentations, but none of them presented with subcutaneous emphysema.

Tracing back the underlying causes, all these eight patients have ever received BNT vaccination, but none had respiratory illness (such as asthma exacerbation and respiratory infection) before the onset of pneumomediastinum. SARS-CoV-2 polymerase chain reaction (PCR) of nasopharyngeal swabs was negative in all patients. The mean time interval between the onset of pneumomediastinum and vaccination of BNT is 31.6 days (7–59 days in range). After further analyzing the histogram of this time interval, bimodal peak was found in around 10 and 60 days after BNT vaccination [Figure 1]. All patients were under observational treatment and recovered uneventfully.

The diagnosis of pneumomediastinum was mostly confirmed only by chest radiography (6/8), chest CT was further performed in two patients. Barium esophagography was done in five patients to exclude esophageal perforation. Reviewing the radiographic characteristics of these patients [Figure 2].

Discussion

In the history of vaccine development, live, killed, and subunit vaccines have been used to control the spread of infectious diseases. After the pandemic of COVID-19, the mRNA technology was first applied to develop the vaccines

Table 2: Clinical symptom, outcome, and radiographic characteristics

Case No.	Chest pain	Swallowing discomfort	Macklin effect	Hospital days
1	+	+	+	3
2	+	+	+	1
3	+	−	−	0
4	−	+	+	3
5	+	+	−	3
6	+	−	+	3
7	+	−	+	2
8	+	+	+	2

Table 1: Demographic data of patients

Case No.	Gender	Age (years)	BW (kg)	BH (cm)	BMI	BMI percentile	Onset interval after BNT (days)
1	M	16.2	67	183	20	15–50	8
2	M	14.3	49	162	18.7	15–50	22
3	M	15	38.8	160.5	15.1	<3	7
4	M	14.7	65	165	23.9	85–97	41
5	M	15	55	176	17.8	3–15	50
6	F	16.7	44	157	17.9	3–15	59
7	M	12	34.8	152.4	15	3–15	8
8	M	14.7	62	175	20.2	50–85	59
Mean (SD)		14.8 (1.4)	52.0 (12.2)	166.4 (10.6)	18.6 (1.0)		31.6 (23.1)

BH = body height, BMI = body mass index, BW = body weight, SD = standard deviation

against SARS-CoV-2. After the allowance of emergency use authorization by Food and Drug Administration in December 2020, billions of doses of BNT vaccine have been administered globally. The adverse events have been reported by several literature,[6,7] and chest pain was among the common constitutional complaints after immunization in adolescent population.[8] However, no definite diagnosis was confirmed for the etiology of chest pain. Herein, this case-series report indicated pneumomediastinum-associated chest pain can be a possible adverse event after the immunization of BNT vaccine.

From the pathogenetic point of view, a pneumomediastinum can be resulted from injury of aerodigestive tract or air dissection of bronchovascular sheath (Macklin effect). The Macklin effect indicated a process starting with alveolar rupture followed by sequent separation of bronchovascular sheath even toward hilum and mediastinum.[3] Pneumomediastinum, which resulted from this pathogenesis after excluding perforation of aerodigestive tract, has been categorized as "spontaneous" origin. Although chest CT was only performed in two patients, the Macklin effect could be recognized in six patients after excluding the etiology of aerodigestive tract injury. This result hints the pathogenesis of SPM after BNT vaccination has closely related to alveolar rupture.

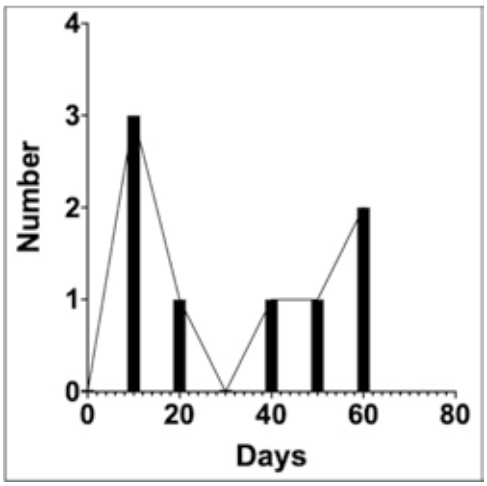

Figure 1: Histogram of time interval between SPM onset and BNT vaccination

Since the beginning of COVID-19 pandemic, several cases with complicated pneumomediastinum have been described in patients with COVID-19 pneumonia.[9,10] A recent study from New York state revealed that the incidence of pneumomediastinum even increased more than 6–7 folds compared with non-COVID-19 pneumonia.[9,11] Nevertheless, the comorbid pneumomediastinum did not attribute to poorer clinical outcomes, namely higher mortality rate and longer hospital stay. However, the pathophysiological process of pneumomediastinum in patients with COVID-19 is unclear. Lemmers's study showed that its etymology may be increased lung frailty, instead of barotrauma mechanism, since significant Macklin effects were observed in radiographs of COVID-19 patients with pneumomediastinum.[11] Although similar Macklin effects were also found in most patients in this study, the mechanism of pneumomediastinum after COVID-19 pneumonia and BNT vaccination is still vague.

Although serious outcome was rarely identified in phase 3 trials because of limited sample size and restrictive trial participants, several suspected adverse events have been reported after global vaccination of BNT vaccine. The nationwide study of Israel revealed that BNT vaccine was not related to a higher risk of adverse events observed, but it was mildly associated with elevated risk of myocarditis.[12]

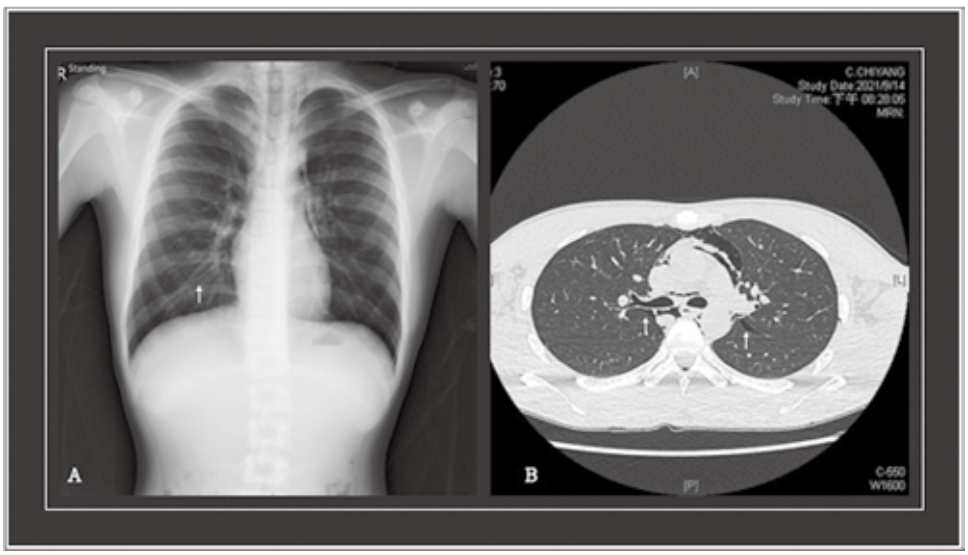

Figure 2: Air dissection along bronchovascular sheath toward hilum and mediastinum, namely Macklin effect (indicated with arrows), was shown in chest radiography (A) and computed tomography (B)

However, some thoracic and mediastinal adverse events have still been reported in European and Korean data.[13,14] It is unclear whether pneumomediastinum has been ever reported among these adverse events of thorax and mediastinum. In this study, we report a possible adverse effect of thoracic and mediastinal systems after the inoculation of BNT vaccine.

There are some limitations in this study. First, the findings of this case-series study might not exactly reflect population-based results. However, the hospitalizations due to pneumomediastinum really increased after the period of BNT vaccination. It would need population-based investigation to further quantify the increasing trend. Second, despite Macklin effect was found in the majority of our patients, it is difficult to conclude the direct insult of alveolar rupture after BNT vaccination. Further delicate experimental investigation will be needed to clarify the mechanism. Third, bimodal peak was found in around 10 and 60 days after BNT vaccination. However, it is difficult to know if SPM can occur later because this study only enrolled cases in the 3-month period.

In conclusion, although the immunization of BNT vaccine is quite safe, few adverse events of thoracic system are still reported. Among these events, SPM should be considered especially in an adolescent complaining chest pain. And, the precise association between pneumomediastinum and BNT vaccination is needed for further investigation.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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Failed Intubation in a COVID-Positive Syndromic Neonate

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Abstract

Videolaryngoscopy (VL), supraglottic devices (SGDs), and high-flow nasal cannula (HFNC) have been introduced in the algorithms for the management of difficult airway in neonates but dysmorphism in various anatomical sites such as nasopharynx, oropharynx, mandible, maxilla, larynx, trachea, and cervical spine limit the use of the above equipment. We report the airway management in a neonate in which retrognathia, microtia, microstomia, and macroglossia limited visualization of glottis with a VL; cleft palate precluded the use of SGD and choanal atresia precluded the use of HFNC. Concomitant infection with severe acute respiratory syndrome coronavirus 2 necessitated a need to limit repeated airway manipulations. A timely decision in favor of a surgical airway, thus, prevented hypoxia and its related consequences.

Keywords: Choanal atresia, COVID-19, difficult airway, supraglottic devices (SGD), syndromic neonate, videolaryngoscope (VL)

Introduction

The incidence of difficult tracheal intubation in neonates and infants is reported to be 5.8%.[1] The incidence is higher but variable in neonates with various syndromes namely Pierre-Robin, Treacher-Collins, and Goldenhar. The utility of other oxygenation devices such as supraglottic airways and high-flow nasal cannula (HFNC) is limited in patients with craniofacial dysmorphism. Airway management practice is further modified in patients with coronavirus disease 2019 (COVID-19) infection to minimize transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Protected intubation (use of personal protective equipment) further decreases the performance/efficiency of the anesthesiologist during laryngoscopy and is of major concern in a "Cannot intubate" neonate.[2,3]

Case Report

A 2.2 kg, 3-day-old neonate was admitted with respiratory distress in pediatric emergency during the first wave of the pandemic after a full-term elective cesarean section secondary to nonprogress of labor. The APGAR scores were 7 and 9 at 1 and 5 min after birth. The baseline respiratory rate was 68/min, oxygen saturation was 40%–55%, and bilateral air entry was equal on auscultation. The neonate had dysmorphic facial features including retrognathia, cleft palate, choanal atresia, absent thumb, microtia, microstomia, and large tongue. A presumptive diagnosis of CHILD (congenital hemidysplasia with ichthyosiform erythroderma and limb defects)/CHARGE (Coloboma, heart defects, atresia choanae, growth retardation, genital abnormalities, and ear abnormalities) syndrome was made.[4,5] Nasal continuous positive airway pressure (CPAP) was administered, which increased oxygen saturation to 65%–75%.

Nasopharyngeal samples for GeneXpert and SARS-CoV-2 reverse transcription-polymerase chain reaction were sent to the laboratory immediately after primary stabilization of the neonate, which were subsequently reported as positive. The patient was shifted to a dedicated COVID care block where a decision to intubate the child was made by the neonatologist in view of low partial pressures of oxygen with nasal CPAP. However, all three intubation attempts made by the neonatologist failed; Cormack-Lehane grade

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Website: www.prccm.org

DOI: 10.4103/prcm.prcm_1_23

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Submitted: 13-01-2023 **Revised:** 24-03-2023
Accepted: 29-03-2023 **Published:** 21-06-2023

How to cite this article: Samra T, Chander A, Nair RS. Failed intubation in a COVID-positive syndromic neonate. Pediatr Respirol Crit Care Med 2023;7:37-9.

was 4 on direct laryngoscopy. The anesthesiologist posted in the "COVID operation theater (OT)" was notified, and a pediatric bronchoscope, pediatric laryngeal mask airway (LMA, I-gel) size 1, and videolaryngoscope (VL) (C-MAC®, Karl Storz Video Macintosh Laryngoscope) were made available. The patient was taken inside OT, all monitors attached, and bag and mask ventilation was done using 100% oxygen. The patient was put under induction with inhalational agent Sevoflurane. No sedative was given as premedication as difficult airway was anticipated. Intravenous access was taken in the left upper limb with 22G cannula. After achieving adequate depth of anesthesia, bag and mask ventilation was done, and no difficulty was encountered. Laryngoscopy was done with VL but glottis could not be visualized. A second intubation attempt was made by a senior anesthesiologist but it led to desaturation. LMA (I gel of size 1) was inserted but a proper seal could not be established. HFNC was also available but its use was precluded in view of choanal atresia. The benefits and risks of a surgical airway, that is, tracheostomy were weighted against bronchoscopy-assisted intubation. Repeated intubations had caused airway trauma and the presence of blood in the airway precluded the use of a bronchoscope. Failure in the placement of an LMA prevented its use as a conduit for bronchoscopy-assisted intubation. Minimization of aerosol generation was also warranted in view of COVID-19 infection. Thus, an early decision for tracheostomy was taken, and the neonate was subsequently transferred after tracheostomy to the neonatal intensive care in the dedicated COVID block.

Discussion

Feasibility and merits/demerits of different airway management techniques namely awake intubation, intubation after general anesthesia, preservation of spontaneous ventilation, use of invasive techniques of intubation, use of VL, fiberoptic bronchoscope, and HFNC are to be considered after taking into account the various craniofacial and mandibulo-facial anomalies present in a syndromic neonate. This is followed by the formulation of a primary and alternative strategy for intubation in case the former fails.

Success rate of LMA in syndromic neonates is low with conventional techniques.[6] Ease of insertion of an LMA and its stability in patients with cleft palate is a matter of debate. The use of HFNC and transnasal humidified rapid-insufflation ventilatory exchange increases the apnea time and is, thus, recommended for apneic oxygenation in neonates with difficult airway. However, choanal atresia is a relative contraindication.[7,8] Fiberoptic bronchoscopy is the gold standard for difficult airway management but success is limited in a neonate with airway trauma secondary to multiple intubation attempts.

In our case, a presumptive diagnosis of CHARGE/CHILD syndrome was made. It is reported that 50% of these patients require tracheotomy not only for their associated airway abnormalities but also for the prevention of chronic aspiration of the retained saliva due to associated swallowing disorder.[9] Thus, an early decision for a surgical airway was taken in this case.

Another reason for minimizing the airway manipulations was the presence of COVID-19 infection. Research suggests that only about 2%–5% of infants born to women with COVID-19 near the time of delivery test positive for the virus in the days after birth.[10] Early testing may lead to false positives (e.g., if the neonate's nares, nasopharynx, and/or oropharynx are contaminated by SARS-CoV-2 RNA in maternal fluids) or false negatives (e.g., RNA may not yet be detectable immediately after exposure following birth). Intrauterine, intrapartum, or peripartum transmission from the mother in our case is refuted as the latter tested negative for COVID-19. Transmission of SARS-CoV-2 in this neonate is thought to have occurred through the respiratory droplets during the postnatal period when the neonate was exposed to a caregiver with SARS-CoV-2 infection.

Conclusion

Bronchoscopy-assisted intubation is the gold standard in a difficult airway of a COVID-positive neonate provided the anesthesiologist is using the highest level of personal protective equipment. But the availability of a neonatal bronchoscope and the expertise to perform intubation with the same may not be available at all centers. Adequate preoxygenation and repeat intubation attempts or use of a supraglottic airway device with the HFNC in place increases time to intubate and prevents desaturation and, thus, should be preferred but the presence of a cleft palate and choanal atresia limits the same. Prolonged and repeated airway manipulations in a COVID-positive syndromic neonate lead to aerosolization of SARS-CoV-2, and thus, an early decision for a surgical airway is advocated.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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