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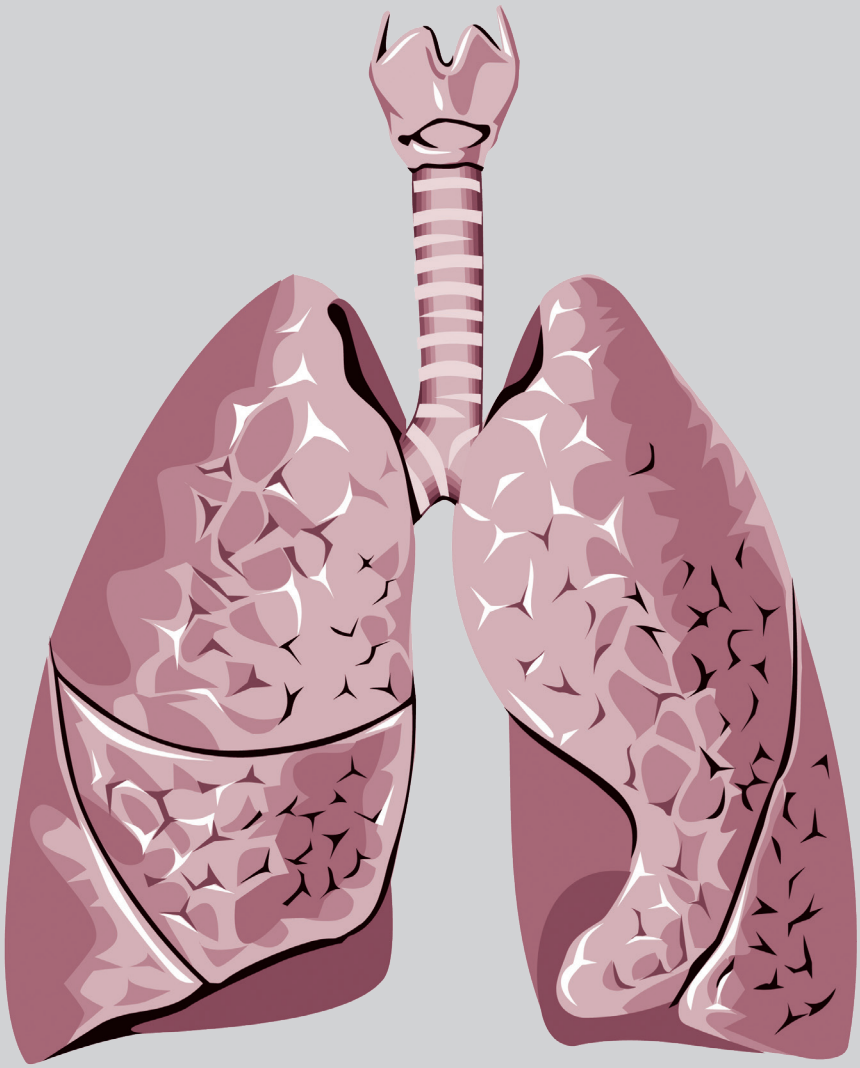

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CONTENTS

Impact of High Eosinophil Counts on Clinical Outcomes of COPD Patients Who Have Received Inhaled Corticosteroids Therapy

Tsu-Chuan Li[1], Chen-Chuan Hsu[1], Shih-Wei Huang[1], Bing-Chen Wu[1], Hao-Ming Wu[1], Shu-Min Lin[1, 2, 3, 4, *]

Introduction: COPD patients on inhaled corticosteroids (ICS)-based therapy typically have more severe profiles. Although ICS is recommended for those with high blood eosinophils, its effectiveness in reducing exacerbations is uncertain. This study evaluated clinical outcomes of COPD patients on ICS, focusing on an absolute eosinophil count (AEC) ≥300 cells/μL.

Methods: A retrospective study was conducted at Linkou Chang Gung Memorial Hospital (2014–2020) using GOLD criteria. Patients underwent tests including a 6-minute walk test, echocardiography, pulmonary function tests, and blood analyses. They were divided into ICS (+) and ICS (–) groups, with the ICS group further stratified by AEC. Outcomes measured over 3 years included acute exacerbations (AEs), emergency visits, hospitalizations, and mortality. Logistic regression identified risk factors for AEs.

Results: Among the 142 patients, the ICS (+) group (n = 48) had worse clinical profiles than the ICS (–) group (n = 94), including higher mMRC scores, elevated AEC and BODE indices, poorer lung function, and greater FEV_1 decline. Within the ICS-treated group, patients with AEC ≥300 cells/μL (n = 24) experienced more AEs. Multivariate analysis identified high AEC (OR 16.074, $p = 0.004$) and lower FEV_1 (OR 0.923, $p = 0.005$) as independent predictors of AEs.

Conclusion: An elevated AEC (≥300 cells/μL) independently predicts higher AE risk in COPD patients on ICS, suggesting that ICS-based therapy may be insufficient for high-risk patients and that personalized treatments are needed. ***(Thorac Med 2026; 41: 95-104)***

Key words: eosinophil, COPD, inhaled corticosteroids, outcomes

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Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive and debilitating respiratory disorder that remains one of the leading causes of morbidity and mortality worldwide [1]. Its impact on public health is profound, not only because of the chronic deterioration in lung function and quality of life [2], but also due to the significant socioeconomic burden associated with frequent hospitalizations and long-term care [3-4]. Acute exacerbations (AE) of COPD (AECOPDs) are pivotal events that accelerate disease progression, further impair lung function, and substantially increase the risks of emergency department visits, hospitalizations, and mortality. Among the various factors that predispose patients to AECOPDs, a prior history of exacerbation stands out as one of the most reliable predictors of future adverse events and overall prognosis [5-6].

While neutrophilic inflammation has traditionally been viewed as the hallmark of COPD, approximately 20%–40% of COPD patients exhibit an eosinophilic phenotype [7-8]. This subgroup is characterized by a type-2 inflammatory response, which shares similarities with the inflammatory processes observed in asthma [9]. Elevated blood eosinophil counts have been proposed as a biomarker not only for predicting the risk of AECOPDs, but also for identifying patients who may benefit from inhaled corticosteroid (ICS) therapy [10-12]. However, despite the current guideline recommendations that favor ICS use in patients with higher eosinophil levels [13-15], there remains a lack of consensus regarding the association between elevated eosinophils and other clinical outcomes, such as emergency visits, hospitalization, and mortality.

Previous studies have produced conflicting results regarding the prognostic implications of elevated blood eosinophils in COPD. Some investigations suggest that higher eosinophil levels may predict an increased risk of exacerbation and even mortality, while others have reported more modest or even inverse relationships [16-17]. Many of these discrepancies could be attributed to study designs that rely heavily on population-based data or insurance claims, which often lack detailed clinical information such as baseline characteristics, lung function measurements, and exercise capacity assessments.

To address these gaps, our study retrospectively examined a cohort of COPD patients who underwent comprehensive evaluations—including 6-minute walk tests (6MWTs), echocardiography, pulmonary function tests, and blood tests—over a 3-year period at a single tertiary care center in Taiwan. By integrating detailed clinical parameters with longitudinal outcome data, we aimed to elucidate the impact of an elevated absolute eosinophil count (AEC) ≥300 cells/μL on a spectrum of outcomes, including AECOPDs, emergency room (ER) visits, hospitalizations, and mortality, among patients receiving ICS therapy.

Methods

Study Design and Cohort

This single-center retrospective cohort study included patients with COPD who underwent comprehensive evaluations—including 6MWTs, echocardiography, and blood tests—over a 3-year period at Linkou Chang Gung Memorial Hospital, Taiwan, from January 2014 to December 2020. COPD was diagnosed by pulmonologists according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD)

criteria, defined as a post-bronchodilator FEV1/FVC ratio of <0.70, the presence of respiratory symptoms (e.g., persistent dyspnea, chronic cough, or sputum production), and a smoking history of >10 pack-years or exposure to other risk factors (such as occupational dust) [18]. Patients with a current or prior diagnosis of asthma or those lacking AEC data were excluded.

Data Collection

Data was collected from the patients' electronic medical records. The variables included baseline characteristics; comorbidities (e.g., hypertension, coronary artery disease, heart failure, atrial fibrillation, diabetes mellitus, and chronic kidney disease); and pulmonary function test results (FVC, FEV1, and FEV1/FVC) at baseline (enrollment) and at the 3-year follow-up. Exercise capacity was assessed using the 6MWT, with measurements recorded for the 6-min walk distance (6MWD), resting oxygen saturation, nadir oxygen saturation, and the presence of exercise-induced dyspnea. Clinical scores such as the modified Medical Research Council (mMRC) dyspnea scale and the BODE index (body mass index, airflow obstruction, dyspnea, and exercise capacity) were also documented. Information regarding maintenance medications prescribed for at least 3 months—including ICSs—was recorded. The 3-year follow-up period was counted from the time of COPD diagnosis. ICS use was determined at the patient's initial enrollment visit during the study period, rather than based on whether the patient ever used ICS during the entire follow-up. An eosinophilic phenotype was defined as having a peripheral blood AEC of ≥300 cells/μL at any time within the preceding year [19].

Covariates and Outcomes

The primary clinical outcomes assessed during the 3-year follow-up included AECOPDs, ER visits, hospitalization episodes, and mortality. AECOPD was defined as an event requiring the prescription of systemic corticosteroids at an outpatient visit, an ER visit related to exacerbation, or hospital admission. ER visits and hospitalizations were considered COPD-related events. However, mortality was reported as all-cause mortality. In addition, data on ICS treatment was collected.

Statistical Analysis

Continuous variables are presented as mean ± standard deviation (SD) and were compared between groups using Student's t-test. Categorical variables were analyzed using the chi-square test. Logistic regression analysis was initially performed for each clinical outcome (AECOPDs, ER visits, hospitalization, and mortality) to identify potential risk factors. Since only the AECOPD outcome reached statistical significance, further analyses were focused on AECOPDs. Univariate logistic regression was performed to identify factors associated with AECOPDs, and variables with a p-value <0.1 were subsequently included in multivariate logistic regression models. The results are reported as odds ratios (ORs) with 95% confidence intervals (CIs), and a p-value <0.05 was considered statistically significant. All statistical analyses were conducted using IBM SPSS Statistics version 26.0 (SPSS Inc., Chicago, IL, USA).

Results

A total of 156 COPD patients who completed the 6MWT were enrolled. We excluded 14 patients because of missing AEC data. The remaining 142 COPD patients were eligible for

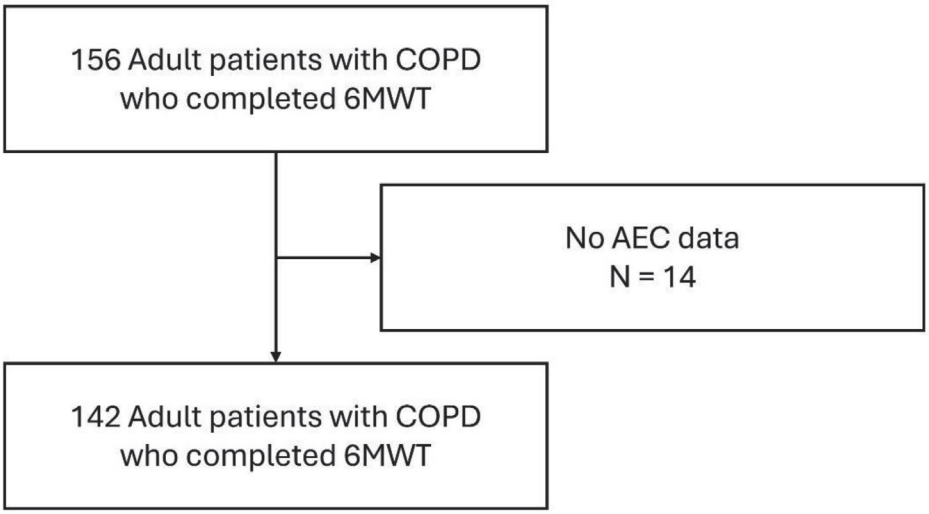

Fig. 1. Flow-chart of patient selection

analysis. Figure 1 provides the study flowchart. Based on ICS use, patients were divided into 2 groups: the ICS(+) group (n = 48) and the ICS(–) group (n = 94) (Table 1). Both groups were similar in age, gender, and BMI, and in smoking status and most comorbidities. However, the ICS(+) group had significantly higher mMRC scores (1.7 ± 0.8 vs. 1.0 ± 0.6, p = 0.001), AEC (323.7±296.0 vs. 172.9±153.5, p<0.001) and BODE indices (3.4 ± 1.8 vs. 2.3 ± 1.7, p = 0.001), along with poorer lung function, as demonstrated by lower FVC (%) (66.8 ± 15.6 vs. 74.0 ± 18.6, p = 0.017), lower FEV1 (L) (1.15 ± 0.49 vs. 1.39 ± 0.56, p = 0.010), lower FEV1 (%) (45.9 ± 16.9 vs. 56.2 ± 18.1, p = 0.001), and lower FEV1/FVC ratio (69.5 ± 16.1 vs. 78.4 ± 14.1, p = 0.002). In addition, the ICS(+) group exhibited a marked decrease in FEV1, which was observed 3 years later (1.12 ± 0.48 L vs. 1.40 ± 0.60 L, p = 0.003). Clinically, ICS(+) patients had significantly more AE episodes (4.2 ± 7.1 vs. 2.2 ± 3.3, p = 0.019), more ER visits (1.9 ± 3.4 vs. 0.6 ± 1.6, p = 0.003), more hospitalizations (1.4 ± 2.2 vs. 0.5 ± 1.2, p = 0.004), and higher all-cause mortality (20.8% vs. 6.4%, p = 0.010).

Further stratification by AEC was performed for the ICS(+) patients (Table 2). Patients with an AEC ≥300 cells/μL (n = 24) and those with an AEC <300 cells/μL (n = 24) were similar in terms of age, gender, BMI, most comorbidities, and lung function. A notable difference was observed in prior smoking status (p = 0.043). Regarding clinical outcomes (Table 3), the AEC ≥300 cells/μL subgroup experienced significantly more AE episodes (6.5 ± 9.0 vs. 1.9 ± 3.2, p = 0.023), while differences in ER visits, hospitalizations, and all-cause mortality were not statistically significant.

Univariate logistic regression analysis for AE among ICS(+) patients identified active smoking (OR 4.250, p = 0.049), AEC ≥300 cells/μL (OR 7.000, p = 0.009), a higher BODE index (OR 1.620, p = 0.044), lower FEV1 (%) (OR 0.945, p = 0.011), and lower FEV1 (3 years) (OR 0.153, p = 0.014) as significant fac-

Table 1. Baseline characteristics of patients with COPD stratified by the ICS.

	Total n=142	ICS(-) N=94	ICS(+) N=48	*P value*
Age, yr	69.8±9.2	69.9±9.7	69.6±8.4	0.843
Male gender	132 (93.0%)	87 (92.6%)	45 (93.8%)	0.792
Body mass index	24.0±4.0	23.7±3.7	24.7±4.5	0.192
Active smoker	56 (39.4%)	36 (38.3%)	20 (41.7%)	0.698
Prior smoker	74 (52.1%)	49 (52.1%)	25 (52.1%)	0.996
Comorbidities				
Hypertension	74 (52.1%)	52 (55.3%)	22 (45.8%)	0.284
Coronary artery disease (CAD)	16 (11.3%)	12 (12.8%)	4 (8.3%)	0.429
Heart failure (HF)	21 (14.8%)	14 (14.9%)	7 (14.6%)	0.961
Atrial fibrillation (Af)	16 (11.3%)	11 (11.7%)	5 (10.4%)	0.819
Diabetes mellitus	29 (20.4%)	21 (22.3%)	8 (16.7%)	0.428
Chronic kidney disease[#]	33 (23.2%)	24 (25.5%)	9 (18.8%)	0.365
AEC, cells/μL	223.9±223.3	172.9±153.5	323.7±296.0	<0.001
mMRC	1.2±0.7	1.0±0.6	1.7±0.8	0.001
BODE	2.7±1.6	2.3±1.7	3.4±1.8	0.001
FVC, L	2.29±0.71	2.36±0.76	2.15±0.60	0.078
FVC, %	71.6±17.9	74.0±18.6	66.8±15.6	0.017
FEV1, L	1.31±0.54	1.39±0.56	1.15±0.49	0.010
FEV1, %	52.7±18.3	56.2±18.1	45.9±16.9	0.001
FEV1/FVC, %	75.4±15.4	78.4±14.1	69.5±16.1	0.002
FEV1 (3 years after), L	1.30±0.57	1.40±0.60	1.12±0.48	0.003
FEV1 decline in 3 years[*], L	0.06±0.17	0.05±0.16	0.08±0.03	0.429
6MWD, meters	429.6±106.8	438.8±108.2	411.5±102.8	0.144
Resting heart rate (/min)	83.8±14.6	83.5±14.6	84.2±14.8	0.784
Resting O2 saturation, %	94.2±2.7	94.7±2.6	93.3±3.2	0.009
Nadir O2 saturation, %	88.4±6.1	89.5±5.3	86.5±6.9	0.011
Exercise-induced dyspnea	59 (41.5%)	35 (37.2%)	24 (50%)	0.144
Clinical Outcomes				
AE episodes	2.9±5.0	2.2±3.3	4.2±7.1	0.019
ER visits	1.1±2.5	0.6±1.6	1.9±3.4	0.003
Hospitalizations	0.8±1.6	0.5±1.2	1.4±2.2	0.004
Mortality	16 (11.3%)	6 (6.4%)	10 (20.8%)	0.010

Acronyms: AEC, absolute eosinophil count; CVD, cardiovascular diseases; mMRC, modified Medical Research Council; BODE, Body mass index, Airflow Obstruction, Dyspnea, and Exercise capacity; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; 6MWD, six-minute walk distance; AE, acute exacerbation; ER, emergency room

Chronic kidney disease (CKD) was defined as CKD stage 3 or higher.

* FEV1 (3 years after) represents the median FEV1 measured after 3 years of follow-up.

Table 2. Baseline Characteristics of COPD Patients Receiving Inhaled Corticosteroids Stratified by Absolute Eosinophil Count.

	Total n=48	**AEC <300/uL N=24**	**AEC ≥300uL N=24**	***P* value**
Age, yr	69.6±8.4	71.2±7.9	68.1±8.7	0.205
Male gender	45 (93.8%)	23 (95.8%)	22 (91.7%)	0.551
Body mass index	24.6±4.5	24.9±4.7	24.4±4.5	0.726
Active smoker	20 (41.7%)	7 (29.2%)	13 (54.2%)	0.079
Prior smoker	25 (52.1%)	16 (66.7%)	9 (37.5%)	0.043
Comorbidities				
Hypertension	22 (45.8%)	14 (58.3%)	8 (33.3%)	0.082
Coronary artery disease (CAD)	4 (8.3%)	2 (8.3%)	2 (8.3%)	1.000
Heart failure (HF)	7 (14.6%)	2 (8.3%)	5 (20.8%)	0.220
Atrial fibrillation (Af)	5 (10.4%)	4 (16.7%)	1 (4.2%)	0.156
Diabetes mellitus	8 (16.7%)	4 (16.7%)	4 (16.7%)	1.000
Chronic kidney disease[#]	9 (18.8%)	4 (16.7%)	5 (20.8%)	0.712
mMRC	1.5±0.8	1.3±0.7	1.6±0.8	0.266
BODE	3.4±1.8	3.3±1.6	3.4±2.0	0.938
FVC, L	2.15±0.60	2.19±0.72	2.10±0.46	0.604
FVC, %	66.8±15.6	65.8±17.7	67.9±13.5	0.636
FEV1, L	1.15±0.49	1.16±0.54	1.14±0.44	0.872
FEV1, %	45.9±16.9	44.9±16.5	46.9±17.6	0.686
FEV1/FVC, %	69.5±16.1	70.3±15.5	68.8±17.1	0.738
FEV1 (3 years after)[*], L	1.12±0.48	1.15±0.56	1.09±0.38	0.704
FEV1 decline in 3 years, L	0.08±0.18	0.06±0.17	0.09±0.18	0.677
6MWD, meters	411.5±102.8	412.5±117.8	410.4±87.8	0.944
Resting heart rate (/min)	84.2±14.8	82.1±12.1	86.4±17.0	0.320
Resting O2 saturation, %	93.3±3.2	92.8±3.8	93.8±2.5	0.290
Nadir O2 saturation, %	86.5±6.9	86.8±6.8	86.2±7.3	0.759
Exercise-induced dyspnea	24 (50.0%)	14 (58.3%)	10 (41.7%)	0.248

Acronyms: AEC, absolute eosinophil count; CVD, cardiovascular diseases; mMRC, modified Medical Research Council; BODE, Body mass index, Airflow Obstruction, Dyspnea, and Exercise capacity; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; 6MWD, six-minute walk distance

Chronic kidney disease (CKD) was defined as CKD stage 3 or higher.

* " FEV1 (3 years after)" represents the median FEV1 measured after 3 years of follow-up.

tors (Table 4). In multivariate analysis, only an AEC ≥300 cells/μL (OR 16.074; 95% CI: 2.409–107.247; $p = 0.004$) and lower FEV1 (%) (OR 0.923; 95% CI: 0.873–0.975; $p = 0.005$) remained independently associated with AE occurrence.

Kaplan–Meier analysis (Fig. 2) demonstrated that among ICS(+) patients, those with an

Table 3. The Relationship Between Clinical Outcomes and Absolute Eosinophil Count in COPD Patients Receiving Inhaled Corticosteroid Treatment.

Clinical Outcomes	Total n=48	AEC <300 cells/μL N=24	AEC ≥300 cells/μL N=24	*P* value
AE episodes	4.2±7.1	1.9±3.2	6.5±9.0	0.023
ER visits	1.9±3.4	1.2±3.3	2.6±3.5	0.156
Hospitalizations	1.4±2.2	0.8±1.8	1.9±2.4	0.097
Mortality	10 (20.8%)	4 (16.7%)	6 (25.0%)	0.477

Acronyms: AE, acute exacerbation; ER, emergency room.

Table 4. Key Factors Associated with Acute Exacerbation in Patients with Chronic Obstructive Pulmonary Disease Receiving Inhaled Corticosteroids Treatment.

	Univariate			Multivariate		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Active smoker	4.250	1.009-17.895	0.049			
AEC ≥300 cells/μL	7.000	1.641-29.854	0.009	16.074	2.409-107.247	0.004
BODE	1.620	1.013-2.592	0.044			
FVC, %	0.959	0.916-1.004	0.075			
FEV1, %	0.945	0.904-0.987	0.011	0.923	0.873-0.975	0.005
FEV1, Liter (3 years after)*	0.153	0.034-0.681	0.014			
Lowest O2 saturation <94%	0.328	0.092-1.170	0.086			

Acronyms: CVD, cardiovascular disease; AEC, absolute eosinophil count; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; mMRC, modified Medical Research Council; 6MWD, six-minute walk distance

* " FEV1, Liter (3 years after)" represents the median FEV1 measured after 3 years of follow-up.

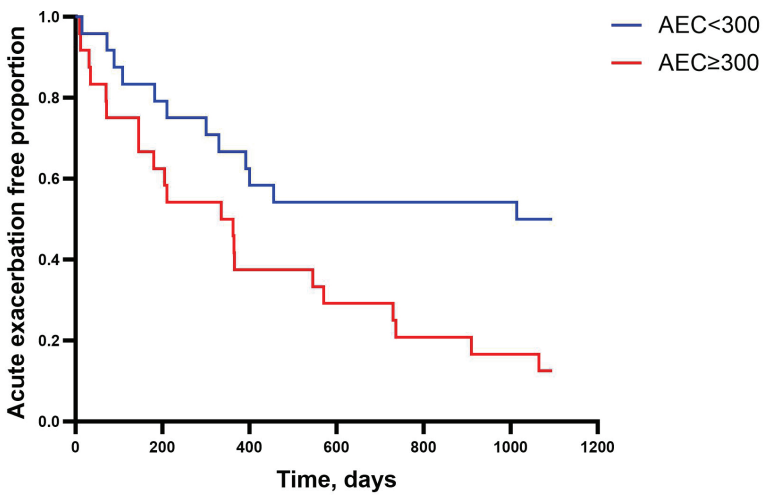

Fig. 2. Time to first exacerbation over the 3-year follow-up period.

The analysis was performed using a multivariate Cox proportional-hazards model. Hazard ratio: 2.52; 95% confidence interval: 1.23-5.15; p = 0.012. Acronym: AEC, absolute eosinophil count. Use “exacerbation-free” below.

Separate: AEC <300, AEC >300.

AEC ≥300 cells/μL had a significantly shorter time to first AE compared with those with an AEC <300 cells/μL (HR 2.52; 95% CI: 1.23–5.15; $p = 0.012$).

Discussion

This study found that COPD patients receiving ICS-based therapy represent a high-risk group. Compared with non-ICS patients, those on ICS exhibited more severe clinical profiles—with higher mMRC scores, elevated BODE indices, poorer lung function, and a greater decline in FEV_1 over 3 years—and experienced more frequent AEs, hospitalizations, and higher mortality. In the ICS-treated subgroup, a higher proportion of patients had blood eosinophil counts ≥300 cells/μL, which is consistent with current GOLD guideline recommendations that favor ICS use in patients with elevated eosinophils [2]. Higher FEV_1 values were significantly associated with a lower risk of AE.

Within the ICS-treated cohort, our results show that patients with an AEC ≥300 cells/μL continue to experience a significantly higher rate of exacerbations. This suggests that even though ICS therapy is intended to modulate type 2 inflammatory pathways [15, 20], it may not fully mitigate the risk in patients with persistently high eosinophil levels. Additionally, the variability in functional capacity—as measured by the 6MWT—indicates that these patients often have a more severe disease phenotype, which further contributes to adverse outcomes, including mortality.

However, our findings must be interpreted in the context of contrasting evidence. For example, the pooled analysis by Singh *et al*. [16] did not identify a strong or clinically significant relationship between baseline blood eosinophil counts and exacerbation rates; while patients with ≤150 cells/μL tended to have the lowest exacerbation rates, the increases observed in higher eosinophil subgroups were modest (rate ratios ranging from 0.97 to 1.17). Similarly, a review by Pradeesh *et al*. [17] underscores that although elevated eosinophil levels may predict a better response to ICS treatment in some patients, they do not uniformly confer protection against exacerbations. These discrepancies may be partly attributable to the inherent variability of blood eosinophil levels over time and differences in study designs, suggesting that eosinophil counts should be considered alongside other clinical parameters to more accurately predict treatment response and exacerbation risk.

Clinically, our results reinforce the importance of integrating blood eosinophil measurements with other clinical indicators—such as exacerbation history, lung function, and 6MWD—to refine risk stratification and optimize treatment decisions in COPD. Although the GOLD guidelines advocate for ICS in patients with higher eosinophil counts, our findings indicate that even within this subgroup, an AEC ≥300 cells/μL independently predicts a higher risk of exacerbations. This observation highlights a potential gap in current management, suggesting that ICS-based therapy may be insufficient for some high-risk patients [20].

Our study found that a lower FEV_1 is an independent risk factor for AE in COPD patients receiving ICS-based therapy. Notably, the 3-year rate of FEV_1 decline did not differ significantly between ICS and non-ICS patients. This finding is consistent with previous literature, which indicates that while ICS treatment may provide a modest short-term improvement in FEV_1—typically increasing by 45 to 96 ml

within the first 1 to 6 months—this benefit diminishes over longer periods, with the rate of decline eventually resembling that of non-ICS patients [21, [21]. These results suggest that although short-term gains in FEV_1 are achievable, maintaining a higher FEV_1 is crucial for reducing the risk of AE, and additional therapeutic strategies may be necessary to sustain long-term lung function.

Given these findings, further large-scale prospective studies are warranted to better define the eosinophilic COPD phenotype and to evaluate whether intensive monitoring and tailored treatment strategies—possibly incorporating additional anti-inflammatory or targeted therapies—can improve outcomes. Such studies should also address whether repeated blood eosinophil measurements can overcome the limitations posed by their inherent variability and thereby better predict treatment response and long-term prognosis.

Our study has several limitations. The retrospective design introduces potential biases and limits causal inference. Moreover, our analysis was confined to patients capable of completing the 6MWT, which may not be representative of the broader COPD population, particularly those with severe functional impairment. Finally, the variability of blood eosinophil counts over time could lead to misclassification when relying on a single measurement.

Conclusion

In conclusion, our study demonstrates that COPD patients receiving ICS-based therapy represent a high-risk group, characterized by more severe clinical profiles, diminished lung function, and increased rates of AEs, hospitalizations, and mortality compared with non-ICS patients. Within the ICS-treated cohort, those with blood eosinophil counts ≥300 cells/μL experienced a higher rate of exacerbations, indicating that ICS therapy alone may not fully mitigate risk in this subgroup. Additionally, a lower FEV_1 was identified as an independent risk factor for AEs. These findings highlight the need for tailored treatment strategies and further large-scale prospective studies to better define high-risk COPD phenotypes and improve long-term outcomes.

Declarations

Conflicts of interest

The authors declare that they have no potential conflicts of interest regarding the research, authorship, or publication of this article.

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Author contributions

All authors contributed substantially to study conception, design, and execution, as well as data acquisition, analysis, and interpretation. Additionally, all authors participated in drafting, revising, or critically reviewing the manuscript; provided approval for publication; agreed on the journal for submission; and accepted accountability for all aspects of the study.

Availability of data and materials

The datasets analyzed in this study are available from the corresponding author upon reasonable request.

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Asthma Control Test (ACT) as a Predictive Tool for Asthma Control Defined by GINA Guidelines: A Retrospective Study

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Introduction: Both the Asthma Control Test (ACT) and the Global Initiative for Asthma (GINA)-based assessment are widely used tools for monitoring treatment outcomes, yet they have been found to yield differing assessments of asthma control. This study aims to correct the discrepancies between the ACT score and GINA classification.

Methods: This retrospective study enrolled adult patients diagnosed with asthma who visited the chest OPD in Tri-Service General Hospital from February 2024 to October 2024. The GINA classification served as the reference standard to evaluate asthma control, while the ACT score was considered the predictive measure. We used receiver operating characteristic (ROC) curve analysis and Youden's index to find the optimal ACT cut-off point for prediction of well-controlled asthma.

Results: A total of 967 patients with asthma were included in our study. When using the cut-off point of ≥20 for ACT well-controlled asthma, the ACT score predicted GINA to be “well controlled” and showed sensitivity of 100% and specificity of 35.4%, while Youden's index was 0.354. When using the cut-off point of ≥24 for ACT well-controlled asthma, the ACT score showed sensitivity of 87.4% and specificity of 87.2%, while Youden's index was 0.747.

Conclusion: Based on the ROC curve and Youden's index, the optimal ACT cut-off point defining “well-controlled” was ≥24. The discrepancy underscores the importance of using both ACT and GINA criteria in conjunction to achieve optimal asthma management. ***(Thorac Med 2026; 41: 105-114)***

Key words: asthma, GINA, Asthma Control Test

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Introduction

Asthma is a heterogeneous disease characterized by chronic airway inflammation. It affects approximately 300 million people globally, and has significant impacts on morbidity, mortality, and healthcare systems worldwide [1]. Achieving good asthma control through treatment is the most effective strategy to reduce acute exacerbations, hospitalizations, and mortality, and improve patients' quality of life. To monitor treatment outcomes effectively, various tools are employed in clinical practice, including the Asthma Control Test (ACT) and the Global Initiative for Asthma (GINA)-based assessment [2].

The GINA guidelines provide a comprehensive framework for assessing asthma control using both subjective patient-reported symptoms and objective clinical measures. According to current guidelines, well-controlled asthma is defined by the following criteria: no limitations in daily activities, absence of nocturnal symptoms, minimal or no daytime symptoms, and minimal or no reliance on rescue medication.

The ACT is a validated patient-completed questionnaire designed for simplicity and ease of use in clinical settings. It includes 5 questions that evaluate daily activity limitations, shortness of breath, nocturnal symptoms, use of rescue medications, and the patient's overall perception of asthma control over the preceding 4 weeks. According to GINA guidelines, ACT scores ranging from 20 to 25 are classified as indicating "well-controlled" asthma [1].

While both tools are widely used, discrepancies often arise in their classification of asthma control levels, which can lead to inconsistent treatment decisions. Such discrepancies are clinically significant as they may result in under- or over-treatment of patients. Chao *et al*. reported that the ACT demonstrates a good correlation (complete agreement was 71.7%, kappa agreement = 0.524) with GINA-based criteria in assessing asthma control, highlighting that ACT is a convenient tool to evaluate asthma control rapidly. However, discrepancies between the 2 methods, including overestimation (15.5%) or underestimation (12.9%) of asthma control in this patient population, highlight the need for cautious interpretation in clinical practice [22].

Panettieri *et al* suggested that specialists commonly overestimated the level of asthma control relative to ACT scores in patients with severe asthma [23]. A single measurement of the ACT could be used for assessing asthma control and predicting risk of exacerbation, and as an adjunct to treatment decisions in asthmatic patients in Hong Kong [5]. Previous studies have shown that optimal ACT cut-off points vary across populations with differences in demographics, healthcare access, and cultural factors. However, only limited research has explored how these thresholds align with GINA-defined asthma control in Taiwan.

To address this gap, our study aimed to evaluate the relationship between ACT scores and GINA-defined asthma control in a Taiwanese population. Using receiver operating characteristic (ROC) curve analysis and Youden's index, we sought to identify an optimal ACT cut-off point that maximizes sensitivity and specificity for predicting well-controlled asthma according to GINA criteria.

Methods

Study design

This retrospective study was conducted at the Chest Clinic of Tri-Service General Hospi-

tal in Taiwan. Patient data were retrospectively collected from medical records of individuals aged 18 years or older who visited the clinic between February 2024 and October 2024. This study was approved by the Tri-Service General Hospital Institutional Review Board (TSGHIRB No.: A202405141). All patients included in the study had a prior diagnosis of asthma, which was established based on documented clinical symptoms (e.g., wheezing, shortness of breath, cough, or chest tightness) and lung function assessments recorded in their medical charts. Each asthma patient underwent an evaluation of their GINA asthma control level and ACT score conducted by our asthma case manager and a chest physician, with the results documented in the outpatient medical records. In addition to clinical data, demographic information such as sex, smoking status, and use of inhaled medications was also collected from the medical records. Data on ACT scores and GINA classification were extracted during the retrospective review. These variables were analyzed to evaluate the correlation between ACT scores and GINA-defined asthma control and to determine the optimal ACT cutoff values for well-controlled asthma.

Statistical analysis

The objective of this study was to evaluate the predictive validity of the ACT score in identifying GINA-defined well-controlled asthma. The GINA classification served as the reference standard, while the ACT score was considered the predictive measure. The analysis focused on distinguishing GINA-defined well-controlled asthma from partly controlled or uncontrolled asthma using an optimal ACT score cut-off.

To determine the optimal ACT score cut-off, we calculated the sensitivity, specificity, and overall classification accuracy at different cut-off points. A sensitivity analysis was conducted to refine the selection of the most appropriate cut-off value, highlighting the reclassification of asthma control categories at different thresholds.

The relationship between the ACT score thresholds and GINA classification was assessed using ROC curve analysis. Key performance metrics, including sensitivity, specificity, and Youden's Index, were summarized to evaluate the predictive performance of ACT scores. Youden's Index was calculated as the sum of sensitivity and specificity minus 1, which is a common simplification, though it is more accurately represented as a measure of the difference between the true positive and false positive rates.

Results

A total of 967 asthma patients who met the inclusion criteria were enrolled in the study; their demographic and clinical characteristics are summarized in Table 1. The mean age of the participants was 54.6 years, with a predominance of females, accounting for approximately 66.5% of the cohort. Most patients visited our chest clinic at a frequency of 1-3 times (89%), reflecting the frequency of follow-up required for asthma management. The majority of patients were prescribed inhaled corticosteroids (ICS) combined with long-acting beta-agonists (LABA) (ICS + LABA, 82.1%), which are considered the cornerstone of asthma treatment, while 5.8% received biologic agents, indicating a subset with severe asthma. These data provide a comprehensive overview of the patient population and highlight the variability in disease severity and treatment approaches within the cohort. Using the GINA-recommended asthma

Table 1. Demographic Data of the Patients (n=967).

Variable	Value
Age	Average: 54.6 years
Gender	Female: 643 (66.5%) Male: 324 (33.5%)
Smoking	Current: 115 (11.9%) Quit: 67 (6.9%) Never: 785 (81.1%)
Number of medical visits in 9 months	1-3 times: 862 (89%) 4-9 times: 99 (11.4%) >9 times: 6 (0.6%)
Inhaled medicines	ICS: 4 (0.4%) ICS+LABA: 794 (82.1%) ICS+LABA+LAMA: 168(17.4%) LAMA: 1(0.1%)
Biologic treatments	Underwent biologic treatments: 56 (5.8%) Did not undergo biologic treatments: 911 (94.2%)

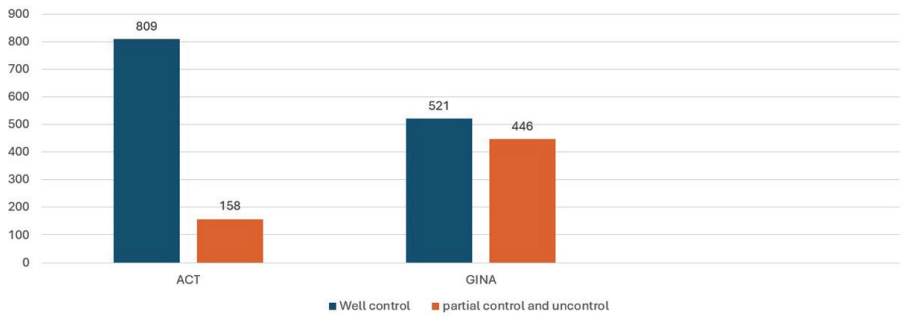

Fig. 1. Histogram showing the distribution of study participants based on ACT scores (cut-off point: >20) and GINA classification. Use "well controlled", "partially controlled and uncontrolled" in the figure below.

control tool, 521 patients (53.9%) were classified as having well-controlled asthma, while 446 patients (46.1%) were classified as having partly or uncontrolled asthma (Fig. 1).

When using an ACT cut-off point score ≥ 20 to identify well-controlled asthma, 809 patients (83.6%) were classified as having well-controlled asthma, and 158 patients (16.3%) were classified as having partly controlled or uncontrolled asthma. At this cut-off point, the ACT score achieved a sensitivity of 100%, indicating that all patients classified as well-controlled by GINA criteria were correctly identified. However, the specificity was only 35.4%,

reflecting a high rate of false positives where patients with partly controlled or uncontrolled asthma were misclassified as well-controlled (Table 2). This discrepancy highlights the limitations of using an ACT cut-off of 20 in accurately distinguishing between GINA-defined asthma control categories.

The Sankey diagram in Fig. 2 further illustrates the reclassification of asthma control groups when applying an ACT cut-off of 20 compared to GINA-defined categories. A significant proportion of patients classified as "partly controlled" or "uncontrolled" by GINA were misclassified as "well-controlled" under this ACT threshold, underscoring the potential overestimation of asthma control. While an ACT cut-off score of ≥ 20 ensures high sensitivity for identifying well-controlled asthma, its low specificity limits its ability to accurately differentiate between GINA-defined asthma control levels. These findings suggest that relying solely on this threshold may lead to overestimation of asthma control in clinical practice, emphasizing the need for a more stringent cut-off point to improve classification accuracy.

To address the limitations of using an ACT cut-off score of 20, we performed ROC curve analysis to identify the optimal ACT score

Table 2. Distribution of ACT Scores vs GINA Scores with Correlation Statistics (ACT cut-off point: > 20).

		GINA	
		Well controlled	Partially controlled & uncontrolled
ACT	Well controlled	521	288
	Partially controlled & uncontrolled	0	158

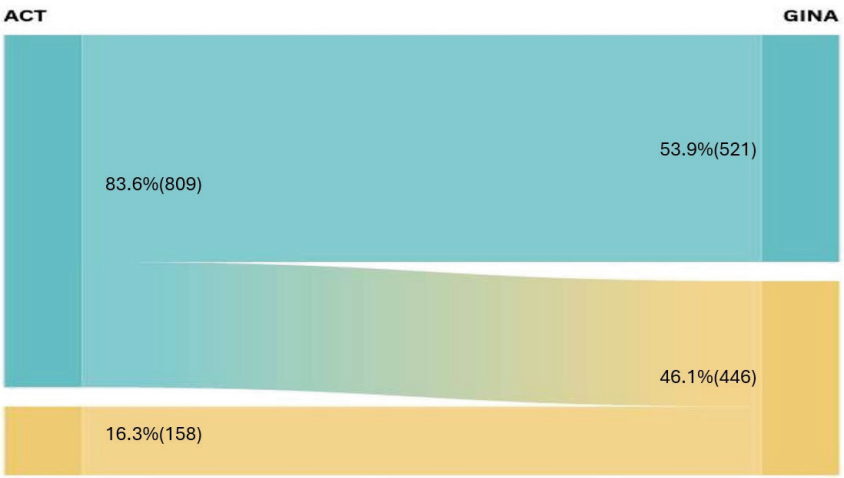

Fig. 2. Sankey diagram showing reclassification of asthma control groups when 2 different methods (ACT cut-off point > 20 vs GINA) were used. Separate the percentages and numbers below (53.9% (521)).

for predicting GINA-defined well-controlled asthma (Fig. 3). The ROC curve demonstrated excellent discriminatory ability, with an area under the curve (AUC) of 0.91, indicating that the ACT score is a reliable predictor of asthma control as defined by GINA guidelines. Table 3 summarizes the sensitivity, specificity, and Youden's index for each ACT score cut-off

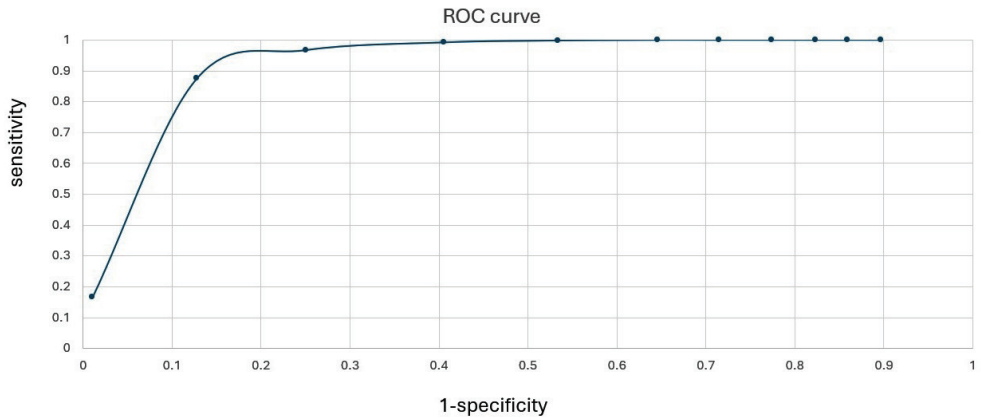

Fig. 3. Receiver operating characteristics (ROC) curves for the Asthma Control Test score predicting the Global Initiative for Asthma control classification for the 967 patients included in the survey.

Table 3. Performance of the ACT Score at Different cut-off Points in Predicting GINA Categories of well-Controlled Asthma for all Patients (n=967).

	Sensitivity	**Specificity**	**Youden's Index**
≥15	1	0.103	0.103
≥16	1	0.141	0.141
≥17	1	0.177	0.177
≥18	1	0.226	0.226
≥19	1	0.285	0.285
≥20	1	0.354	0.354
≥21	0.998	0.466	0.464
≥22	0.992	0.594	0.586
≥23	0.967	0.749	0.716
≥24	0.875	0.872	0.747
=25	0.167	0.989	0.156

Table 4. Distribution of ACT Scores vs GINA Scores with Correlation Statistics (ACT cut-off point: > 24).

		GINA	
		Well controlled	Partially controlled & uncontrolled
ACT	Well controlled	456	57
	Partially controlled & uncontrolled	65	389

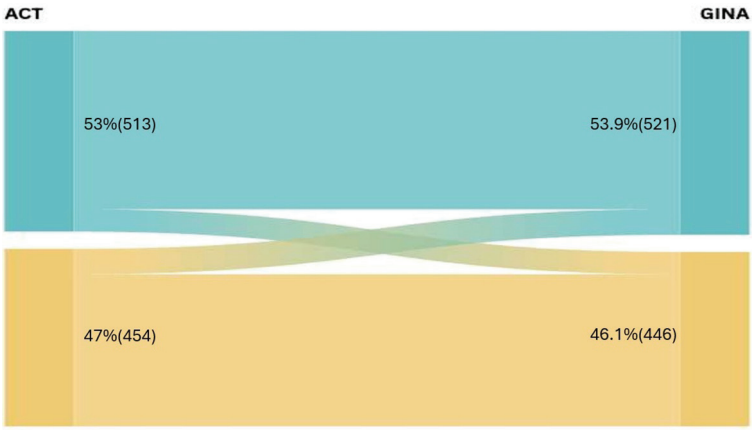

Fig. 4. Sankey diagram showing reclassification of asthma control groups when 2 different methods (ACT cut-off point > 24 vs GINA) were used. Separate the percentages and numbers below.

point. Among the tested cut-off points, an ACT score of 24 was identified as the optimal threshold based on the highest Youden's index (0.747). At this cut-off point, the ACT score achieved a sensitivity of 87.4% and a specificity of 87.2%, reflecting a balanced performance in correctly identifying well-controlled asthma while minimizing false positives and negatives. The ROC curve analysis confirmed that an ACT score of 24 provides the optimal balance between sensitivity and specificity for predicting GINA-defined well-controlled asthma. This threshold improves upon the limitations observed with a cut-off score of 20 and offers a more accurate tool for clinical decision-making in asthma management.

Based on the ROC curve analysis and the maximum Youden's index, we chose an ACT score of 24 as the optimal cut-off point for distinguishing GINA-defined well-controlled asthma. Fig. 4 illustrates the Sankey diagram, which visualizes the reclassification of asthma control categories when applying this ACT cut-off compared to GINA-defined control levels. The diagram highlights that an ACT score of 24 achieves a better alignment with GINA-defined well-controlled asthma, reducing the overestimation observed at lower cut-off points such as 20. Specifically, fewer patients classified as "partly controlled" or "uncontrolled" by GINA were misclassified as "well-controlled" under this threshold.

The Sankey diagram also demonstrates the distribution of patients across different asthma control categories, providing insights into how the ACT score reclassifies patients relative to GINA standards. This visualization underscores the improved accuracy of using an ACT score of 24, as it minimizes both false positives (patients incorrectly classified as well-controlled) and false negatives (patients incorrectly classified as not well-controlled).

Discussion

In this study, we analyzed data from 967 asthma patients to evaluate the accuracy of the ACT score in predicting GINA-defined well-controlled asthma. When using an ACT score cut-off of ≥20, the sensitivity was 100%, but the specificity was only 35.4%, resulting in a substantial overestimation of well-controlled asthma cases. To address this limitation, we performed an ROC curve analysis to identify the optimal ACT cut-off point. The analysis revealed that an ACT score of 24 provided the highest Youden's index (0.747), achieving a sensitivity of 87.4% and a specificity of 87.2%, indicating a more balanced performance in distinguishing well-controlled asthma from partly controlled or uncontrolled asthma.

Furthermore, the Sankey diagram demonstrated how applying an ACT cut-off of 24 reclassified patients into GINA-defined asthma control categories. This threshold significantly reduced misclassification compared to lower cut-off points, aligning ACT-based assessments more closely with GINA criteria. These findings suggest that an ACT score of 24 is a more accurate and reliable tool for clinical decision-making in asthma management, offering improved precision in evaluating asthma control levels.

In the early guidelines, the GINA classified asthma severity into 4 levels: intermittent asthma, mild persistent asthma, moderate persistent asthma, and severe persistent asthma. The assessment criteria included the frequency of daytime and nighttime symptoms, lung function, and the occurrence of exacerbations [9, 12]. After 2006, GINA shifted its focus from asthma severity to asthma control, categorizing it into 3 classifications: well-controlled, partly controlled, and uncontrolled asthma. The assessment criteria for control included the frequency of daytime symptoms, nighttime awakenings, activity limitations, the need for reliever medication, lung function, and exacerbations. This paradigm shift emphasized a more dynamic and patient-centered approach, aiming to guide treatment adjustments based on current disease control rather than static severity classification [10, 12, 18].

After 2014, GINA introduced a 2-component approach to asthma control, comprising symptom control and future risk assessment. The criteria for evaluating symptom control included daytime symptoms, nighttime awakenings, activity limitations, and the need for reliever medication. Meanwhile, lung function was considered a key metric in assessing the risk of future exacerbations [13-14, 19].

The ACT was a validated tool designed to assess the level of asthma control in patients. It was a simple, patient-based questionnaire that helped quantify asthma control, providing insights into the effectiveness of treatment and guiding therapeutic decisions [11, 20]. The ACT was widely used due to its ease of administration and ability to provide a quick assessment of asthma control, which was crucial for managing this chronic condition effectively [15]. Both the

ACT and GINA symptom control assessment were notable for their roles in guiding treatment decisions and improving patient outcomes, yet they had been found to yield differing assessments of asthma control.

The optimal cut-off point for the ACT varied across different populations and settings, as evidenced by several studies. In adult populations, according to GINA guidelines, an ACT score of ≥20 was the optimal cut-off point defining well-controlled asthma [1, 21]. However, it might not have been universally applicable, as GINA's stricter criteria often highlighted a lower overall control rating among patients, leading to potential discrepancies in treatment strategies [8]. Such differences were crucial as they could have significantly affected management plans and patient adherence to therapy, underscoring the importance of selecting appropriate evaluation tools.

Research suggested that the ACT cut-off point should have been adjusted based on geographical and ethnic differences to improve the accuracy of asthma control assessments [4, 5, 16, 17]. Some studies found that ACT and GINA scores had only a weak positive correlation or a negative correlation if the optimal ACT cut-off point defining well-controlled asthma was ≥20 [2, 3]. In a previous study, Ko *et al*. showed that the ACT cut-off for uncontrolled asthma was ≤19 and for partly controlled asthma was ≤22 in a Hong Kong population [5]. Thomas *et al*. showed that an ACT score of ≤19 correctly predicted GINA-defined partly controlled and uncontrolled asthma 94% of the time, while an ACT score of >20 predicted GINA-defined well-controlled asthma only 51% of the time. The study also found that for asthma subjects aged >12 years, the median (interquartile range) ACT scores for GINA categories were 14 (11–17), 20 (17–22), and 23 (21–25) for uncontrolled, partly controlled, and well-controlled asthma in European and U.S. populations [4]. In another study, Ko *et al*. found that the optimal ACT cut-off points for adults were ≤19 for uncontrolled asthma (sensitivity 0.73, specificity 0.67) and ≤22 for partly controlled asthma [6].

Asthma educators worked with patients to create personalized asthma management plans that incorporated both the ACT findings and the GINA recommendations. These plans detailed medication adherence, strategies for avoiding triggers, and mechanisms for tracking symptoms [7]. By individualizing care, educators empowered patients to take an active role in their asthma management, thereby enhancing treatment adherence and improving overall asthma control.

Our study has several limitations. First, its retrospective design may introduce selection bias and limit the ability to establish causal relationships. Second, the study did not apply specific exclusion criteria, which could affect the generalizability of the findings. Third, the analysis was conducted in a single-center setting, potentially limiting the applicability of results to broader populations.

Conclusion

Our research highlights that the traditional ACT cut-off of ≥20 may lead to an overestimation of asthma control, potentially compromising treatment efficacy. By adopting a more stringent threshold of ≥24, clinicians can better align ACT assessments with GINA-defined well-controlled asthma, thereby enhancing the precision of treatment decisions and ultimately improving patient care.

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Challenges in Using the Mandarin Term for "Nontuberculous Mycobacteria" in Taiwan: A Survey of Healthcare Providers' Perspectives

Yu-Hsun Chiang[1], Sheng-Wei Pan[1], Jia-Yih Feng[1]

Introduction: The Mandarin term for "nontuberculous mycobacteria" (NTM, 非結核分枝桿菌) often confuses Taiwanese patients, as it is easily mistaken for tuberculosis. This study explored whether alternative Mandarin terms would be preferred by healthcare providers for patient communication.

Methods: An online questionnaire was sent to 571 clinical trainees in the Department of Chest Medicine at our hospital (2022–2024), assessing their opinions and preferences regarding alternative Mandarin terms for NTM, including "environmental mycobacteria"(環境分枝桿菌), "atypical mycobacteria" (非典型分枝桿菌), and "mycobacteria other than tuberculosis" (結核以外分枝桿菌). Participants completed pre- and post-tests following a brief introduction.

Results: Of the 70 respondents, 51.4% had cared for NTM patients. Over 85% believed the current Mandarin term causes confusion with tuberculosis. Only 7% found "environmental mycobacteria" potentially confusing, compared to 20% for "atypical mycobacteria" and 71% for "mycobacteria other than tuberculosis" (p = 0.039 and p = 0.001). In the single-choice question, 64.3% selected "environmental mycobacteria" as the most intuitive option, this increased to 77.1% after an educational introduction (p = 0.035). Overall, 75.7% favored it for its clarity and accuracy.

Conclusion: Based on the perspectives of healthcare providers, using the Mandarin term for "nontuberculous mycobacteria" presented challenges due to its potential for confusion with tuberculosis. "Environmental mycobacteria" was a clearer alternative that may better support patient education and understanding. ***(Thorac Med 2026; 41: 115-123)***

Key words: Environmental mycobacteria; Mandarin medical terminology; nontuberculous mycobacteria (NTM); Taiwan

Introduction

Nontuberculous mycobacteria (NTM) are widely distributed in the environment and are commonly found in water and soil. The major NTM species associated with human disease include the Mycobacterium avium complex (MAC), the Mycobacterium abscessus group,

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and Mycobacterium kansasii [1]. In individuals with chronic lung diseases (such as bronchiectasis) or compromised immune systems, NTM can cause pulmonary infections, referred to as NTM-lung disease (NTM-LD). The incidence of NTM-related diseases has continued to rise while the incidence of tuberculosis in Taiwan has gradually declined [2]. A multicenter, longitudinal study by Huang *et al*. in Taiwan reported an incidence rate of 46.0 episodes of NTM-LD per 100,000 hospital-based patient-years from 2010 to 2014 [3].

In Taiwan, the Mandarin term for NTM, a direct translation of "nontuberculous mycobacterium" (非結核分枝桿菌), is often misunderstood by patients and mistaken for pulmonary tuberculosis. This confusion arises because the Mandarin term for "non-tuberculosis" sounds similar to the term "lung tuberculosis" in Mandarin as spoken in Taiwan. This misunderstanding in wording, combined with the stigma associated with tuberculosis-related infectiousness and fear of transmission, may lead to unnecessary worry and contribute to delays in further investigation and to reduced cooperation with anti-NTM treatment [4]. From a public health perspective, this terminological confusion creates a communication barrier for clinicians when explaining NTM-LD, often leading to misconceptions about the disease's infectiousness, treatment, and prognosis. Given the increasing clinical relevance of NTM infections, enhancing public awareness and improving doctor-patient communication are crucial. This is especially important for early-career medical professionals, including medical students, postgraduate year (PGY) doctors, and paramedical staff, who may encounter patients with NTM-LD in clinical settings. However, the extent to which the confusing terminology acts as a communication barrier and contributes to the educational burden on clinicians remains unclear.

Several alternative terms for NTM are currently available, including "atypical mycobacteria" (非典型分枝桿菌), "mycobacteria other than tuberculosis" (結核以外分枝桿菌), and "environmental mycobacteria" (環境分枝桿菌)[5]. In Taiwan, the first 2 alternatives are occasionally used in clinical conversations. However, "atypical mycobacteria" is sometimes misinterpreted as "atypical tuberculosis" (非典型結核菌), while "mycobacteria other than tuberculosis" may unintentionally shift the focus of patient education toward tuberculosis rather than NTM. Although the term "environmental mycobacteria" better represents the nature of these organisms and avoids reference to tuberculosis, it is not commonly used in clinical practice in Taiwan. To date, it is unclear which of these alternative names for NTM is most acceptable or preferred by clinicians in Taiwan—particularly among those involved in the care of patients with NTM-LD—as practical terms for explaining the condition. Understanding clinicians' preferences could help guide professional societies in pulmonary medicine and infectious diseases to revise and standardize the Mandarin terminology used in education, clinical practice, and public health messaging.

This study aimed to assess how clinical personnel—including medical students, PGY doctors, and respiratory therapists—perceive the Mandarin term for NTM and its alternatives. Using an online questionnaire, we evaluated their baseline understanding of NTM, reactions to various translated terms, and the potential for confusion with tuberculosis. The goal was to determine which alternative terminology was more likely to help clinicians understand the nature of NTM and communicate more effectively

with patients.

Methods

Study design and participants

This study is a retrospective analysis of survey data collected from routine post-course questionnaires. At the Department of Chest Medicine in Taipei Veterans General Hospital, monthly NTM health education sessions are held for rotating medical clerks, PGY doctors, newly recruited respiratory therapists, and nurses from specialized units. Following each session, participants are invited to complete an anonymous post-course feedback survey, which is distributed via email and completed voluntarily. During the course, an online questionnaire is distributed via the following link: https://forms.gle/aNAAnmdPTjNXjMCh7. For this study, it was sent to 571 individuals who received clinical training in the Department of Chest Medicine at this hospital between 2022 and 2024.

Online questionnaire

The online questionnaire included both pre-tests and post-tests, with an intervening reminder about the nature of NTM-LD. The pre-test gathered basic demographic information, such as participants' clinical background, level of training, and prior experience with NTM cases. It also assessed their baseline understanding of NTM and their impressions of various alternative Mandarin translations, including "environmental mycobacteria" (環境分枝桿菌), "atypical mycobacteria" (非典型分枝桿菌), and "mycobacteria other than tuberculosis" (結核以外分枝桿菌). After the pre-test, participants were provided with a brief educational introduction to NTM (Table 1), covering its epidemiology, clinical significance, and how it differs from

Table 1. Educational Introduction Provided in the Online Questionnaire.

Original text
Nontuberculous mycobacteria (NTM) 是廣泛存在於土壤及水源的分枝桿菌，又稱為environmental mycobacteria（環境分枝桿菌），在慢性肺部疾病(如支氣管擴張症)或免疫力較差的患者，NTM可造成肺部感染，即NTM-lung disease。儘管NTM和結核菌都屬於分枝桿菌，但NTM沒有人傳人的風險，也不需隔離，所以也稱為atypical mycobacteria(非典型分枝桿菌)或mycobacteria other than tuberculosis（結核以外分枝桿菌）。相較於NTM，結核菌一般不會存在於自然環境中，且台灣的結核病發生率逐年下降，而NTM疾病的發生率卻持續上升，值得台灣醫界高度關注。
English translation
Nontuberculous mycobacteria (NTM) are mycobacteria commonly found in soil and water, that are also known as environmental mycobacteria (環境分枝桿菌). In individuals with chronic lung diseases (such as bronchiectasis) or weakened immune systems, NTM can cause lung infections, referred to as NTM-lung disease. Although both NTM and Mycobacterium tuberculosis belong to the same genus, NTM are not contagious and do not require isolation. Therefore, they are also referred to as atypical mycobacteria (非典型分枝桿菌) or mycobacteria other than tuberculosis (結核以外分枝桿菌). Unlike NTM, M. tuberculosis is generally not found in natural environments. While the incidence of tuberculosis in Taiwan has been declining year by year, the incidence of NTM disease continues to rise, warranting significant attention from the medical community in Taiwan.

Mycobacterium tuberculosis. This was intended to provide consistent baseline knowledge before re-evaluating their perceptions. The post-test then reassessed participants' opinions on the clarity, intuitiveness, and appropriateness of each translated term using a similar set of questions.

Statistics

Survey data were presented as number with percentage. The pie chart and related figures were created using Microsoft PowerPoint. The McNemar test was used to compare paired pre-test and post-test responses, as well as to assess differences between alternative NTM terminologies in terms of their potential to be confused with tuberculosis.

Results

Participants' characteristics and perception

A total of 70 responses were collected, representing a diverse group of clinical personnel, including 27 medical students (clerks, 38.5%), 21 PGY1 and PGY2 doctors (30.0%), 12 nurses (17.1%) and 10 respiratory therapists (14.3%). A majority of the participants (n=69) reported they were already familiar with the Mandarin term for NTM, and 51.4% had prior experience participating in the care of patients with NTM-LD.

As shown in Fig. 1, 86% of respondents believed that the Mandarin term for NTM, a translation of "nontuberculous mycobacteria" (非結核分枝桿菌), could lead to confusion with the Mandarin term for tuberculosis among patients and their families, potentially impacting disease awareness and management. Correspondingly, 70% believed it created difficulties when explaining NTM-LD to patients and their families. Importantly, up to 89% of respondents felt that the term was not easily understood by the general public.

Confusion over alternative names for NTM

Considering the risk of confusion among alternative names, only 7% of respondents felt that the Mandarin term for "environmental mycobacteria" could lead to confusion, compared to 20% for "atypical mycobacteria" and 71%

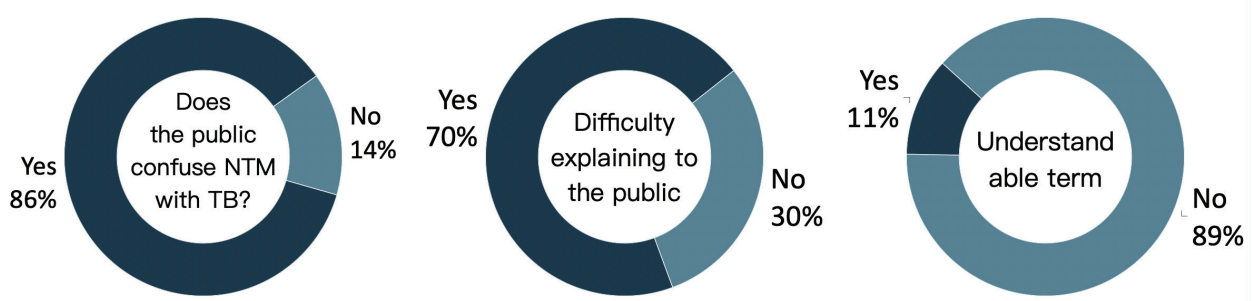

Fig. 1. Perception of the Mandarin term for NTM (非結核分枝桿菌) among respondents.
Use "Understand-able" in the figure above, if the word cannot be written "Understandable".

for “mycobacteria other than tuberculosis”. As shown in Fig. 2, conversely, 92.8% of respondents believed that “environmental mycobacteria” was unlikely to be confused with *Mycobacterium tuberculosis*, compared to 80.0% for “atypical mycobacteria” and only 28.5% for “mycobacteria other than tuberculosis”. Notably, among these alternative Mandarin names for NTM, “environmental mycobacteria” was associated with a significantly lower perceived risk of confusion with *Mycobacterium tuberculosis* compared to the other 2 alternatives (p = 0.039 and $p < 0.001$, respectively).

Preference for alternative names for NTM

In the pretest, as shown in Fig. 2, 57.1% of respondents believed “environmental mycobacteria (環境分枝桿菌)” best reflected the microbiological characteristics of NTM and 64.3% identified it as the intuitive term for NTM. After reading the basic introduction to NTM, post-test results showed a clear shift in preferences: the proportion rose to 75.7% for microbiological relevance (p = 0.011), and to 77.1% for perceived intuitiveness (p= 0.035).

As shown in Fig. 4, when considering professional accuracy, public comprehension, and ease of explanation, 75.7% of participants indicated that “environmental mycobacteria (環境分枝桿菌)” was the most helpful alternative term for doctor-patient communication. Overall, 75.7% of participants identified the Mandarin term for “environmental mycobacteria” as their most preferred choice in this survey.

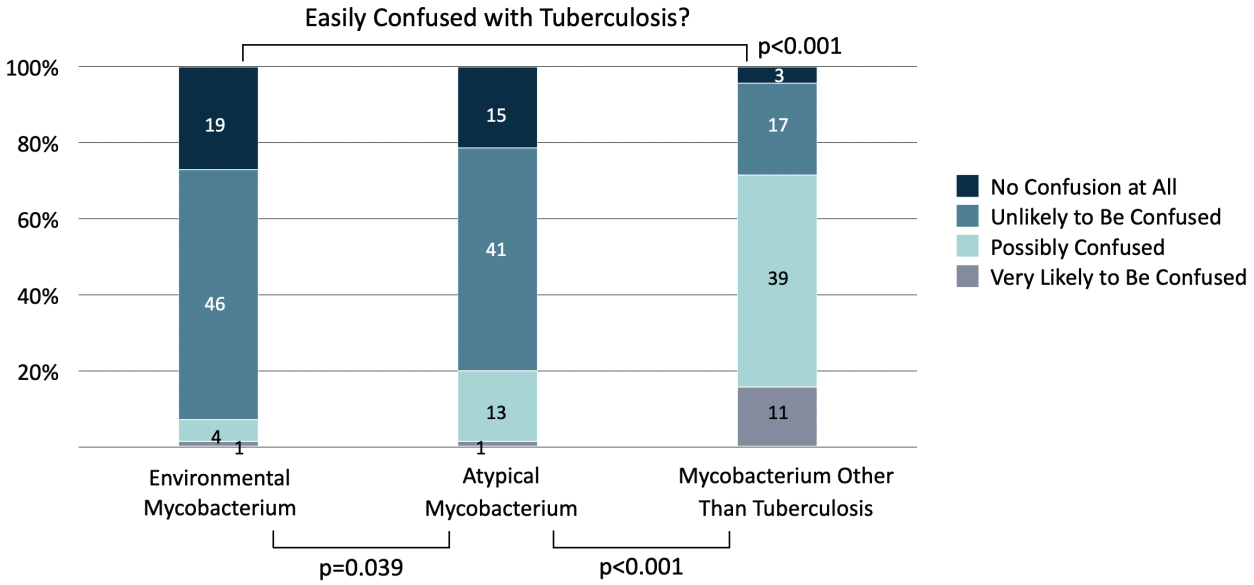

Fig. 2. Likelihood of confusion between alternative terminologies of NTM and tuberculosis.

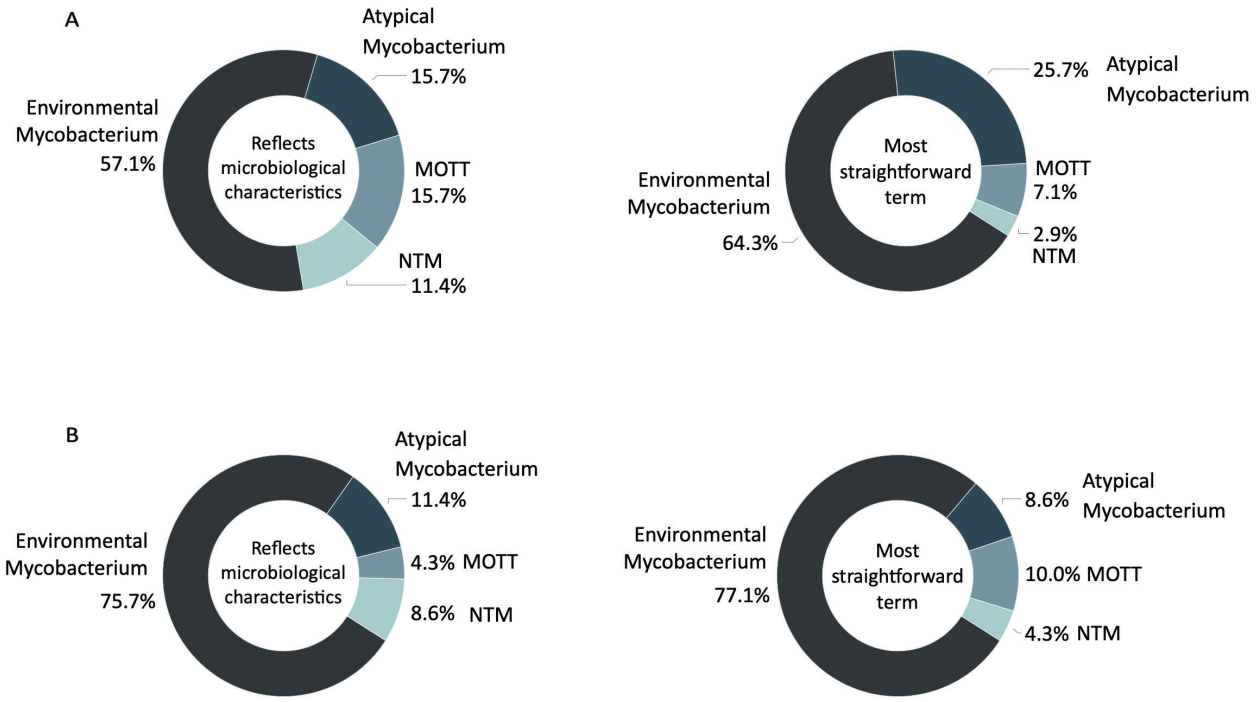

Fig. 3. Pre-test results (A) and post-test results (B) on preferences for terminologies referring to nontuberculous mycobacteria based on biological accuracy and intuitiveness.

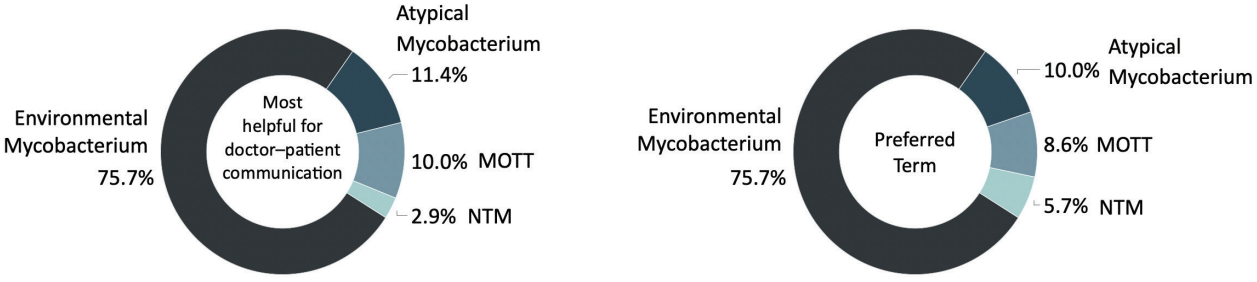

Fig. 4. Post-test results on alternative terminologies for nontuberculous mycobacteria: clinical communication, and overall preference.

Discussion

In this survey of medical students, junior residents, respiratory therapists and nursing staff, we found that the Mandarin translation of "nontuberculous mycobacteria" (非結核分枝桿菌) posed challenges in patient-physician communication, due to its potential for confusion with tuberculosis, which continues to carry social stigma in Taiwan. In contrast, the Mandarin translation of "environmental mycobacteria" (環境分枝桿菌), an alternative name for NTM,

was perceived as a less confusing and more intuitive term. In the post-test, following a brief educational introduction to NTM, over 75% of respondents agreed that “environmental mycobacteria”, as a Mandarin term, best reflected the microbiological characteristics of NTM and was the most intuitive name. Therefore, based on input from medical personnel, “environmental mycobacteria” may serve as a more suitable Mandarin term for NTM in the context of patient-physician communication in Taiwan.

Although the incidence of tuberculosis has gradually declined in Taiwan, the prevalence of NTM-LD continues to rise. In our survey, it was surprising to find that half of the participants—all of whom had received chest medicine training in recent years—reported prior experience in caring for patients with NTM-LD and most believed they were familiar with the Mandarin term for NTM. However, 70% agreed that the current Mandarin translation of “nontuberculous mycobacteria” often causes confusion with tuberculosis among patients. This confusion can lead to unnecessary anxiety, misconceptions about disease transmission, and potential delays in seeking appropriate medical care in patients with NTM-LD. Although this issue of terminology has been present for decades, it has largely gone unrecognized—perhaps because NTM-LD itself was long overlooked.

Thus, to address concerns that the current Mandarin term for “nontuberculous mycobacteria” (非結核分枝桿菌) may be confused with the term for tuberculosis, the present study aimed to explore more patient-friendly alternative terms. In a comparison of alternative Mandarin names for NTM in this survey, both “environmental mycobacteria” (環境分枝桿菌) and “atypical mycobacteria” (非典型分枝桿菌) were associated with significantly lower concern about confusion, compared to “mycobacteria other than tuberculosis” (結核以外分枝桿菌). Specifically, confusion concerns were reported by 10%, 20%, and 70% of respondents for the 3 terms, respectively. Thus, “environmental mycobacteria” was associated with the lowest perceived risk of confusion with tuberculosis, underscoring its greater clarity and suitability for medical staff in clinical communication with patients about NTM infection, helping to avoid confusion with tuberculosis.

In a follow-up analysis in which respondents were asked to choose their preferred Mandarin translation for NTM from 4 options, “environmental mycobacteria” emerged as the most intuitive and effective term, outperforming “nontuberculous mycobacteria” and other alternatives in reflecting the nature of NTM. The shift in preferences from the pre- to post-test, following an educational introduction to NTM, further supports that “environmental mycobacteria” remained the top choice among medical personnel for improving patient understanding and communication. These findings suggest that the current Mandarin terminology used in clinical and public health settings warrants reconsideration to reduce misunderstanding and improve awareness of NTM-related diseases.

Recently, a similar issue was noted with the Mandarin translation of chronic obstructive pulmonary disease (COPD), whose original Mandarin translation was complex and difficult for the public to understand. In Taiwan, the commonly used Mandarin term for COPD was simplified to “lung obstruction” (肺阻塞, pronounced fèi zǔ sè) to improve public awareness and facilitate more effective communication between healthcare providers and patients. Based on the results of this survey, we believe that applying a similar strategy for NTM—by adopt-

ing a clearer and less misleading Mandarin term such as "environmental mycobacteria" (環境分枝桿菌)—could significantly enhance health education and public understanding.

We believe this survey, incorporating input from medical students, junior residents, and nursing staff, suggests that the Mandarin translation of "environmental mycobacteria" is a promising alternative term for NTM, with the potential to enhance communication between healthcare providers and patients. Thus, we propose retaining the English term "nontuberculous mycobacteria (NTM)" for scientific and professional use, while adopting the Mandarin term for "environmental mycobacteria" for clinical communication in Taiwan. We believe that standardizing a more patient-friendly translation could improve disease recognition, support clearer doctor–patient communication, and enhance public understanding of NTM-LD. However, this study did not include input from patients or the general public. Further research is needed to confirm whether patients and their family members also consider "environmental mycobacteria" an appropriate and effective term for introducing NTM-LD in Taiwan.

Several limitations should be acknowledged in the present study. First, the relatively small sample size may reduce the statistical power and limit the generalizability of the findings. Second, the questionnaire used in this study lacks established measures of validity and reliability. This may introduce potential bias or measurement error, which could influence the interpretation of participants' responses. Third, the study did not include senior clinicians, such as experienced pulmonologists and infectious disease specialists, whose perspectives may offer additional insights and clinical depth. Larger-scale studies involving a more diverse cohort of healthcare professionals are warranted to validate these findings. In addition, future investigations should aim to develop questionnaires specifically tailored for patients, family members, and the general public. This would enable a more comprehensive assessment of how medical terminology related to NTM-LD influences disease perception, understanding, and patient–clinician communication across different audience groups.

Conclusion

In conclusion, our survey among medical trainees and clinical staff indicates that the current Mandarin term for "nontuberculous mycobacteria" (非結核分枝桿菌) may impede patient-physician communication due to confusion with tuberculosis. In contrast, the Mandarin term "environmental mycobacteria" (環境分枝桿菌) was perceived as more intuitive and accurate, with over 75% of participants endorsing it after a brief educational intervention. Future studies should engage a broader population and include validated questionnaires to assess public and patient perspectives.

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Pulmonary Alveolar Proteinosis Secondary to Pulmonary Tuberculosis

Mu-Han Peng[1], Po-Hsin Lee[1], Jing-Tong Fu[2], Yen-Hsiang Huang[1], Tsung-Ying Yang[1]

Pulmonary alveolar proteinosis (PAP) is a rare lung disease characterized by the accumulation of lipo-proteinaceous materials within the alveoli. Currently, whole lung lavage is the gold standard of treatment. Secondary PAP is secondary to a number of conditions, such as infections, hematological diseases, occupational exposure, and toxin inhalation. Cases secondary to pulmonary tuberculosis (TB) are rarely reported.

We present a case of PAP secondary to pulmonary TB, with symptoms and image findings showing significant improvement after anti-TB treatment alone, without whole lung lavage. Our findings underscore the necessity to check for pulmonary TB in patients diagnosed with PAP, and emphasize the need for further research on the association of PAP and pulmonary TB. ***(Thorac Med 2026; 41: 124-130)***

Key words: pulmonary alveolar proteinosis; pulmonary tuberculosis

Introduction

Pulmonary alveolar proteinosis (PAP), first reported by Rosen *et al* in 1958 [1], is a disease characterized by lipo-proteinaceous materials accumulating within the alveoli, causing respiratory symptoms. Some of these cases are found secondary to infections, hematological diseases, occupational exposure or toxin inhalation [2]. In Taiwan, a case secondary to invasive rhinocerebral aspergillosis has been reported [3]. Few reports on PAP secondary to pulmonary tuberculosis (TB) have been published [4-8]. PAP patients are also known to have higher risks of secondary infections, including pulmonary TB, which is likely related to macrophage dysfunction [9]. In Taiwan, pulmonary TB remains an important issue. In 2023, the incidence of TB was 28.2 cases per 100,000 population [10]. Awareness of TB in patients diagnosed with PAP is crucial.

We present here a case of PAP secondary to pulmonary TB, with improvement of both symptoms and image findings observed after treatment with an anti-TB agent only.

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Case Report

An 82-year-old woman had progressive exertional dyspnea for 1 month. Accompanying symptoms included occasional cough with scanty whitish sputum, and poor appetite for 2 weeks. She had no fever, chills, audible wheezing, chest pain or tightness, orthopnea, limbs edema, body weight loss, night sweating, abdominal discomfort, tarry stool, or frequent choking.

She visited our outpatient department, with oxygen saturation of 86% in room air. She was transferred to our emergency department, where her body temperature measured 36.4°C, heart rate 67 beats/min, respiratory rate 20 breaths/min, blood pressure 166/83 mmHg, and oxygen saturation 98% under oxygen support at 3L/min with nasal cannula. Physical examination revealed diffuse fine rales in bilateral basal lungs, regular heartbeat, with no murmur, nor pitting edema in the limbs. Laboratory data showed a white blood cell count of 9,850/uL, with neutrophils 86.7%, lactate 8.1 mg/dl, D-dimer 1.41 mg/l fibrinogen equivalent unit, and lactate dehydrogenase 326 U/L. The result of the HIV-ELISA test was negative. Chest X ray showed a bilateral alveolar pattern (Fig. 1A). Chest computed tomography (CT) showed bilateral peribronchial and subpleural crazy paving, with bilateral ground glass opacity and foci of consolidation (Fig. 2A).

Suspecting PAP and atypical infection, a bronchoscopy was performed, which found yellowish tissue coating at the orifice of the right lower lung. Biopsy was then performed, and the pathological findings were mycobacterial infection with caseating granulomatous inflammation. Bronchoalveolar lavage (BAL) was also done. The BAL fluid appeared white and

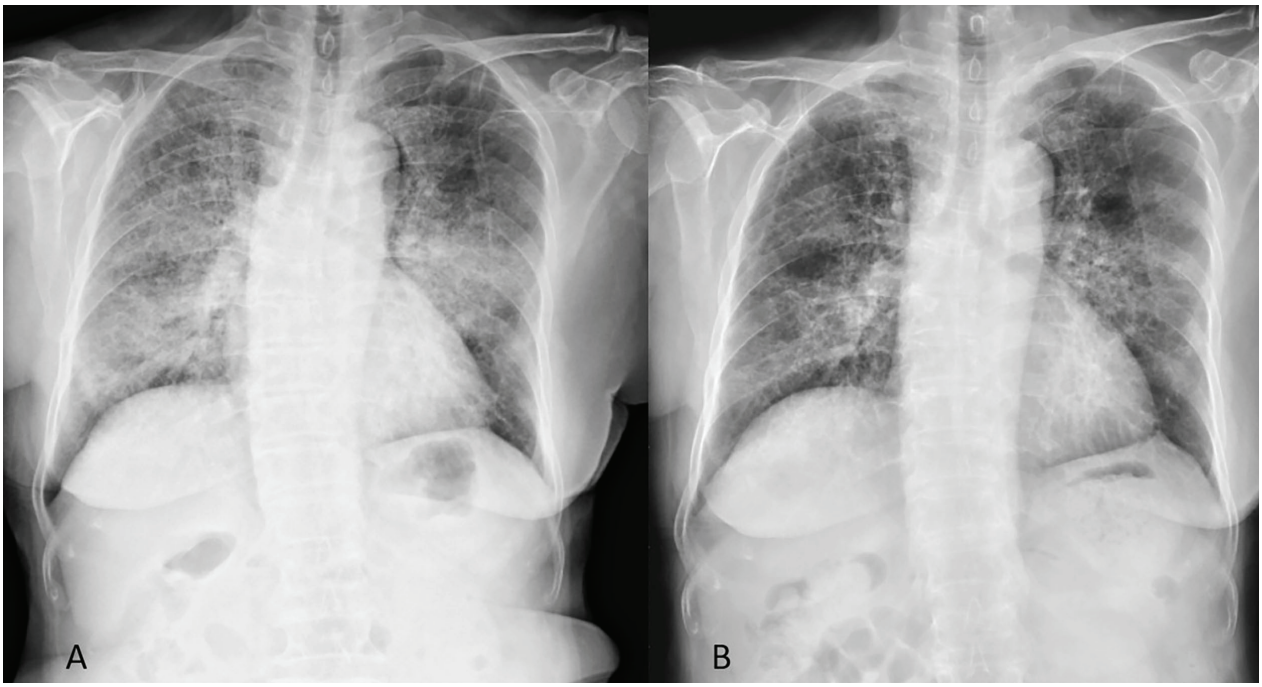

Fig. 1. (A) Chest X-ray in November 2020, showed increased alveolar infiltrates bilaterally. (B) Chest X-ray in December 2020, showed improvement of bilateral alveolar infiltration.

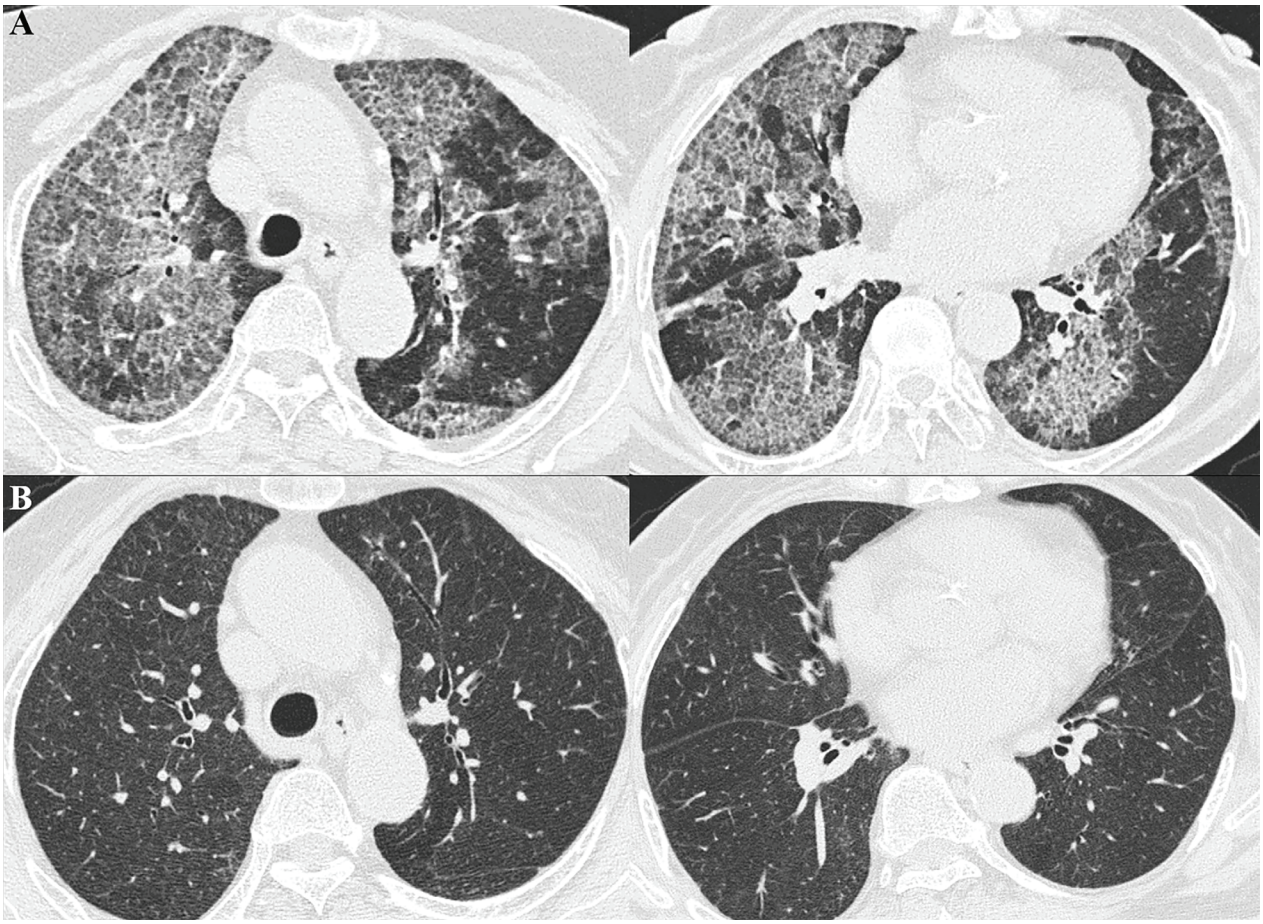

Fig. 2. (A) Chest CT in November 2020, revealed bilateral ground glass opacity and crazy paving. (B) Chest CT in May 2021, revealed total remission of the lesions found previously.

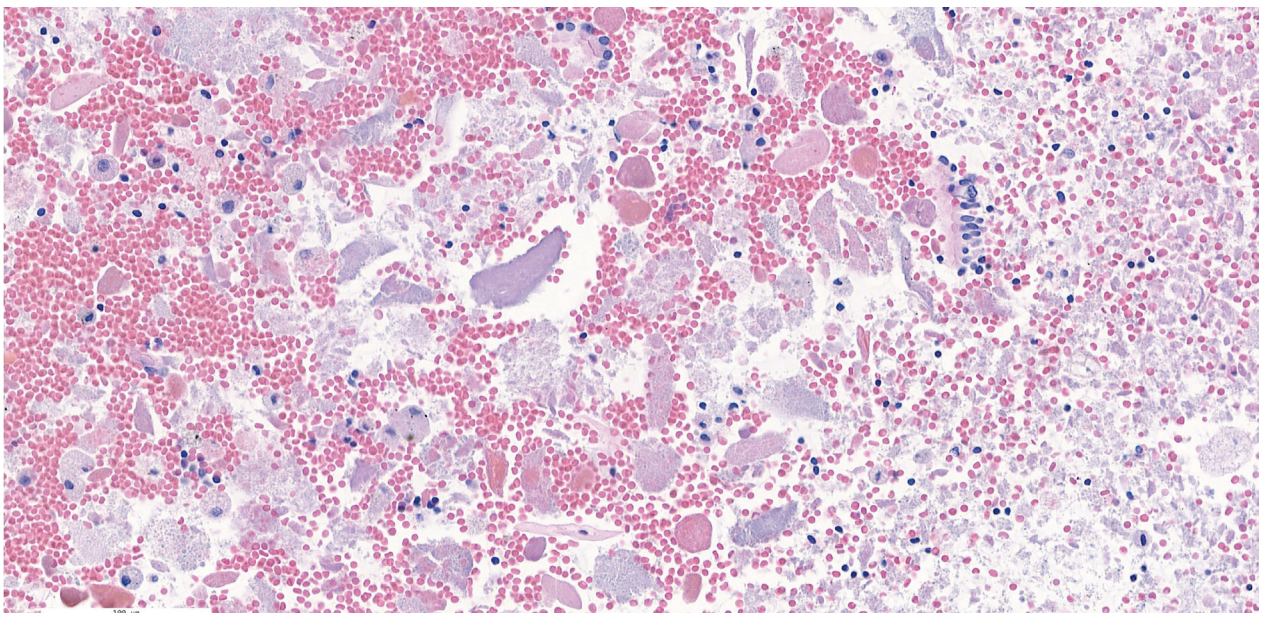

Fig. 3. Eosinophilic materials filling in alveolar spaces. Periodic acid-Schiff stain turned out positive.

cloudy, with the presence of proteinaceous materials positive for periodic acid-Schiff staining (Fig. 3). The BAL fluid tested positive for acid-fast staining and *Mycobacterium tuberculosis* polymerase chain reaction (TB-PCR). Culture of the BAL fluid later confirmed *Mycobacterium tuberculosis*, with no bacterial growth. PCR testing of the BAL fluid was negative for both cytomegalovirus and *Pneumocystis jirovecii*.

The diagnosis of pulmonary TB and PAP was finally made. We started to treat the patient with a combination of rifampin, isoniazid, pyrazinamide, and ethambutol. She had improved oxygen saturation (94% on ambient air). One month later, chest X-ray also showed improvement of the alveolar pattern bilaterally (Fig. 1B). The patient was then discharged with regular outpatient follow-up. After completing a 6-month anti-TB course in 2021/05, her chest CT showed total resolution of the crazy-paving pattern and ground glass opacity (Fig. 2B).

Discussion

PAP is a rare disease characterized by abnormal surfactant accumulation in pulmonary alveoli. Its prevalence is 6.87 ± 0.33 per million population in the United States [11], 8.7 per million in Japan [6], and 3.7 per million in Israel [12]. Clinical symptoms are nonspecific, with an insidious onset of respiratory symptoms (dyspnea, cough, sputum production, chest tightness) or systemic symptoms (fatigue, body weight loss) lasting for a few months before evaluation or initial diagnosis. Hemoptysis or fever is less common, found often in the context of superimposed infection [13]. Symptom severity varies across patients, with some being asymptomatic [14]. Chest CT findings typically include diffuse ground-glass opacities with sharply defined margins reflecting lobular or lobar boundaries (geographic appearance), septal thickening (crazy paving) and subpleural sparing [14]. PAP can be identified by the presence of opaque, milky BAL fluid or by histological evaluation of a lung biopsy sample [13].

Based on the pathogenesis, PAP is classified into 3 types: primary, congenital, and secondary PAP. According to previous studies, 89.0-92.0% of cases were primary PAP, and 3.7-9.9% of cases were secondary PAP [5-6, 15]. In the PAP cohort in Taiwan, 36% of patients were identified as secondary PAP [8].

Primary PAP, caused by signaling disruption of the granulocyte–macrophage colony-stimulating factor (GM-CSF), includes autoimmune PAP (due to autoantibodies to GM-CSF) and hereditary PAP (due to mutations in genes encoding GM-CSF receptor subunits). Congenital PAP is caused by surfactant production disorders due to mutations causing a deficiency in surfactant proteins or a deficiency in the lipid transporter ATP-binding cassette subfamily A member 3 (ABCA3), or due to mutations affecting lung development (NKX-2.1). Secondary PAP is related to reduced functions and/or numbers of alveolar macrophages caused by a variety of conditions, like hematological disorders, malignancies, immunodeficiency, chronic inflammatory conditions, infections, toxic inhalation, or mutations affecting functions or numbers of mononuclear phagocytes, such as mutations in MARS and SLC7A7 [2, 14].

Among secondary PAP cases, 0.0-44.4% are attributed to TB [4-7]. This wide range of cases reported across countries might be due to regional differences in TB incidence rate. In Taiwan, a PAP cohort found 14% of PAP patients had a history of TB [8]. An increase in the serum level of pulmonary surfactant

protein A was observed both in patients with TB and in patients with PAP, compared with healthy subjects [16]. According to a previous study, infections like TB stimulate the type II pneumocyte to secrete large quantities of surfactant that activate and overwhelm the alveolar macrophage system, with the lysosomes of the macrophage being compromised, leading to excessive surfactant accumulation and the release of hydrolytic enzymes into the alveoli. Finally, the surfactant is transformed into amorphous granular material and myeloid bodies. This process spreads to the adjacent alveoli through the pores of Kohn [17]. These are the possible mechanisms explaining how TB might lead to PAP.

On the other hand, PAP patients are known to be susceptible to infections, with TB representing 10.7-28.0% of all the opportunistic infections [18-19]. Mice lacking expression of GM-CSF were unable to control the growth of *Mycobacterium tuberculosis* and eventually succumbed to the infection [20]. Neutrophil dysfunction characteristic of PAP was reproduced in a dose-dependent fashion in blood specimens from healthy subjects after the specimens were incubated with affinity-purified GM-CSF autoantibodies isolated from PAP patients [21]. Macrophage monolayers incubated with soluble SP-A from alveolar proteinosis patients (APP SP-A4) and recombinant rat SP-A (SP-Ahyp) showed better adherence to *Mycobacterium tuberculosis* [22], as surfactant protein D binding to *Mycobacterium tuberculosis* bacilli could reduce phagocytosis [23]. Macrophages in PAP patients were dysfunctional with decreased phago-lysosome fusion [9]. Pulmonary washings from PAP patients could support the growth of *Mycobacterium tuberculosis* [24]. These findings provide insights into the mechanisms by which TB develops as a secondary infection in PAP patients.

The association between PAP and TB is seemingly bidirectional. TB could occur before, after, or concurrently with the diagnosis of PAP [18]. In our case, TB was found simultaneously with PAP. A literature review found another 7 similar cases, with patients clinically improving after receiving only anti-TB medications, without therapeutic lavage [7, 25-28]. Regarding the timing to treatment response, mentioned only in 1 of the cases, relieving of symptoms and regression of chest CT findings were found 1 month after anti-TB medication use [26]. On the other hand, during lung tissue biopsy on 149 active pulmonary TB patients, Steer *et al* found focal alveolar proteinosis in 11 patients, who were all cured by anti-TB drugs only [29]. PAP in these cases was suspected to be secondary to TB. Interestingly, in previous studies on 3 cases with TB diagnosed after PAP, 2 had their PAP improved after anti-TB treatment without therapeutic lavage [30-31], while in the third patient, the initial PAP-related lesions on CXR improved even more after anti-TB drugs than after previous therapeutic lavage [32]. In these cases, TB might have also been the initial event.

Nevertheless, spontaneous improvement of PAP has been reported in 5.0-7.9% of patients [2]. In cases with TB detected, remission of PAP may also occur spontaneously, even in the absence of anti-TB therapy. Establishing the definite diagnosis of PAP secondary to TB remains challenging. We have to increase the availability of GM-CSF autoantibody testing or investigate new biomarkers to distinguish secondary PAP from other types of PAP.

Conclusion

PAP is a rare disease, and can be classified as primary, congenital, or secondary. For patients with secondary PAP, treating the underlying disease can increase the cure rate. Hence, when facing a patient with PAP, one should make all efforts to determine the possibility of secondary PAP. Considering the burden of TB in Taiwan, it's always important to evaluate TB as a potential underlying cause.

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Case Report: Transthoracic Echocardiography for Dissection Flap in Descending Thoracic Aorta

Da-Chun Hsu[1], Sheng-Wei Pan[1]

Aortic dissection is a potentially fatal condition that requires timely diagnosis and management. Point-of-care ultrasound has been reported to aid in the diagnosis of this condition. However, diagnosing dissection in a descending thoracic aorta remains challenging due to limited acoustic windows for transthoracic ultrasound. We reported the case of a 46-year-old man who presented with chest tightness and right lower limb pain. A dissection flap in the descending thoracic aorta was identified using bedside transthoracic echocardiography (TTE), and subsequently was confirmed by computed tomography. This case highlights the potential of using TTE to facilitate the rapid identification of descending aortic dissection, which can significantly influence early clinical decision-making. ***(Thorac Med 2026; 41: 131-134)***

Key words: aortic dissection; echocardiography; point-of-care ultrasound (POCUS)

Introduction

Aortic dissection is a life-threatening condition with a mortality rate exceeding 50% [1-3]. Early diagnosis of this illness is critical for patient outcome and reduces mortality by 30% to 60% [4-6]. Although computed tomography (CT) remains the gold standard of diagnosis, the use of point-of-care ultrasound (POCUS) has emerged and demonstrated its advantages in early detection [7-9]. A combination of these 2 imaging modalities appears to be the best way to diagnose and assess the details of acute aortic syndrome, leading to appropriate management [10]. Using bedside ultrasound, a skilled physician can identify a dissection flap in the ascending aorta or abdominal aorta in a practical way. However, it is still challenging for a physician to identify a dissection flap in the descending thoracic aorta using transthoracic echocardiography (TTE) [7]. Hence, such ultrasound images are rarely reported, despite the frequency of the condition.

Case Presentation

A 46-year-old previously healthy man presented to the emergency department with a 1-day

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history of chest tightness and intractable pain in the right groin and leg. Physical examination revealed blood pressure of 162/83 mmHg, a heart rate of 90 beats/minute, and diminished right femoral pulses. A sonography showed a decreased blood flow in the right femoral artery. TTE disclosed a dissection flap in the descending thoracic aorta, using a parasternal long axis view (Fig. 1, Panel A, arrow). CT revealed an intimal flap from the aortic arch and descending aorta (Fig. 1, Panel B, arrow, and Panel C) to bilateral common iliac arteries, causing nearly total occlusion of the right iliac artery. The patient then received treatment with beta-blockers and morphine administration. Despite his refusal to undergo surgery, he continued medical treatment after admission and recovered from the aortic dissection. Six months after this presentation, the patient still received beta-blocker treatment and remained asymptomatically stable.

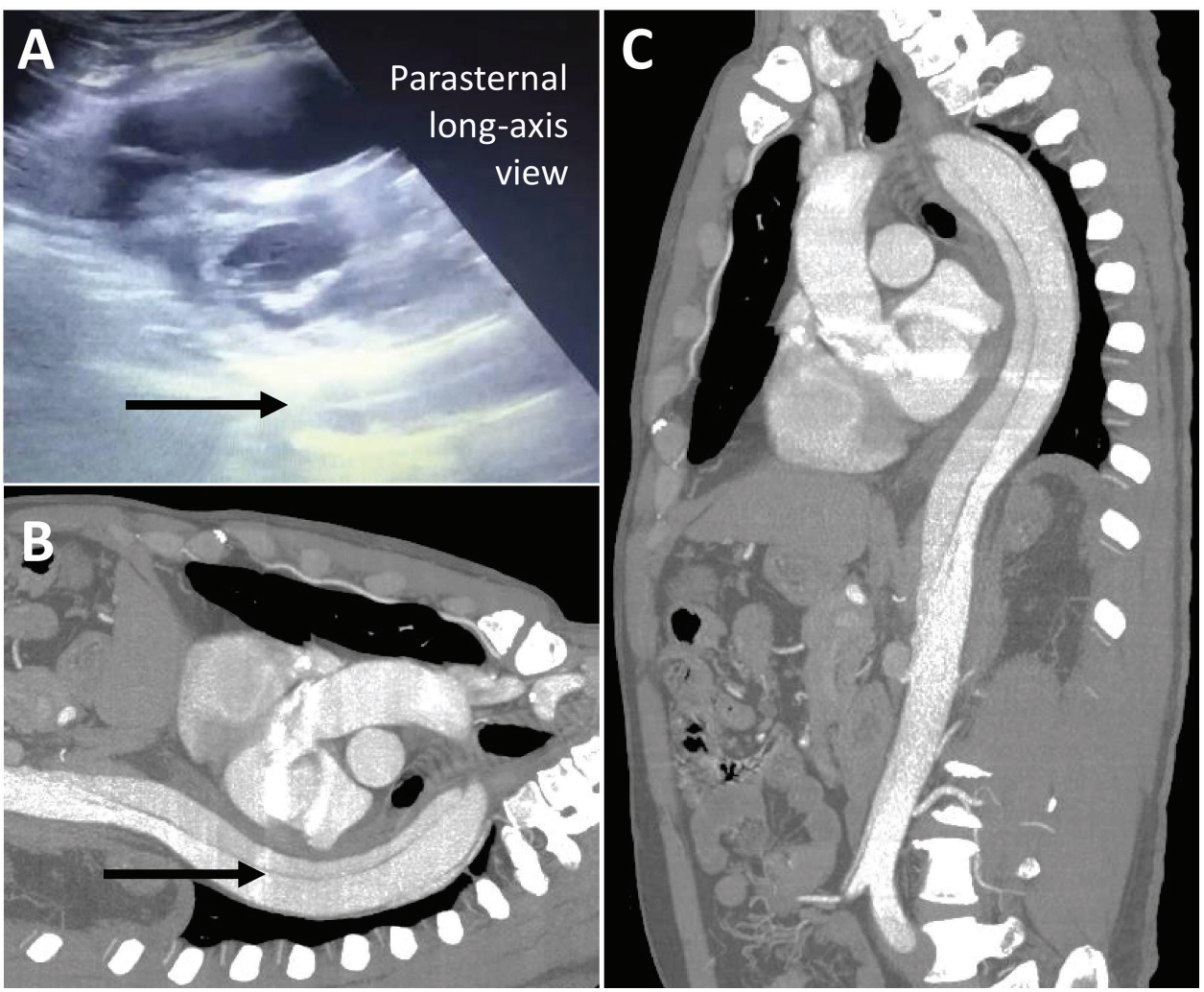

Fig. 1. Transthoracic echocardiography (Panel A) and CT scans (Panels B and C).

Discussion

Aortic dissection is a life-threatening condition that results from a tear in the intimal layer of the aorta, leading to blood entering and splitting the medial layer. It is classified anatomically as Stanford type A (involving the ascending aorta) and type B (involving the descending aorta only). The mortality rate can exceed 50%, particularly when diagnosis and treatment are delayed or complications arise [1-2]. Epidemiological data suggest that aortic dissection is often under-recognized in emergency settings, contributing to high early mortality. The American College of Cardiology and the American Heart Association have developed a risk scoring system to improve early detection, that yields high sensitivity (>95%), but relatively low specificity (<40%) [11-12].

The clinical presentation is highly variable and often nonspecific, making the diagnosis challenging. While 70% to 85% of patients experience sudden-onset chest or abdominal pain, other signs such as dyspnea, syncope, or neurological deficits, and even asymptomatic cases have been reported. History and physical examination alone are not sufficiently sensitive or specific to reliably identify aortic dissection. Misdiagnosis occurs in 16% to 39% of cases due to symptoms overlapping with other conditions [13]. Notably, a study reported that emergency physicians correctly suspected aortic dissection in only 43% of patients who were ultimately confirmed to have the condition, highlighting the need for improved awareness and diagnostic strategies [14].

Computed tomography angiography of the chest, abdomen, and pelvis remains the gold standard for diagnosing aortic dissection, offering sensitivity above 95%. However, it requires patient stability and access to imaging resources, which may not be feasible in some critical situations. Alternative imaging modalities such as transesophageal echocardiography, magnetic resonance imaging, and D-dimer assays have also demonstrated high sensitivity, especially for type A dissections. TTE, while less sensitive for type B aortic dissection (33% to 70%), is more accessible and can be performed at bedside. Recent studies support the use of POCUS by emergency physicians to expedite diagnosis [7-9]. Treatment strategies vary by dissection type, with type A typically requiring surgical repair, while type B may be managed medically or with endovascular intervention [15-17].

In our case, with acute chest tightness and intractable pain in the right lower limb, we performed TTE immediately at the emergency room and, fortunately, identified the dissection flap in the descending thoracic aorta by using a parasternal long axis view. During echocardiography, a parasternal long-axis view involves placing the transducer just to the left of the sternum, in the third or fourth intercostal space. This view allows for the assessment of cardiac function and the evaluation of additional structures, including the descending aorta situated behind the left atrium. Consequently, the patient received a CT scan to confirm the diagnosis of descending aortic dissection and started treatment without delay in the emergency room. We believe that the ultrasound image and supplementary video may provide important teaching points to intensivists who may be evaluating patients with chest pain and suspected aortic dissection.

Conclusion

Transthoracic echocardiography, particu-

larly the parasternal long-axis view, can play a role in the early detection of descending thoracic aortic dissection. Although CT remains the gold standard for diagnosis, echocardiography offers a non-invasive, bedside tool that can assist emergency physicians in promptly identifying life-threatening vascular conditions. This case emphasizes the value of POCUS in enhancing diagnostic efficiency and optimizing initial management in acute care settings.

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A Case of Cytomegalovirus Lung Abscess in a Patient with Community-Acquired Pneumonia

Hsi-Yang Chen[1], Yen-Hsiang Tang[1], Shun-Han Dai[1]

This article presents a rare case of lung abscess caused by cytomegalovirus (CMV) in a 76-year-old man initially presenting with symptoms of pneumonia. Despite broad-spectrum antibiotics, his condition worsened, prompting further investigation that revealed high CMV viral loads in the blood and bronchoalveolar lavage fluid, and histopathology confirmed CMV tissue invasion. The patient was treated with antiviral therapy and surgical resection of the abscess, leading to clinical improvement. However, he ultimately succumbed to complications related to gastrointestinal bleeding and respiratory failure. This case highlights the importance of considering CMV as a potential pathogen in lung abscesses, especially in immunocompromised or high-risk patients, and underscores the need for timely diagnosis and targeted antiviral treatment. It also emphasizes that CMV-associated lung abscesses are often underdiagnosed due to their rarity and non-specific presentation, which can delay appropriate management. Early recognition and combined medical and surgical interventions can improve outcomes, but severe complications remain a significant challenge. ***(Thorac Med 2026; 41: 135-142)***

Key words: cytomegalovirus, lung abscess

Introduction

Cytomegalovirus (CMV) infection is a well-recognized cause of substantial morbidity and mortality in immunocompromised patients [1]. Severe infections are rare in immunocompetent patients and are often underdiagnosed or diagnosed inadequately [2]. Among the different infection sites, the lung is rarely involved, and the presentation on chest radiographs is non-specific and can vary, including interstitial infiltrates, focal or diffuse pulmonary opacification, and nodules [3]. Lung abscess is usually caused by polymicrobial infection, which requires a relatively long course of broad-spectrum antibiotics covering both aerobes and anaerobes; CMV is almost never considered as a primary pathogen [4]. This empirical approach to treatment is supported by multiple reports in the literature illustrating the epidemiology and microbiology of lung abscess [4-6]. This may lead to delayed diagnosis of the CMV abscess,

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potentially delaying treatment and increasing morbidity and mortality [7]. We report the case of a 76-year-old man presenting with an unusual case of CMV-associated lung abscess, treated with antiviral medication followed by surgical intervention.

Case Presentation

A 76-year-old man with a medical history of type 2 diabetes mellitus, hypertension, stage 3 chronic kidney disease, and chronic obstructive lung disease presented to the emergency department with general malaise and shortness of breath for 1 week. His vital signs included hypothermia (35.5°C) and hypotension (83/56 mmHg). Blood tests revealed leukocytosis with 95% neutrophils and elevated C-reactive protein. Chest X-ray revealed bilateral air bronchograms and consolidation (Fig. 1), which supported our initial diagnosis of pneumonia. Arterial blood gas analysis showed pH 7.26, pCO_2 41 mmHg, HCO_3^- 18 mmol/L, and pO_2 119 mmHg on supplemental oxygen via a simple mask at 6 L/min. He developed acute hypercapnic respiratory failure and received endotracheal intubation with mechanical ventilation support. He was subsequently admitted to the intensive care unit (ICU).

Broad-spectrum empirical antibiotics with moxifloxacin 400 mg IV QD were prescribed to cover atypical pathogens, since chest X-ray showed bilateral pneumonia. However, a follow-up chest X-ray (Fig. 2) on day 3 of ICU admission showed disease progression. Resistant pathogens, disseminated infection, and oth-

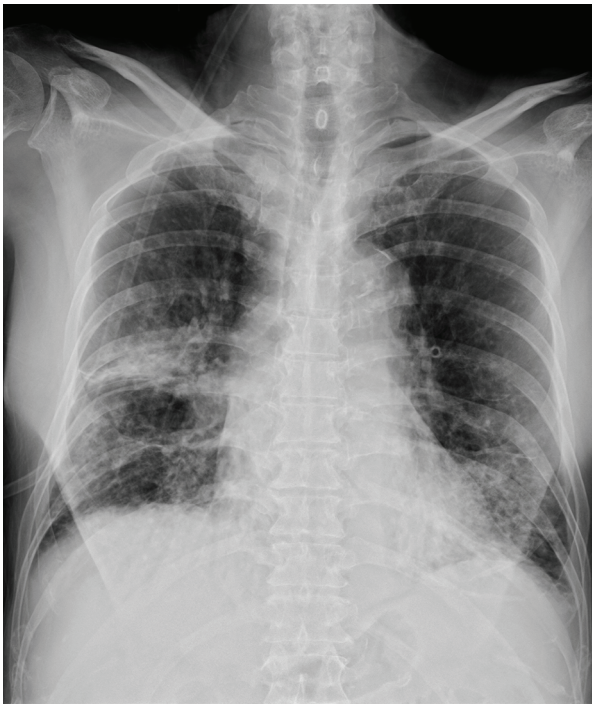

Fig. 1. Initial chest X-ray taken in the emergency department revealed bilateral air bronchograms and consolidation.

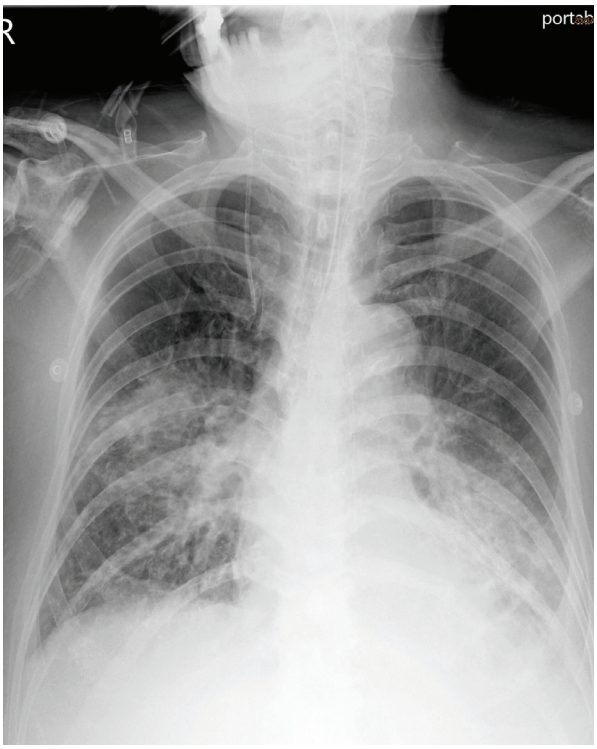

Fig. 2. A follow-up chest X-ray taken after 1 week in the intensive care unit showed disease progression despite broad spectrum antibiotics use.

er diagnoses were considered possible causes of treatment failure. Therefore, blood culture was repeated, and antibiotics were escalated to meropenem 500 mg Q12H. Blood culture later in the week yielded *Haemophilus influenzae*, which was susceptible to meropenem. Follow-up chest X-ray on day 7 of ICU admission still showed bilateral air bronchogram without significant improvement. Bronchoscopy with bronchoalveolar lavage (BAL) then was arranged. BAL fluid on day 7 revealed a viral load of 1,320,000 IU/mL, with a positive blood CMV viral load of 354,000 IU/mL. CMV pneumonia with CMV bacteremia was then diagnosed. Ganciclovir was added on day 7 of ICU admission. Chest computed tomography (CT) scans (Figs. 3-4) showed multifocal ill-defined peribronchial opacities, patchy consolidations in both lungs, bilateral pleural effusions, bronchiectasis in the right lower lobe, and a lung abscess in the left upper lobe. Hemothorax was diagnosed via thoracentesis of the left pleural effusion.

A thoracic surgeon performed VATS, during which bloody pleural effusion was evacuated along with some fibrin and hematoma. The left upper lobe abscess was identified and underwent wedge resection. Pathology showed lung tissue with abscess formation and chronic inflammation. Viral inclusions (Fig. 5) were noted in the tissue, and CMV immunostaining was positive. PAS-D stains showed no other microorganisms.

Ganciclovir was continued and the patient's condition improved. Follow-up bronchoscopy with BAL after surgery showed a decrease in the viral load of 566,000 IU/mL. His blood CMV viral load was 354,000 IU/mL on ICU day 7, which decreased to 155,000 IU/mL by day 12, and further declined to 16,700 IU/mL on day 19, 4580 IU/mL on day 26, 766 IU/mL on day 33, and undetected after 47 days of gan-

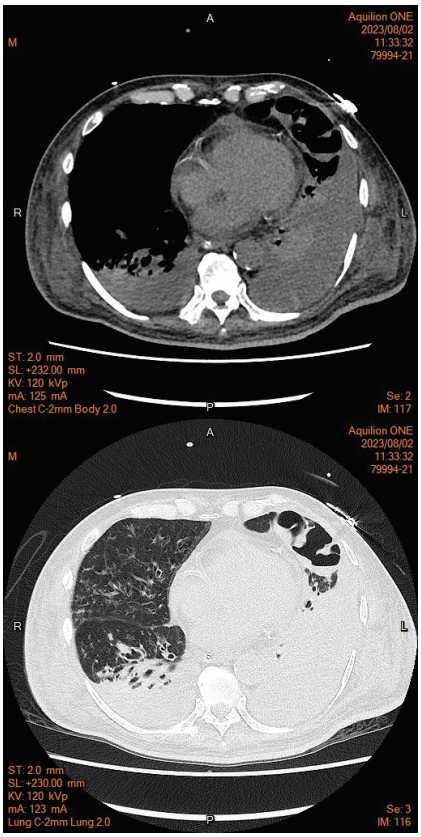

Fig. 3-4. Chest computed tomography scan demonstrated multifocal ill-defined peribronchial opacities, patchy consolidations in both lungs, bilateral pleural effusions, bronchiectasis in the right lower lobe, and a lung abscess in the left upper lobe.

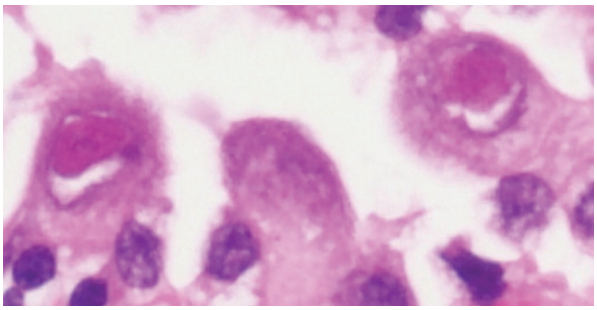

Fig. 5. Viral inclusions were noted in the tissue, and CMV immunostaining was positive.

ciclovir 1.25 mg/kg IV QD treatment. His vital signs stabilized, vasopressors were discontinued, and oxygen demand decreased, allowing for weaning from ventilator support by day 29 at the respiratory care center. However, he developed severe upper gastrointestinal bleeding associated with acute-on-chronic kidney disease. The family decided against further invasive treatment, and the patient died on hospital day 55.

Discussion

Standard broad-spectrum antibiotic treatment was prescribed after admission, but the patient's clinical condition deteriorated after admission, meeting the criteria of late treatment failure (respiratory failure >72 hours) [8]. According to the Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults, when late treatment failure is suspected, the following factors must be taken into consideration: resistant microorganism, uncovered pathogen, inappropriate by sensitivity, parapneumonic effusion or empyema, nosocomial superinfection, complication of pneumonia, and misdiagnosis [9], Therefore, pathogen identification was performed again via BAL to obtain faster results with greater specificity. CT revealed a lung abscess. Instead of the typical pathogens more often described in past studies and literature, CMV was isolated from BAL samples and surgical debridement tissue, which might explain the possible cause of treatment failure.

A lung abscess is the result of lung tissue necrosis, most commonly due to a polymicrobial infection, and its clinical course is usually relatively subacute or chronic. A lung abscess can be primary or secondary. Primary lung abscess is most commonly associated with different forms of aspiration, either a large volume emesis or frequent episodes of small-volume microaspiration [10].

Lung abscess is usually described as a polymicrobial infection in textbooks, including Murray and Nadel's *Textbook of Respiratory Medicine*. Anaerobic bacteria such as *Peptostreptococcus, Fusobacterium, Prevotella*, and *Bacteroides* species are the most commonly isolated microorganisms [4]. Other bacteria, such as *Staphylococcus aureus, Streptococcus pyogenes, Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, can also cause lung abscess. Takayanagi *et al*. reviewed the microbiology of community-acquired lung abscesses and found that Streptococcus species were the most common (60.5%), followed by anaerobes (42.1%), Gemella species (13.2%), Staphylococcus aureus (5.3%), and *Haemophilus influenzae* (5.3%) [5]. Jiun-Ling Wang *et al*. (2005) focusing on the microbiology of lung abscesses, found that a high proportion (21%) of cases were due to Klebsiella pneumoniae, differing from previous studies [6].

CMV lung abscess is extremely rare; therefore, precise epidemiological data specifically for CMV lung abscess are lacking. However, data from CMV pneumonia can provide context. Tamm M *et al*. published a prospective study, and reported a 20 to 30% occurrence in HIV-positive patients, in patients following stem cell or renal transplantation, and in patients with autoimmune disease or lung fibrosis treated with immunosuppressive agents [11]. Kanika A *et al*. conducted a systematic search in 2023 on the MEDLINE (PubMed) database. In 45 published cases of pulmonary CMV infection, they found that 64% (29/45) of cases

occurred in immunocompromised individuals. The same review found that 36% (16/45) of pulmonary CMV infection cases occurred in immunocompetent individuals [12]. Very few review articles or literature reports have identified CMV as a primary cause of lung abscess [7, 13]. Gonçalves *et al*. published a case report of acute CMV infection in a 29-year-old male presenting with fever and dyspnea despite standard antimicrobial therapy for community-acquired pneumonia [14].

CMV pulmonary infection, while classically associated with immunocompromised hosts, can also affect immunocompetent individuals, though the risk is significantly higher in certain populations. Older age has been identified as a significant risk factor for CMV infection. In 1 cohort, patients with CMV infection were significantly older than those without (median age 76 vs. 69 years, p=0.030) [15]. However, this study population was composed of patients with antibody-associated vasculitis, and therefore could not represent the general population. Another study conducted by Kwak SH *et al*. suggested that lymphopenia and high doses of steroids may be important risk factors for CMV reactivation in lung transplant patients [16].

While conservative medical treatment is usually sufficient for lung abscesses, some complicated cases require invasive procedures such as percutaneous chest drainage or surgical intervention. Pagès *et al*. in 2012 indicated that 11–20% of lung abscess cases did not resolve with medical therapy alone. In such cases, drainage (endoscopic or percutaneous) should be considered [17-18].

The diagnostic approach to CMV pneumonitis can be challenging in various clinical settings due to its rarity and the overlap of clinical and radiological features with other pulmonary infections. The diagnostic strategy typically integrates clinical suspicion, imaging, laboratory testing, and histopathological confirmation. Viral culture was the primary diagnostic method in the past; however, it is time-consuming and labor-intensive, limiting its utility, especially in ICUs where rapid results are often needed [19]. Quantitative real-time PCR (qRT-PCR) is the most sensitive and widely used method for detecting CMV DNA in blood and BAL fluid. In hematologic malignancy and transplant patients, qRT-PCR allows quantification of the viral load, which can help distinguish between asymptomatic infection and active CMV disease. However, there is no universally accepted viral load cut-off for diagnosing CMV pneumonia or lung abscess, and some studies even suggested different cut-off values might be needed to be applied considering a patient's baseline condition. Lee HY *et al*. retrospectively reviewed the microbiologic and pathologic results of bronchial washing fluid and biopsy specimens in 2017. A total of 565 CMV qRT-PCR assays were performed using bronchial washing fluid from patients with hematologic malignancies. A cut-off of 28,774 copies/mL in BAL fluid yielded a sensitivity of 75% and specificity of 88.6% [20]. While CT findings can be variable, the presence of ground-glass opacities, consolidations, and abscess formation should raise suspicion for CMV infection [3,21]. Detection of CMV pp65 antigen in leukocytes can support the diagnosis, particularly in transplant recipients, but is less commonly used in pulmonary disease due to technical limitations [22]. Conventional imaging can suggest the diagnosis, but definitive confirmation typically requires both virological and histopathological evidence. The presence of characteristic viral inclusions on histopathology remains the definitive diagnosis of CMV

infection [23]. In our case, the extremely high CMV viral load in both blood and BAL fluid (1,320,000 IU/mL in BAL and 354,000 IU/mL in blood) provided strong evidence of active CMV disease. This diagnosis was confirmed by pathological findings of viral inclusion bodies in pneumocytes.

Prophylactic or empirical treatment for CMV is generally suggested for bone marrow transplant patients but is rarely employed in patients who are relatively immunocompetent [24]. Most guidelines recommend a combination of a β-lactam plus a β-lactamase inhibitor for empiric treatment regimens in severe community acquired pneumonia. Nonetheless, CMV infection should always be considered if antimicrobial treatment alone does not produce a significant response, regardless of the patient's immune status [2,7]. Treatment of CMV pneumonitis generally involves intravenous ganciclovir, with response monitored via serial viral load measurements. Oral valganciclovir, the prodrug of ganciclovir, may be used for less severe cases or as maintenance therapy after initial intravenous treatment. In cases of ganciclovir resistance or intolerance, foscarnet is an alternative [25].

This case demonstrated an appropriate virological response, with a steady decrease in blood CMV levels over 6 weeks. In some cases, tube drainage or even surgical intervention may be indicated. Herth *et al*. reported a 90% improvement rate in 42 patients using small-bore catheters, with a 5% complication rate and no mortality [26]. Van Sonnenberg *et al*. found 100% resolution in 19 patients with CT-guided drainage, with only 3 requiring subsequent surgery [27]. Surgical intervention is considered when patients with lung abscess, including those cases caused by CMV, fail to respond to appropriate antimicrobial and antiviral therapy, typically after 7–14 days, or when complications arise (e.g., life-threatening hemoptysis, rupture with empyema, or persistent sepsis). Surgery is also indicated for abscesses larger than 6 cm, chronic abscesses (>6 weeks), suspicion of underlying malignancy, or when tube drainage fails. Lobectomy is the most common surgical approach for large, central, or multiloculated abscesses. Wedge resection may be considered for smaller, peripheral lesions. Pneumonectomy is rarely required but may be indicated for extensive disease or gangrene [27]. Zhang J-H *et al*. also reported that surgical resection is necessary in about 10% of all lung abscess cases. Mortality rates after surgery range from 5–15% for lobectomy and are higher for pneumonectomy, especially in immunocompromised patients. Postoperative complications include bronchopleural fistula (5–8%), prolonged air leak (15–20%), and empyema (10%). Recurrence rates after surgery are lower (5–10%) compared to drainage alone (15–25%) [28].

The prognosis of CMV pneumonia varies by disease severity and underlying health condition. The 30-day, 1-year, and 5-year mortality rates for CMV respiratory infection are 21.6%, 51.4%, and 69.2%, respectively. Organ transplant recipients have the lowest 30-day mortality rate (6.8%), while patients with nephrotic syndrome have the lowest 1- and 5-year mortality rates (30.9% and 38.3%). In contrast, non-immunocompromised patients still face substantial long-term mortality (1- and 5-year rates: 53.8% and 68.3%). Other poor prognostic indicators include the presence of interstitial pneumonia, respiratory failure, high Pneumonia Severity Index (PSI) and CURB-65 scores, and persistent lymphocytopenia. Advanced age and delayed diagnosis are also associated with

worse outcomes [29].

Conclusion

This case illustrates the complex nature of CMV pneumonitis and lung abscess, particularly in patients with multiple comorbidities. Successful management requires early recognition, appropriate diagnostic testing, including both molecular and histopathological studies, and careful monitoring of treatment response via viral load measurements. The potential for severe complications, including bacterial superinfection, necessitates vigilant clinical monitoring and aggressive intervention when needed. This case highlights the importance of considering CMV in the differential diagnosis of severe pneumonia, particularly in immunocompromised patient populations.

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