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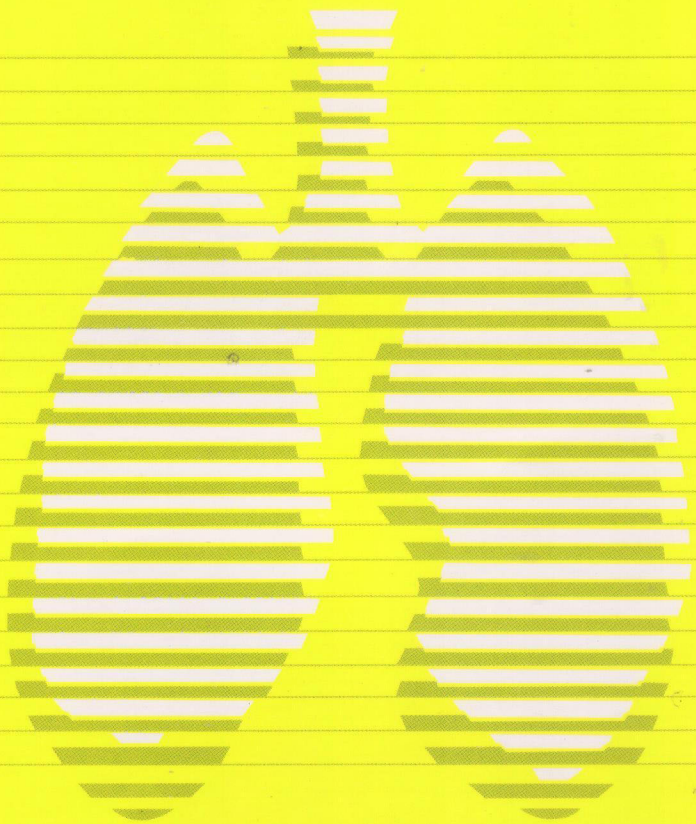

台灣胸腔暨重症加護醫學會

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Comparison of New Impedance Cardiography versus Ventricular Angiography in Measuring Hemodynamic Variables

Jui-Ying Fu, Chao-Hsin Cheng*, Kuo-Chin Kao, Ning-Hung Chen,
Ying-Huang Tsai, Chung-Chi Huang

Background: Hemodynamic variables provide crucial information to a critical care clinician. Non-invasive, safe, easily reproducible continuous hemodynamic monitoring is helpful in diagnosing and guiding treatment in critically ill patients. This study determined the correlation and agreement of measuring stroke volume (SV) and left ventricular ejection fraction (LVEF) using new generation impedance cardiography (ICG) and ventricular angiography (Cath).

Methods: Biplanar left ventriculograms were done to calculate SV and LVEF among patients who underwent cardiac catheterization from October 2004 to December 2004. ICG was performed to obtain concurrent SV and LVEF. Thirty-six comparative measurements were obtained. Pearson's r correlation coefficients and Bland-Altman comparisons were calculated.

Results: Thirty-six patients (30 acute coronary syndromes, 3 congestive heart failure and 3 valvular heart disease; mean New York Heart Association Class 2 +/- 1) were examined using the 2 methods. The average age of the patients was 53 +/- 15 years. The correlation coefficient between the values of SV_{ICG} and SV_{cath} was r = 0.50 (p<0.01; n = 36; bias = -1 ml; standard deviation = 19.6 ml). The correlation coefficient between the values of EF_{ICG} and EF_{cath} was r = 0.67 (p<0.01; n = 36; bias = -2.5%; standard deviation = 12.3%). The limits of agreement between SV_{ICG} and SV_{cath} were -40.2 ml to 38.2 ml; the limits of agreement between EF_{ICG} and EF_{cath} were -27.1% to 22.1%.

Conclusions: In our study, the limits of agreement between the new generation ICG and the left ventricular angiogram were wide. We concluded that the new generation ICG should not replace the standard methodology at a single time point. ***(Thorac Med 2008; 23: 73-80)***

Key words: impedance cardiograph, thoracic electrical bioimpedance, ventricular angiography, thermodilution, pulmonary artery catheter, cardiac output, stroke volume

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Division of Pulmonary and Critical Care Medicine, Chang Gung Memorial Hospital, Taipei, Taiwan; *Division of Chest Medicine, Ten-Chen Hospital, Chung-Li, Taiwan
Jui-Ying Fu and Chao-Hsin Cheng contributed equally to the work for this study as first authors.
Address reprint requests to: Dr. Chung-Chi Huang, Division of Pulmonary and Critical Care Medicine, Chang Gung Memorial Hospital, 5, Fu-Shin Street, KweiShan, Taoyang, 333, Taiwan

Introduction

Cardiac output is a primary determinant of global oxygen transport from the heart to the rest of the body, so it is the most important hemodynamic measurement for assessing perfusion status. While augmenting cardiac output to high levels (i.e., > 3.5l/min/m^2) has been shown not to improve survival rates in septic shock [1-2], a very low cardiac output is detrimental and associated with high mortality rates [1]. Reliable hemodynamic measurements help clinicians make appropriate decisions regarding the diagnosis and treatment of critically ill patients.

Over the past 30 years, pulmonary artery catheterization (PAC) has been widely used to measure hemodynamic variables in critically ill patients; however, controversy still exists regarding the use of PAC in these patients. A number of studies were not able to show that measuring PAC had any benefit in determining the prognosis for such patients [3-5]. In addition, the thermodilution method through PAC requires central venous access, which is more invasive and is associated with insertion and infection risks. Hence, hemodynamic variables have been monitored in only the sickest patients during the past decades.

However, hemodynamic measurement is important in many other clinical conditions, including diagnosis of acute dyspnea and shock, as a prognosis predictor and treatment guide for heart failure, in hemodialysis, and in weaning from the mechanical ventilator. Therefore, a simple, reliable, noninvasive, and continuous monitoring of circulatory dysfunction has become indispensable to enable the application of hemodynamic measurement throughout the hospital, and for diverse patients with different degrees of medical severity. The monitoring of continuous real-time hemodynamic variables allows prompt recognition of circulatory abnormalities and early therapeutic intervention.

The impedance cardiograph (ICG) provides such information, but its practicality remains unclear. In the past, the accuracy of ICG was typically validated by Doppler echocardiography and the thermodilutional method [6-10]. However, left ventricular ejection fraction (LVEF) and stroke volume (SV), as measured by ventricular angiography (Cath), is more precise and objective, and is the standard method in patients without pulmonary artery catheter insertion [11-12]. The purpose of this study was to determine the agreement between the LVEF and SV as measured by ICG compared to those values as obtained by Cath.

Materials and Methods

After receiving approval of the protocol, including the consent form, by the institutional ethics committee, patients undergoing elective Cath were considered for enrollment into the study from October 2004 to December 2004. A total of 36 patients were enrolled.

Left ventricular angiograms were performed in our cardiac catheterization laboratory. Biplanar left ventriculograms in 30-degree right anterior oblique (RAO) and 60-degree left anterior oblique (LAO) projections were performed to estimate left ventricular end-systolic and end-diastolic volume, using the standard area-length ellipsoid formula [12]. Afterward, the SV and LVEF were calculated.

A new generation impedance cardiograph (Physio Flow PF-05; Manatec Biomedical; Macheren, France) was used to obtain the bioimpedance data. SV measured by impedance car-

diography (SV_{ICG}) was based on changes in transthoracic impedance (Z) during cardiac ejection. The device we used emits an alternating electrical current of 1.8 mA and 75 kHz via electrodes (Ag/AgCl, Blue Sensor VL; Medicotest; Oelstykke, Denmark). Two sets of 2 electrodes, 1 transmitting and 1 sensing, were applied above the supraclavicular fossa at the left base of the neck and along the xiphoid, respectively. Another set of 2 electrodes was used to monitor a single ECG signal. With the Physio Flow device, there is no need to measure baseline Z.

The Physio Flow System provides a continuous measure of cardiac output and LVEF by measuring the stroke volume of each heart beat and averaging that over a period (chosen by the user). For this study, the recording interval was set at beat to beat, and the Physio Flow device was left connected during the entire process of the Cath examination. We marked the time of starting to measure the left ventricle volume as a vertical line on the screen. Finally, we averaged the measurements over the 10 minutes around the mark. The final value was compared with that obtained from the left ventricular angiogram.

A statistical analysis of the ICG and Cath data (SV and LVEF) were done using Pearson's r correlation coefficients with $p<0.05$ considered significant. In addition, Bland-Altman comparisons with bias (mean difference) and precision (standard deviation [SD] of difference) were carried out to evaluate the agreement between the 2 methods.

Results

A total of 36 patients were enrolled in this study (mean age, 53 years old; 25 males, 11 females; mean New York Heart Association Class 2 +/- 1). Thirty-six comparative measurements were taken using ICG and cardiac ventriculography. The SV range was 43-115 ml in the ICG group and 47-158 ml in the ventriculography group. The regression analysis and Bland-Altman representations are presented in Figure 1. The correlation coefficient between the values of SV_{ICG} and SV_{cath} was r = 0.50 ($p<0.01$; n = 36; bias = -1 ml; standard deviation = 19.6 ml). The limits of agreement between SV_{ICG} and SV_{cath} were -40.2 ml to 38.2 ml. EF range was 25% to 78% in the ICG group and 22% to 84% in the ventriculography group. This data is presented in Figure 2. The correlation coefficient between the values of EF_{ICG} and EF_{cath} was r = 0.67 ($p<0.01$; n = 36; bias = -2.5%; standard deviation = 12.3%), and the limits of agreement between EF_{ICG} and EF_{cath} were -27.1% to 22.1%.

Discussion

After a new generation of ICG became available, a number of studies showed strong correlation and clinically acceptable agreement between cardiac output as measured by bioimpedance and thermodilution, and concluded that the new generation of ICG provided an acceptable alternative for hemodynamic monitoring [8-9,13]. Nevertheless, the thermodilution method via PAC is an inherently inaccurate estimate of cardiac output, with 22% variability reported in the measurement of thermodilution from 1 injection to the next [14], although the pulmonary artery catheter has been used almost exclusively as the method of following cardiac output. SV and LVEF measured by Cath are more precise and objective in patients without pulmonary artery catheter

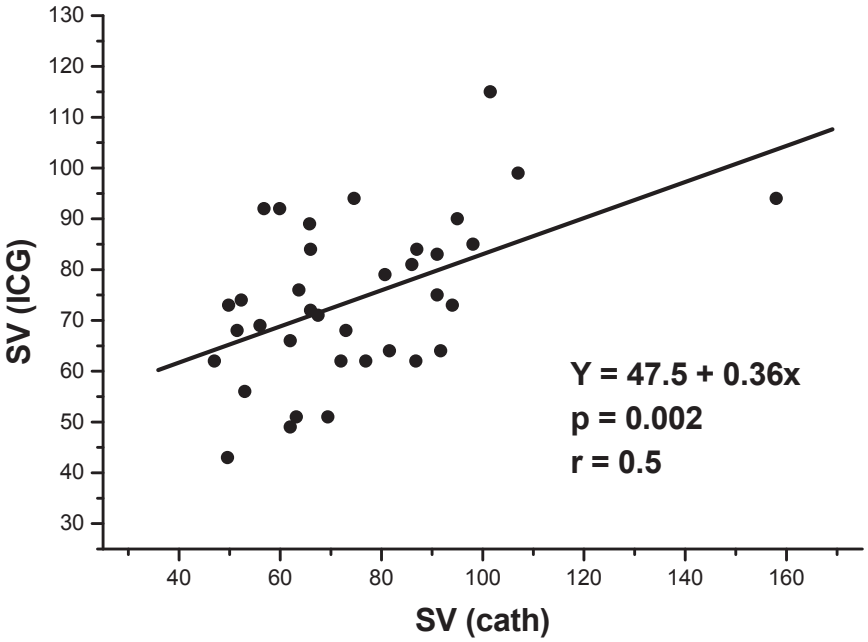

Fig. 1A. Stroke volume comparison using regression analysis. The correlation coefficient was r = 0.50; $p<0.01$.

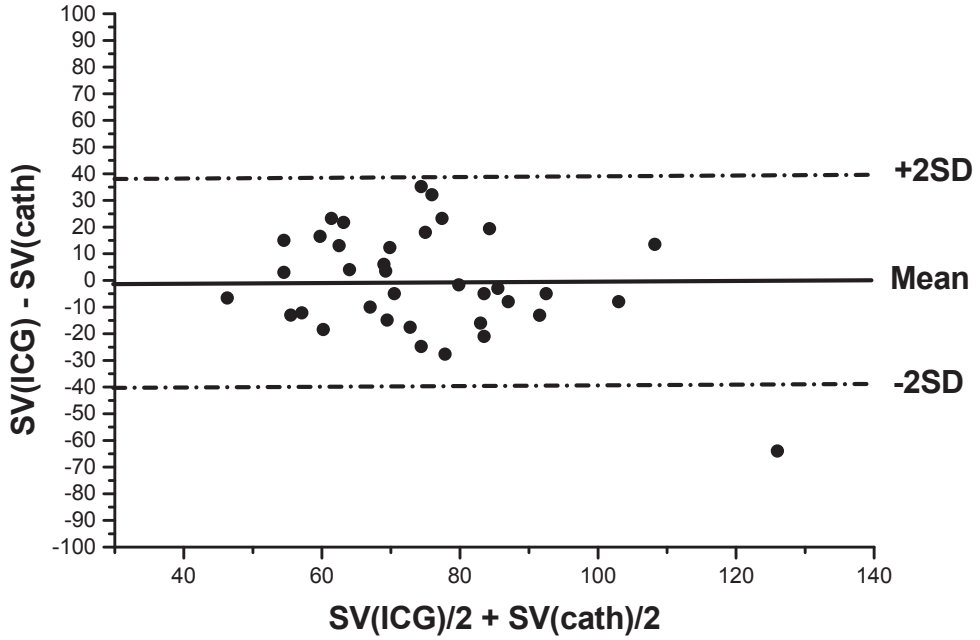

Fig. 1B. Stroke volume comparison using Bland-Altman representation (n = 36). The bias was -1 ml and the standard deviation was 19.6 ml.

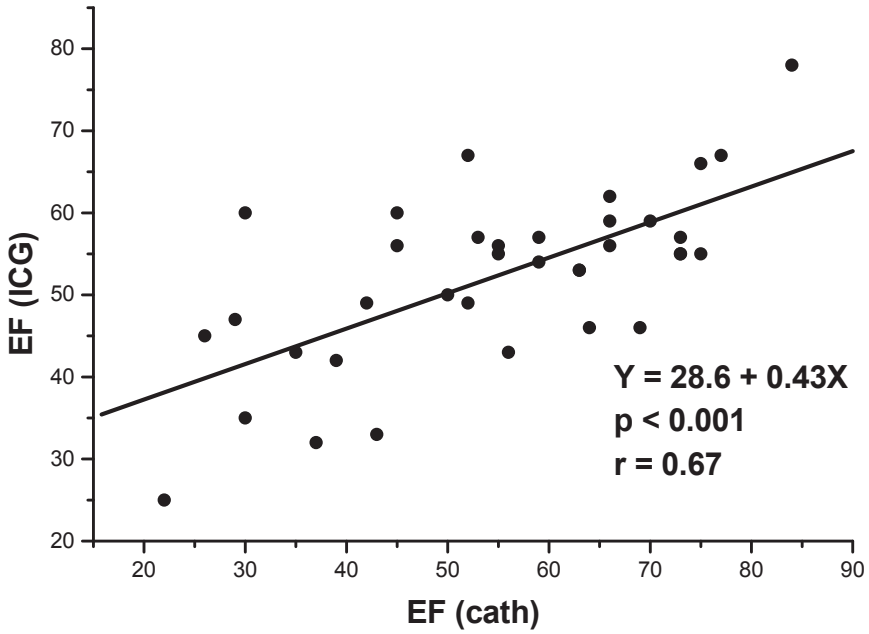

Fig. 2A. Left ventricular ejection fraction comparison using regression analysis. The correlation coefficient was r = 0.67; $p<0.01$.

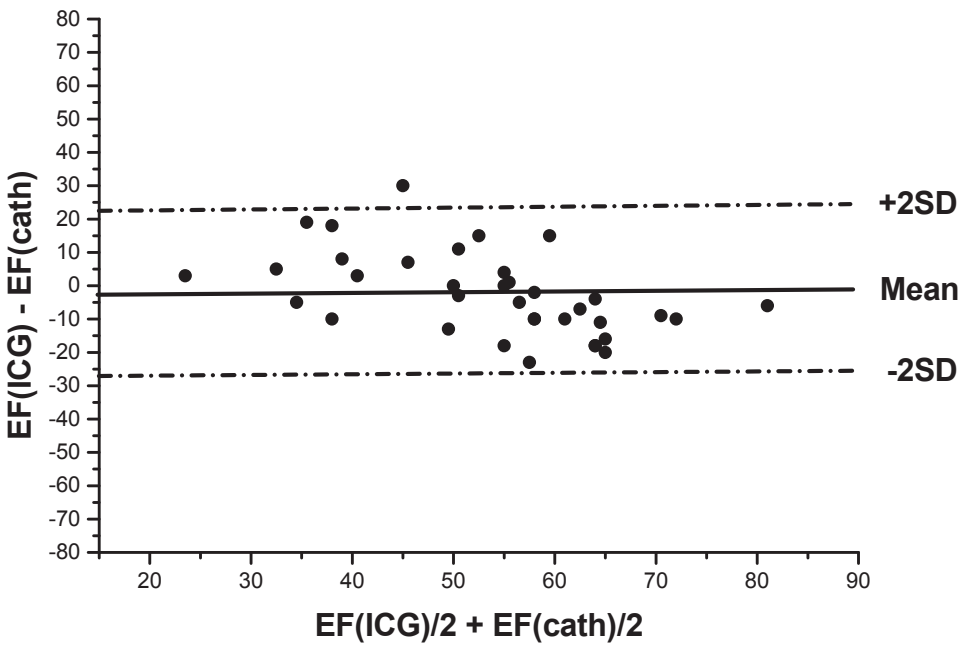

Fig. 2B. Left ventricular ejection fraction comparison using Bland-Altman representation (n = 36). The bias was -2.5% and the standard deviation was 12.3%.

insertion.

Marik *et al*. compared left ventricular ejection fraction and end-diastolic volume estimated by first-generation ICG with measurements determined from left ventricular angiography [15]. The limits of agreement between the ejection fraction estimated by ICG and ventriculography were -35% to 37%; the limits of agreement between the left ventricular end-diastolic volume estimated by ICG and ventriculography were -139 to 113 mL. They concluded that ICG should not replace invasive hemodynamic monitoring.

In our study, the new generation ICG measured beat-to-beat changes of thoracic bioimpedance via sensors applied to the neck and thorax. It used relative values of the impedance signal exclusively, and not absolute values to reduce the influence of lung water [16-18]. But the study results showed wide limits of agreement between the new generation ICG and Cath, in both SV and LVEF, so it is not clinically acceptable to use ICG in place of invasive hemodynamic measurement. It could be argued that changes or trending of SV and LVEF is more important than the absolute value of these variables when making clinical decisions. Further study to determine the longitudinal correlation and agreement would answer this question.

Conclusions

In conclusion, our study showed that the PhysioFlow, a new generation ICG, is an advance over the first-generation system, but does not have sufficient correlation and agreement compared to standard Cath. For the absolute value of hemodynamic variables, it cannot replace the standard method. For monitoring the capabilities and trending of these variables, further investigation is necessary.

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新一代電阻抗心電圖（impedance cardiography）與心導管左心室攝影（left ventriculargraphy）在血流動力學監測上之比較

傅瑞英　鄭朝馨*　高國晉　陳濬宏　蔡熒煌　黃崇旂

背景：新一代電阻抗心電圖（impedance cardiography）（ICG）可以非侵襲性的方法監測血流動力學參數。此研究目的在於比較新一代電阻抗心電圖（impedance cardiography）與心導管左心室攝影（left ventriculargraphy）（Cath）在血流動力學監測上之相關性（correlation）以及一致性（agreement）。

方法：36位接受心導管檢查的病人，於接受左心室攝影時同時利用新一代ICG記錄病人之SV以及LVEF。利用Pearson's r correlation coefficients以及Bland-Altman comparisons計算兩種方法之相關性及一致性。

結果：SVICG與SVcath的相關性為r = 0.50 (p<0.01; n = 36; bias = -1 ml; standard deviation = 19.6 ml)。EF_{ICG}與EF_{cath}的相關性為r = 0.67 (p<0.01; n = 36; bias = -2.5 %; standard deviation = 12.3%)。

結論：新一代ICG所測量的SV及LVEF值仍不能取代左心室攝影（left ventriculargraphy）。***(胸腔醫學 2008; 23: 73-80)***

關鍵詞：電阻抗心電圖（impedance cardiography），左心室攝影（left ventriculargraphy）

林口長庚紀念醫院　胸腔內科，*中壢天晟醫院　胸腔內科
索取抽印本請聯絡：黃崇旂醫師，林口長庚紀念醫院　胸腔內科，桃園縣龜山鄉復興街5號

Assessment of Asthma Control by Correlation of Asthma Control Test and GINA Criteria

Chih-Hao Chao*, Shiang-Ling King*, Chen-Yu Wang**, Ming-Cheng Chan*, Benjamin I Kuo***,****, Jeng-Yuan Hsu*,*****

Background and objective: The GINA asthma guidelines indicate that the rating of asthma control should include the daytime and nocturnal symptoms, limitations of activities, need for rescue treatment, frequency of exacerbations, and measurement of spirometry or peak flow rates. The Asthma Control Test (ACT™), a recently devised tool, evaluates asthma control simply, using a 5-item, self-administered questionnaire. To ensure the clinical applicability of the ACT, we evaluated the correlation of the ACT and the GINA rating criteria in assessing asthma control in our asthmatic patients.

Methods: Asthmatic patients with regular outpatient follow-up at our clinic who completed the ACT were enrolled into this study. The patients were classified according to their ACT questionnaire score: 25 as total control, 20 to 24 as well controlled, and less than 20 as not well controlled.

Results: Among the 116 patients, who accounted for a total of 233 visits, there was a significant correlation between the ACT control level and the GINA rating criteria in assessing asthma control. Complete agreement was observed in 71.7% (kappa agreement = .524). There was a 15.5% and 12.9% over- and underestimation, respectively, of asthma control status by the patients themselves. Sub-group analysis showed a better kappa agreement value in the non-smoking patients.

Conclusions: The ACT correlates well with the GINA rating criteria in assessing asthma control, although some disagreements may still persist. The results of this study confirm that the ACT is a convenient alternative screening tool for use in outpatient follow-up. ***(Thorac Med 2008; 23: 81-88)***

Key words: asthma, asthma control test

*Division of Chest Medicine, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan; **Division of Intensive Care Unit, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan; ***Laboratory of Epidemiology and Biostatistics; ****Department of Medical Research and Education, Veterans General Hospital, Taipei, Taiwan; *****Institute of Medicine, Chung-Shan Medical University, Taichung, Taiwan

Address reprint requests to: Dr. Jeng-Yuan Hsu, Division of Chest Medicine, Taichung Veterans General Hospital, 160, Sec. 3, Chung-Kang Rd., Taichung, Taiwan

Introduction

Asthma is a growing problem in Taiwan. The prevalence of asthma in school children increased more than 10-fold in the past 2 decades, despite reduced mortality [1-2]. The Global Initiative for Asthma (GINA) was formed in 1993 and first described guidelines for asthma management and prevention in 1995 [3]. The GINA guidelines are widely distributed, have been translated into several languages and have been updated several times [4]. These guidelines have been accepted in many countries as the gold standard for asthma treatment and control. A population-based study designed by de Marco *et al*. evaluated the treatment adequacy and control of asthma following the GINA guidelines and concluded that better control of asthma was achieved [5].

According to the recently updated GINA guidelines, the goal of asthma treatment should be optimum asthma control, rather than evaluation of asthma severity [4]. Daytime and nocturnal symptoms, limitations of activities, need for rescue treatment, frequency of exacerbations, and measurement of lung function by spirometry or peak flow meter should be assessed in the control of asthma.

Physicians in Taiwan see a high volume of patients during office hours. Thus, an accurate, reliable, and simple tool would be very helpful in the evaluation of asthmatic patients. Several questionnaire scoring systems have been developed to assess asthma control without measurement of pulmonary function, such as the Asthma Control Questionnaire (ACQ), Asthma Therapy Assessment Questionnaire (ATAQ), and mini-Asthma Quality of Life Questionnaire (mini-AQLQ) [6-8].

The Asthma Control Test (ACT^{TM}), a recently devised tool, evaluates asthma control simply, using a 5-item, self-administered questionnaire. Each item includes 5 response options corresponding to a 5-point Likert-type rating scale [9], which considers the impact of asthma on everyday functioning, shortness of breath, use of rescue medication, nocturnal asthma symptoms, and the patient's rating of asthma control during the past 4 weeks. The ACT provides a more simplified and comprehensive assessment of asthma control than the ACQ, mini-AQLQ and ATAQ. Furthermore, expensive equipment or trained personnel are not required to administer the test.

Although the ACT has been applied in clinical settings in Western countries, to our knowledge, there have not been any reports from Taiwan. The purpose of this study was to evaluate the correlation of the ACT and the GINA rating criteria in assessing asthma control in asthmatic patients.

Method

This study was conducted in an asthma-specific clinic in a medical center in central Taiwan. The diagnosis of asthma was made by an asthma specialist, based on the 2006 GINA rating criteria, including clinical symptoms and a pulmonary function test. From April 2006 to January 2007, 116 asthmatic patients, who accounted for a total of 233 visits to the outpatient department of this hospital, were enrolled. The patients completed the ACT questionnaire before entering the doctor's office. Then, the doctor evaluated the asthma control status on the basis of the GINA rating criteria, while blinded to the patient's ACT score.

For the ACT rating criteria, good control was defined as a total ACT score of 25, well

controlled as an ACT score between 20 and 24, and not well controlled as an ACT score of less than or equal to 19. The 2006 GINA rating criteria categorized the asthma control status as controlled, partly controlled, or uncontrolled. Correlation and agreement were measured after the 2 scoring systems had been completed.

Results

A total of 116 patients (aged 26-86 years (mean 62 yrs.)), who accounted for a total of 233 visits, completed the ACT and were included in this study. Table 1 shows the demographic data of the patients. There was an equal number of male and female patients and more than half were older than 60 years. Around 19% of the patients had a smoking history, including current and ex-smokers. Table 2 shows the distribution of asthma control within the range of the 2 different rating criteria. Table 3 shows the correlation of the ACT control level and the GINA rating criteria in assessing asthma control. The total agreement between the 2 measures was 71.7%. The kappa *p* agreement = .524. Some patients overestimated (n = 36, 15.5%) or underestimated (n = 30, 12.9%) their asthma control, but only 1 level of difference was observed, except in the case of 1 patient.

With the ACT scores cutoff point of 19, 83.7% of our patients were correctly classified, and only 1 patient in the GINA uncontrolled group reported ACT total control. No patient in the GINA controlled group was rated in the ACT not well controlled group.

We then subdivided these patients into smokers and non-smokers and repeated the previous statistical analysis (Tables 4 and 5). The kappa p agreement value increased to 0.533 in non-smokers and decreased to 0.481 in smokers. We also compared the correlation of the ACT levels and the GINA rating levels in different age groups with a cutoff point of 50 years. The kappa p agreement value in patients older than or equal to 50 years was 0.526 and that in patients younger than 50 years was 0.505.

Table 1. Demographic data of the patients

Characteristics	Total (n = 116)
Age (yrs)	
≤30	5 (4.3)
31-40	5 (4.3)
41-50	16 (13.8)
51-60	19 (16.4)
61-70	30 (25.9)
≥70	41 (35.3)
Gender, n (%)	
Male	58 (50)
Female	58 (50)
Initial asthma severity, n (%)	
Intermittent	0 (0)
Mildly persistent	21 (18.1)
Moderately persistent	63 (54.3)
Severely persistent	32 (27.6)
Smoking, n (%)	
Yes	22 (19.0)
No	90 (77.6)
Unavailable	4 (3.4)

Table 2. Distribution of asthma control

Rating criteria	Total (n = 233)
GINA criteria, n (%)	
Controlled	30 (12.9)
partly controlled	105 (45.1)
uncontrolled	98 (42.0)
ACT level, n (%)	
good control	25 (10.7)
well controlled	122 (52.4)
not well controlled	86 (36.9)

Table 3. Correlation of ACT control level and GINA rating criteria in all patients

		ACT control level			
		Good control	Well controlled	Not well controlled	Total
GINA rating criteria	Controlled	13	17	0	30
	Partly controlled	11	81	13	105
	Uncontrolled	1	24	73	98
	Total	25	122	86	233

Kappa agreement = .524

Table 4. Correlation of ACT control level and GINA rating criteria in smokers

		ACT control level			
		Good control	Well controlled	Not well controlled	Total
GINA rating criteria	Controlled	5	6	0	11
	Partly controlled	3	11	3	17
	Uncontrolled	0	4	16	20
	Total	8	21	19	48

Kappa agreement = .481

Table 5. Correlation of ACT control level and GINA rating criteria in non-smokers

		ACT control level			
		Good control	Well controlled	Not well controlled	Total
GINA rating criteria	Controlled	8	11	0	19
	Partly controlled	8	70	10	88
	Uncontrolled	1	20	57	78
	Total	17	101	67	185

Kappa agreement = .533

Table 6. Correlation of ACT control level and GINA rating criteria in patients ≤50 years of age

		ACT control level			
		Good control	Well controlled	Not well controlled	Total
GINA rating criteria	Controlled	4	9	0	13
	Partly controlled	2	12	3	17
	Uncontrolled	0	3	21	24
	Total	6	24	24	54

Kappa agreement = .505

Discussion

Our study shows good correlation between the ACT control level and the GINA rating criteria. The kappa agreement value of 0.524 denotes good reproducibility. The results

Table 7. Correlation of ACT control level and GINA rating criteria in patients >50 years of age

		ACT control level			
		Good control	Well controlled	Not well controlled	Total
GINA rating criteria	Controlled	9	8	0	17
	Partly controlled	9	69	10	88
	Uncontrolled	1	21	52	74
	Total	19	98	62	179

Kappa agreement = .526

corroborate those of previous studies indicating that the ACT is convenient, non-invasive, reproducible, responsive to changes in asthma control, and can be utilized as a screening tool for asthma control both within and outside of the medical environment [10].

The sensitivity and specificity of the ACT for poorly controlled asthma, with a cutoff point score of 19, were 69.2% and 76.2% in the study by Nathan *et al*. [9] and 71.3% and 70.8% in the study by Schatz *et al*., respectively [11]. The percentages of patients who were correctly classified by using this cutoff point of the ACT scores were 74.1% and 71% in the 2 studies, respectively [9, 11]. In our study, 83.7% of patients were correctly classified by the same cutoff point.

The results of this study showed some mismatches between the GINA rating criteria and the ACT scoring system, which may be due to the different criteria used for rating asthma control. An ACT score of 23-25 is rated as "controlled" by the GINA criteria, 17-22 as "partly controlled" and 16 or less as "uncontrolled", respectively.

A recent study found that many patients tend to overestimate their level of asthma control [12]. This was also observed in our study, in which 15.5% of patients overestimated their asthma control. The lack of pulmonary function criteria accounts for the remarkable difference between the ACT and GINA control ratings, and also is the reason why some patients who are asymptomatic, but with impairment of pulmonary function, overestimate the level of their asthma control. Therefore, total agreement between the ACT and GINA control ratings can never be achieved. Nevertheless, our study exhibited a good correlation between these 2 methods of assessing asthma control.

Since the ACT is a self-reported score, some patients may not understand the exact meaning of the questionnaire without help. The study by Nathan *et al*. suggested that a higher degree of concordance was demonstrated if patients were well-informed regarding asthma control and self-monitoring [9]. In our study, some patients used rescue medication regularly on a daily basis or unnecessarily when they experienced symptoms unrelated to asthma, and were thus classified into a lower ACT control level. Better patient education is needed to decrease the unnecessary use of rescue medication and obtain ACT scores reflecting the real status of asthma control.

Since allergic rhinitis is frequently associated with asthma, some patients had a low ACT score for question 3, "How often did your asthma symptoms wake you up at night or earlier than usual in the morning?", because they experienced night cough with sleep disturbance. That was another reason for the

underestimation of asthma control.

Patient age may influence the validity of a self-administered questionnaire, because younger patients may better understand the real meaning of a question. But our results showed that patients older than 50 years had slightly better agreement between the GINA rating criteria and the ACT control level. Several factors may account for this result. First, only a small portion of our patient group was younger than 50 years, since this institute is a veterans' hospital. A sample size that is too small may result in bias in statistical analysis. Second, our patient group included some patients who had previously visited our outpatient department. Every patient that was newly diagnosed as asthmatic received an asthma education program. This may minimize the impact of age on the ACT scores. Further research with a larger patient group may be needed to identify the relationship between age and the ACT.

Those patients who had a smoking history had a higher probability of combined chronic obstructive pulmonary disease (COPD) and asthma. COPD patients usually have more dyspnea and limitation of activity, and therefore they may record lower ACT scores than pure asthma patients. We sub-analyzed the correlation of the GINA rating criteria and the ACT level in smoking and non-smoking patients and found that better kappa value agreement was demonstrated in non-smokers, and even better kappa value agreement in all patients. This finding suggests that the ACT may have better correlation with the GINA rating criteria in pure asthma patients.

Conclusion

The ACT control level correlates well with the GINA rating criteria in assessing asthma control, although some disagreements may still persist. The ACT score seems to be more accurate when applied in pure asthma patients than in patients with other comorbidities. The results of this study confirm that the ACT is a convenient alternative screening tool for use in outpatient follow-up.

Abbreviations and Standard Abbreviations:
GINA: The Global Initiative for Asthma
ACT: Asthma Control Test
ACQ: Asthma Control Questionnaire
ATAQ: Asthma Therapy Assessment Questionnaire
mini-AQLQ: mini Asthma Quality of Life Questionnaire
COPD: Chronic Obstructive Pulmonary Disease

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比較使用氣喘控制測驗及GINA準則對氣喘控制程度評估的相關性

趙志浩* 金湘玲* 王振宇** 詹明澄* 郭英調***,**** 許正園*,*****

前言：GINA氣喘準則指出，評估氣喘控制程度要包括日間及夜間症狀、活動受限狀況、使用急救藥物的次數、急性發作的頻率以及肺功能試驗或是尖峰流速的結果。一個最近被提出的方法－氣喘控制測驗（ACT），是種由病人自行填寫的問卷，其中包含了五個問題，可由問卷評分的結果簡單地評估氣喘控制狀況。本研究目的在比較使用這兩種不同方法對評估氣喘控制程度的關聯性，以確定ACT在臨床上的實用性。

方法：規則於門診追蹤的氣喘病人完成ACT後即加入此研究。ACT依分數將病人分為三組，25分為完全控制，20-24分為控制良好，小於20分為控制不良。

結果：總共116位病人，233次門診中，ACT和GINA準則有良好的關聯性。71.7%的病人有完全相關（agreement Kappa = .524）。分別有15.5%及12.9%的病人高估及低估了自身氣喘的控制。進一步分析發現在沒有抽煙病史的病人中可得到較好的agreement Kappa值。

結論：ACT和GINA準則對氣喘控制程度的評估上有良好的關聯性，然而還是有些病人高或低估了他們的疾病。本研究結果支持ACT可當作病人在門診追蹤時可選用的一種工具。*(胸腔醫學* ***2008; 23: 81-88)***

關鍵詞：氣喘，氣喘控制測驗

*台中榮民總醫院 胸腔內科，**台中榮民總醫院 加護中心，***流病及生統實驗室，****台北榮總 教研部
*****中山醫學大學醫學研究所
索取抽印本請聯絡：許正園醫師，台中榮民總總醫院 胸腔內科，台中市西屯區台中港路三段160號

Orthopnea – Clinical Manifestation of Motor Neuron Disease: A Case Report

Liang-Yu Chen, Jia-Horng Wang, Li-Chi Hsu*

A patient presented with transitional cell carcinoma of the urinary bladder, and had suffered from bilateral lower leg pain and weakness since 1993. Radiculopathy and myelopathy were diagnosed, and the patient underwent a laminectomy, but in vain. Severe orthopnea was complained half a year later, and congestive heart failure was suspected, but clinical data did not support this diagnosis. The pulmonary function test disclosed evidence of neuromuscular disease (NMD), but no further investigation was performed. Unfortunately orthopnea progressed quickly with CO_2 retention. In addition to new abnormal neuromuscular findings, amyotrophic lateral sclerosis (ALS) was diagnosed by electromyogram and nerve conduction velocity test (EMG/NCV). ***(Thorac Med 2008; 23: 89-94)***

Key words: orthopnea, amyotrophic lateral sclerosis

Introduction

Orthopnea is not only a notorious finding of congestive heart failure (CHF) but also a presentation of neuromuscular disease (NMD) involving the diaphragm. We present a patient who had suffered from orthopnea since Feb 2006, and amyotrophic lateral sclerosis (ALS) was diagnosed 1 month later. We also review recent reports concerning the detection of neuromuscular weakness and categorizing inspiratory, expiratory and bulbar types, by pulmonary function test.

Case Report

An 82 year-old male was a military briefer. He had been regularly followed up at our genitourinary department since June 1997 for his transitional cell carcinoma of the urinary bladder, and had received 4 courses of transurethral resection and intravesical chemotherapy up to March 2003.

He had suffered from neck pain and bilateral lower leg pain since May 1993. Computered tomography (CT) showed herniated intervertebral discs at L3/4 and L4/5, and radiculopathy was suspected. Back pain was progressive and bilateral numbness of the legs presented 7 months later. Magnetic

Department of Respiratory Therapy, Taipei Veterans General Hospital, Taiwan; *Department of Neurology, Taipei Veterans General Hospital, Taiwan
Address reprint requests to: Dr. Jia-Horng Wang, Department of Respiratory Therapy, Taipei Veterans General Hospital

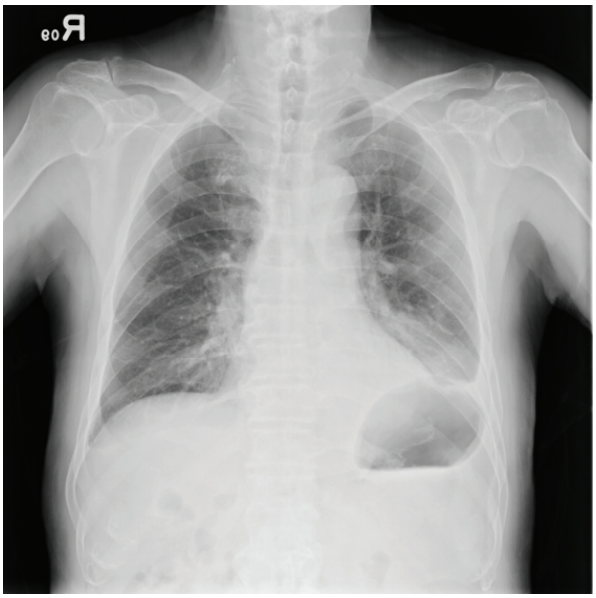

Fig. 1. A standing PA view. Encephalization of blood vessel and left pleural effusion are found

resonance imaging (MRI) of the thoracic spine revealed enhancement at T8. Occult fracture or early metastasis was suspected, but a whole body bone scan (WBBS) did not support this impression. Electromyogram and nerve conduction velocity (EMG/NCV) tests were also arranged for his cramping pain in the bilateral lower legs, and disclosed right L5/S1 radiculopathy. He then underwent a laminectomy on 24 August 2005, but in vain. Follow-up EMG/NCV showed progressive involvement with bilateral L1-S1 radiculopathy.

Unfortunately, obvious dyspnea occurred after laminectomy, so he was sent to the emergency room (ER) on 25 January 2006. No abnormal physical examination was noted, except weakness in the bilateral lower legs. Chest X-ray (CXR) revealed left pleural effusion (Figure 1), and electrocardiogram (EKG) disclosed sinus tachycardia and premature ventricular contraction. Follow up was arranged at chest clinic, and he was admitted to the chest ward due to severe orthopnea on 19 February 2006.

Neither abnormal breathing sounds nor abnormal heart sounds were heard. Pitting edema, jugular vein engorgement, and hepatojugular reflex were not noted. Biochemistry,

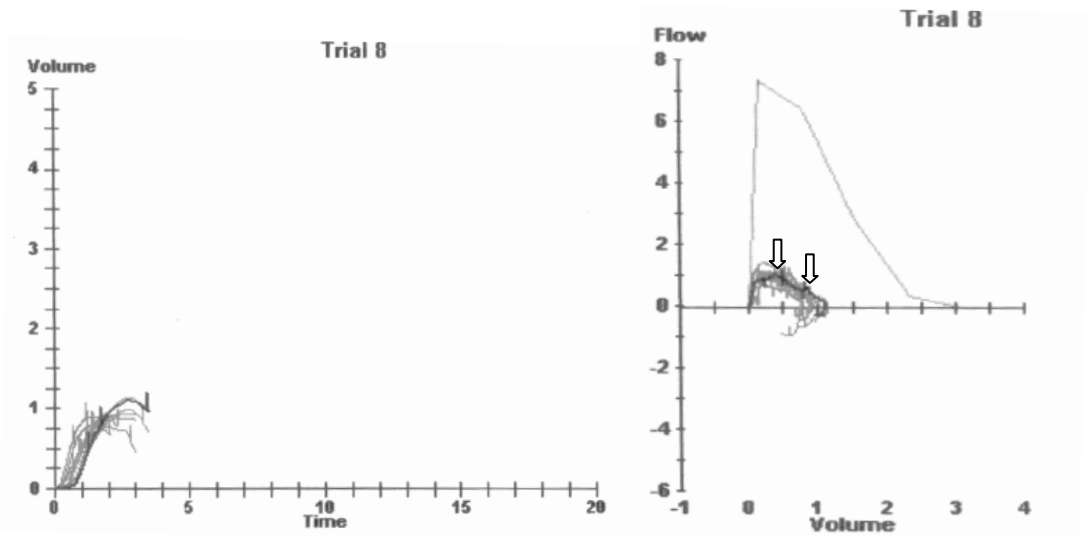

Fig. 2. Spirometry during admission. Poor effort was suspected by diminished peak flow rate and slope of flow-volume curve. A saw tooth curve was also found (arrow).

including renal function, was within normal limits, but blood routine disclosed mild macrocytic anemia. He had euthyroidism, and the pulmonary function test disclosed a reduced forced vital capacity (1.14L, 37% of predicted). The expiratory flow volume (F-V) loop disclosed reduced peak expiratory flow and a saw-tooth curve; however, this was interpreted as poor effort (Figure 2). The nuclear cardiogram showed normal systolic contraction and wall motion, and echocardiography revealed left ventricular over-contraction, no chamber dilation, no valvular abnormality and no pericardial effusion. Digoxin was given, because CHF with a normal systolic function was highly suspected.

Two weeks later, orthopnea progressed, and disorientation was also noticed by his family, so he was sent to the ER on 26 March 2006. An intermittent non-invasive positive pressure ventilator (NIPPV) was used because CO_2 retention was noted (pH = 7.342, PaO_2 = 140.8 mmHg, $PaCO_2$ = 86.5 mmHg, HCO_3^- = 45.8 mmHg on O_2 cannula 3L/min). After recovering consciousness, the patient asked to be discharged against physician advice. He was sent back to the ER the next day because of lethargy in the early morning. This time, interphalangeal muscle atrophy, increased deep tendon reflex of both knees and tongue atrophy with fasciculation were found. Repeated EMG/NCV revealed motor neuron disease, and ALS was then diagnosed.

Discussion

Orthopnea is the main complaint during admission to the chest ward, and is initially suspected to be the presentation of heart failure. But nuclear cardiogram and echocardiography disclosed no abnormality in this patient. It was not until his 3rd visit to the ER, muscle atrophy, tongue fasciculation and CO_2 retention were found and NMD was suspected.

Orthopnea can be seen in patient with CHF, and in those with diaphragmatic weakness. The originof diaphragmatic weakness can be at any point from the central nervous system to the diaphragm. The diagnosis of diaphragmatic weakness depends on fluoroscopic imaging of the diaphragm [1], direct measurement of transdiaphragmatic pressure (Pdi) [2] or a reduction in vital capacity (VC) when changing from the erect to the supine position [3]. Fluoroscopy is poorly sensitive when the hemidiaphragm is not completely paralyzed, and it is particularly misleading in patients with bilateral paralysis [4]. A fall in VC of 25% or more between the upright and supine positions has been a more sensitive indicator of diaphragmatic weakness [3]. The specificity and sensitivity are 90% and 79% respectively. Bilateral diaphragmatic dysfunction can produce closer to a 50% drop of VC, but unilateral dysfunction may show less than a 25% drop [5-6]. As for Pdi, less than 30 cmH_2O, is another sensitive detector of diaphragmatic weakness [7], but it is invasive and poorly tolerated especially in patients with swallowing impairment. Unfortunately, we did not measure this patient's vital capacity in the supine position.

ALS is a disease involving both upper and lower motor neurons, and it does not affect the lung directly, but pulmonary presentations, such as aspiration pneumonia, micro-atelectasis, and respiratory failure, are the results of weakness in the major respiratory muscles, including the expiratory muscles, inspiratory muscles and upper airway muscles [8].

Inspiratory muscle weakness not only leads to respiratory weakness but also reduces chest wall and pulmonary compliance, which results in restrictive ventilatory impairment of the patient. Total lung capacity (TLC) and VC fall below normal limits when muscle power is severely impaired to below 50% of the normal range [9].

Expiratory muscle weakness influences the ability to clear airway secretion. Weak expiratory muscles can not lower thoracic volume, so expiratory reserve volume is reduced, and residual volume (RV) is increased. The increased RV is supposed to be the earliest sign of expiratory weakness in patient with NMD [10]. In addition, the forced expiratory F-V loop became rounded due to reduced peak expiratory flow and the abrupt cut off of end expiratory flow [11-12].

Bulbar neurons control laryngeal muscle and pharyngeal muscles, so their involvement leads to an obstructive expiratory F-V curve. During expiration, irregular adduction of the vocal cord (contraction tremor: 4-8Hz) results in a saw tooth-like flow curve. As for inspiration, the vocal cord can not open completely, so inspiratory flow is lower than expiratory flow [13-14]. Impairment of speech and swallowing are other symptoms of the uncoordination of laryngeal and pharyngeal muscles, so inadequate nutrition and aspiration pneumonia may follow. Besides, bulbofacial weakness causes the patients to occlude the mouthpiece loosely, so the sniff pressure test is another indicator [15].

ALS is difficult to diagnose in the early stages, because the initial presentation is nonspecific. One study showed misdiagnosis in the early course of 43% of patients [16]. Two-thirds of the patients with an initial symptom of dyspnea were misdiagnosed, and 3 patients underwent laminectomies.

As for pulmonary function, NMD is difficultly to differentiate from poor effort, so we may combined this with other examinations, including physical findings and EMG/NCV. The difference in VC between the upright and supine positions may be considered a necessary test if diaphragmatic weakness is suspected.

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端坐呼吸，運動神經元疾病的臨床表現之一：病例報告

陳亮宇　王家弘　許立奇*

陶先生是一位膀胱移行上皮癌的病患，他因雙腳疼痛且無力而求診。由於疑似神經根及脊髓病變，他接受了椎間盤切除術，但是症狀並沒有改善。半年後，因為嚴重的端坐呼吸，又到醫院求診，當時懷疑患有心臟衰竭，但臨床證據並不支持此項診斷。肺功能檢查雖顯示有肌肉疾病，但未被確認做進一步檢查。端坐呼吸的情形快速地惡化，且發現動脈血中二氧化碳濃度逐漸升高，加上有新的異常神經學檢查，最後靠著肌電圖與神經學傳導檢查，肌萎縮側索硬化症才被診斷出來。*(胸腔醫學* ***2008; 23: 89-94)***

關鍵詞：端坐呼吸，肌萎縮側索硬化症

台北榮民總醫院　呼吸治療科，*台北榮民總醫院　神經內科
索取抽印本請聯絡：王家弘醫師，台北榮民總醫院　呼吸治療科，臺北市石牌路二段201號

Primary Pulmonary Lymphoma - Lymphoplasmacytic Lymphoma: A Case Report and Literature Review

Ying-Ming Tsai, Ming-Shyan Huang, Jong-Rung Tsai, Yue-Chiu Su*, Yi-Chang Liu**, Jhi-Jhu Hwang

Bronchogenic carcinoma is a disease with high cancer-related morbidity and mortality despite modern diagnostic equipment and novel treatments. However, a variety of rare benign and malignant tumors other than bronchogenic carcinoma may affect the lung. Thoracic lymphomas, which are located in the mediastinum or hilum, are quite common, and can be either primary or secondary types. Primary pulmonary lymphomas (PPLs) are a rare pulmonary malignancy which has been reported sporadically. Most of the PPLs are low-grade B-cell type lymphomas, which originate from mucosa-associated lymphoid tissue (MALT) of the bronchus. We report a 57-year-old male smoker who suffered from prolonged cough-associated lung mass and weight loss, and who was later proved to have primary pulmonary lymphoma by biopsy. We present this case as a reminder to physicians of this rare disease and to review the relevant literature. ***(Thorac Med 2008; 23: 95-102)***

Key words: primary pulmonary lymphoma, lymphoplasmacytic lymphoma, Waldenstrom macroglobulinemia, mucosa-associated lymphoid tissue (MALT)

Introduction

Primary pulmonary lymphomas (PPL) are uncommon entities that account for less than 1% of all lung malignancies [1]. Most PPLs are mucosa-associated lymphomas; they are low-grade B cell lymphomas and can be referred to as pulmonary mucosa-associated lymphoid tissue lymphomas (MALTOMAs). High-grade pulmonary lymphomas are less frequent and have a worse prognosis and poor treatment response. Secondary pulmonary lymphomas are much more common than primary ones worldwide, with an incidence of 25% to 40% [2-3]. Costa *et al*. [4] stated that non-Hodgkin's lymphomas (NHLs) have a slightly higher incidence in secondary pulmonary involvement than in Hodgkin's disease.

Lymphoplasmacytic lymphoma (LPL), a type of low-grade NHL which primarily involves the lung, has been reported rarely. It is known as as immunocytoma, malignant

Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Department of Pathology*, Department of Hematology and Oncology**, Kaohsiung Medical University, Chung-Ho Memorial Hospital, Kaohsiung Medical University

Address reprint requests to: Dr. Jhi-Jhu Hwang, Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Kaohsiung Medical University Chung-Ho Memorial Hospital, Kaohsiung Medical University, No. 100, Tzyou 1st Road Kaohsiung 807, Taiwan

lymphoma; small lymphocytic, and plasmacytoid in the Working Formulation, and as lymphoplasmacytic/lymphoplasmacytoid lymphoma in the Kiel classification [5]. LPL is frequently associated with Waldenstrom macroglobulinemia, which is defined as a B-cell neoplasm with lymphoplasmacytic infiltration of the bone marrow and a monoclonal immunoglobulin M (IgM) protein, and exludes plasmacytoid/cytic variants. Herein, we present a patient with a lung mass who was later diagnosed with lymphoplasmacytic-type PPL.

Case Presentation

A 57-year-old man without systemic disease had suffered from cough and poor appetite, was easily fatigued for 2 months, and had a small weight loss of 3 kilograms in 6 months. He had recently suffered low-grade fever and chills, and had a history of smoking 30 pack-years, and alcohol consumption. Due to a persistent dry cough, he visited our chest outpatient department. Upon admission, he complained of a mild cough, but no dyspnea, nor dyspnea on exertion. A chest X-ray (Figure 1) revealed a right lung mass and pleural effusion. The chest computed tomography (CT) (Figure 2A) showed a right lower lung consolidated mass with moderate pleural effusion, but without mediastinal lymphadenopathy. Bronchoscopy was performed immediately, and revealed right B8 and B9 orificial narrowing. A transbroncial lung biopsy had a negative result. The characteristics of pleural effusion were the following: exudates, cell count: 17500/μl, and P/M ratio: 5/95%. The cytologic smear showed malignant cells which were plasma cell-like. A blood biochemistry study showed total protein/albumin: 7.31/2.93 mg/dl, LDH: 157 U/L, β2

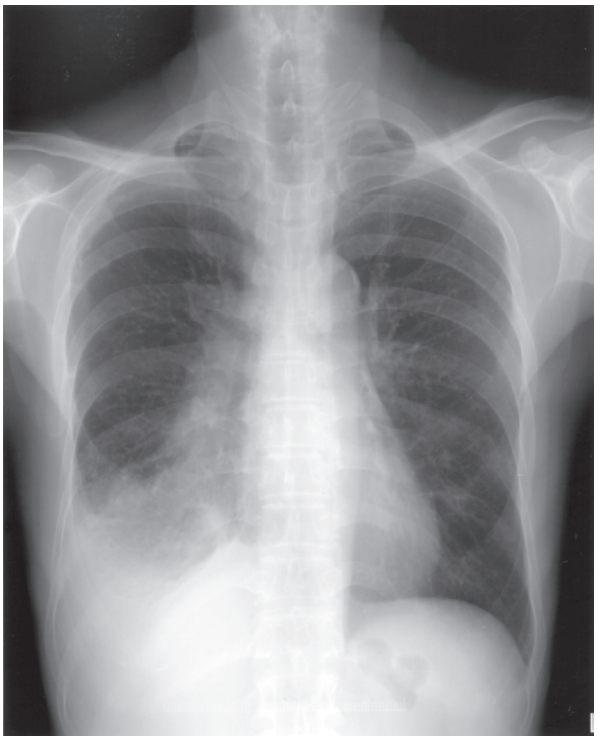

Fig. 1. Chest radiograph initially showed an opacifying mass-like lesion in the right lower lung field with a blunted lateral costophrenic angle.

microglobulin: 268.0μg/dl (normal range: <215.7 μg/dl), immunoglobulin G/A/M: 785.0/91.9/2840.0 mg/dl (normal range: 917.2-1891.2/183.9-322.2/102.6-200.2). From the pleural effusion study and M component protein, multiple myeloma was suspected. Serum protein immunoelectrophoresis revealed IgM lambda monoclonal gammopathy. The bone marrow aspiration and biopsy were normal. An abdominal sonography and gallium-67 scan were done, and neither revealed positive findings in the abdomen.

Due to the non-definite diagnosis, lung tissue biopsy was performed by video-assisted thoracic surgery (VATS). The pathologic report of the right upper lobe and right lower lobe samples showed a cellular infiltrate comprising small mature lymphocytes and plasmacytoid

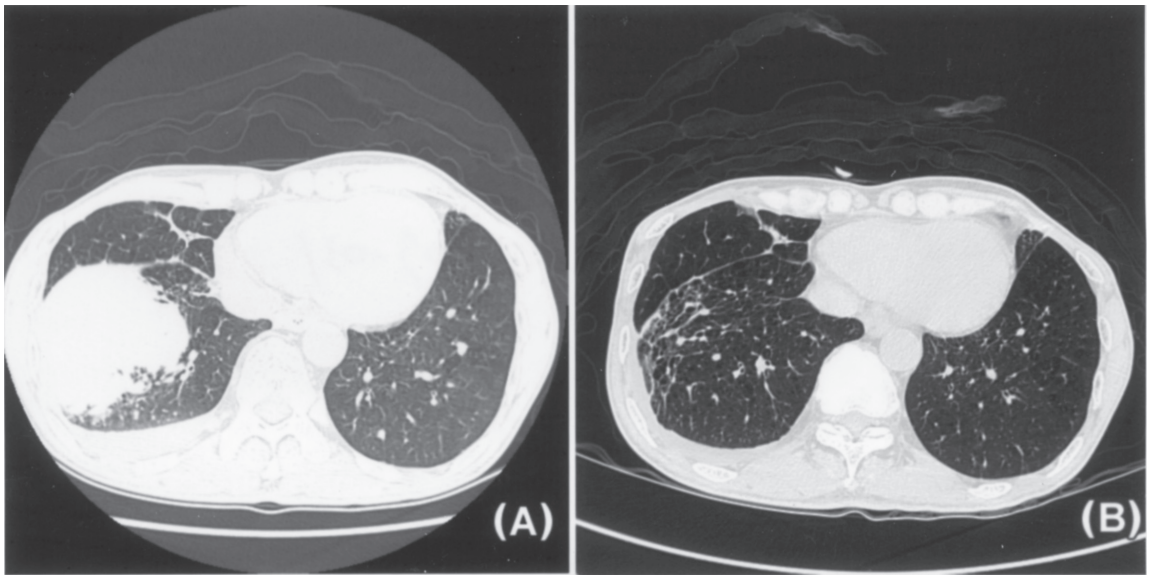

Fig. 2. (A) High-resolution CT revealed the mass with an irregular border. (B) After treatment of more than 10 months, high-resolution CT showed near disappearance of the tumor with little fibrotic change.

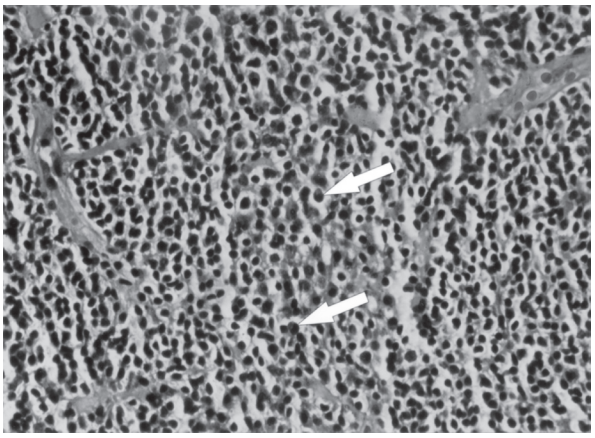

Fig. 3. The pathologic findings of the lung mass: the H&E stain (200X) revealing a mixture of small lymphocytes and plasmacytoid cells (arrow)

lymphocytes, diffusely infiltrating into the lung parenchyma (H&E stain, Figure 3). The tumor cells were positive for leukocyte common antigens, the small lymphocytes were positive for B cell lineage (CD20) (not shown), and the plasmacytoid cells were positive for VS38C (Figure 4B), but negative for CD5 (Figure 4A) According to the histopathologic features and the results of immunohistochemical studies, a LPL was favored.

Later, this patient received chemotherapy with cyclophosphamide (750 mg/m^2), vincristine (1.4 mg/m^2), and prednisolone (60 mg/m^2) for 8 doses, followed by oral medications with chlorambucil (4 mg qd) and prednisolone (10 mg qd). After 10 months of treatment, the patient was well and the mass had disappeared from the chest CT study (Figure 2B). In addition, the IgM level showed improvement (from 2840.0 mg/dl initially to 503.0 mg/dl now).

Discussion

PPL is defined as a clonal lymphoid proliferation affecting 1 or both lungs (parenchyma and/or bronchi) in patients without detectable extrapulmonary involvement at diagnosis or in the subsequent 3 months [6]. In order to exclude extrathoracic lymphoma, a bone marrow biopsy

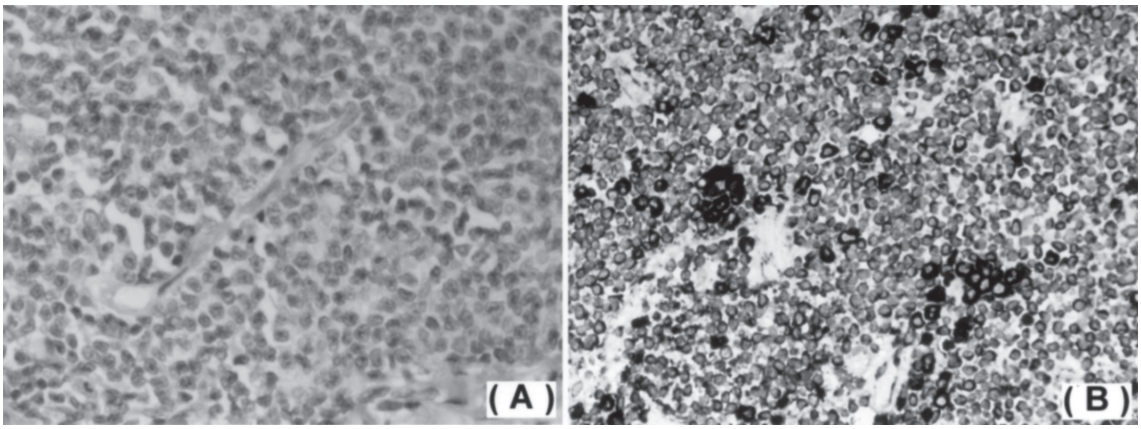

Fig. 4. Immunohistochemical staining (IHC) was negative for CD5 (400X) (A), positive for VS38C (400X) (B).

and CT of the abdomen should be performed [3]. As reported, most of the primary pulmonary NHLs were marginal zone B-cell lymphomas of the mucosa-associated lymphoid tissue type (MALT lymphoma), followed by diffuse large B cell type [3, 7]. Pulmonary MALT lymphoma has some similarities to the well-known gastric MALTOMA, which is strongly related to *H. pylori* infection. The prognosis and natural history of MALT lymphomas in different organs seem the same. However, there are still no proven obvious relationships between specific pathogens and pulmonary MALTOMA.

The clinical presentations of PPLs depend on the grade of the lymphomas. More than half of patients with low-grade types were asymptomatic, and they were found by a routine chest X-ray study [8-9]. Non-specific pulmonary complaints were cough, chest pain, crackle on chest auscultation [1, 10], hemoptysis [11], and constitutional features such as fever and weight loss [3, 11]. Most of the high-grade PPLs are symptomatic.

The median age at diagnosis as shown in other studies ranges from 50 to 70 years of age [11-12]. Male patients have a higher risk than female patients of acquiring primary pulmonary lymphoma, however, other reports have shown an equal risk [8, 10]. And, in a recent case report, the male/female ratio was 1:2 in T cell lymphomas [13]. In recent years, the disease incidence has increased in patients with an immunocompromised status, such as acquired immunodeficiency syndrome [14-16], autoimmune diseases such as Sjogren's syndrome [17], and post-transplantation [18-19].

The most common CT findings of PPLs are air-space consolidation (45-50%) and/or mass and lung nodules (15%) [10]. Other reports have shown that pulmonary infiltration is the most common, consisting of 42%-69% [2-3, 11]. The major differences in radiographic presentation may be related to the grades of lymphomas. Low-grade lymphomas tend to manifest as solitary, well delineated soft-tissue masses, rather than diffuse infiltrations along the bronchovascular bundles, interlobular septa, and extensive lobar infiltrates [20]. Pleural effusion has been found, as well (9%-15%) [3, 10]. CT is useful for detecting mediastinal involvement and the extent of lymphomas [12]. Atelectasis was mentioned in 1 study, and

was related to bronchial stenosis. Fiberoptic bronchoscopic findings showed normal features macroscopically in most cases (34/60, 57%), and the most common abnormality was bronchial stenosis [9].

The diagnostic methods included bronchoscopy (transbronchial needle aspiration, or transbronchial lung biopsy), CT-guided biopsy, open thoracotomy, and VATS [3]. Because of poor accuracy during relatively less-invasive procedures such as bronchoscopy, most of the diseases are diagnosed by frozen section intraoperatively and confirmed postoperatively by immunostaining if the result was negative [11]. In serum protein electrophoresis or immunoelectrophoresis studies, most do not show up abnormally, and 30% of patients revealed monoclonal gammopathy, which IgM gammopathy predominates [9]. To differentiate between a reactive process and a lymphoma, monoclonality of the lymphoma cells needs to be determined by immunophenotyping, using immunohistochemistry or the more sensitive flow cytometry [13].

The treatment of PPL included conservative treatment for the low-grade lymphoma with regular follow-up, chemotherapy with different regimens (CHOP [cyclophosphamide, doxorubicin, vincristine, prednisolone], CVP [cyclophosphamide, vincristine, prednisolone], etc.), complete resection of the tumor with/without adjuvant chemotherapy [2, 11], and radiotherapy. Vanden Eynden *et al*. reported that complete resection is a promising treatment for localized low-grade lymphoma, which is associated with a 90% long-term survival rate [11]. For low-grade PPLs, there are still no standard treatments, such as chemotherapy, surgery, radiation, or combined therapy [2, 9-10, 21].

Waldenstrom's macroglobulinemia is a distinct B-cell lymphoproliferative disorder with the features of bone marrow lymphoplasmacytic cell infiltration, and the demonstration of IgM monoclonal gammopathy [22]. However, in a recent modification of the NHL classification, this disease was considered to be LPL [23]. LPL, which is a tissue presentation of Waldenstrom's macroglobulinemia, is a type of indolent lymphoma that involves the bone marrow, peripheral blood, and spleen. Rarely has the lung been involved with a presentation of pulmonary infiltrates, nodules, or pleural effusion [24]. LPL is rarely reported, and is around 1.2% in non-Hodgkin's lymphomas [25]. However, the prevalence of primary pulmonary lymphoplasmacytic lymphoma is 2% in PPLs [3]. The involved patients frequently had an IgM paraprotein (Waldenstrom's macroglobulinemia) that may lead to symptoms of hyperviscosity, autoimmune phenomena, or neuropathies. Not all patients with LPL need treatment, only the symptomatic patients. The main treatment choices for Waldenstrom's macroglobulinema include alkylating agents (chlorambucil, cyclophosphamide, mephalan), purine analogues (cladribine, fludarabine), and monoclonal antibody (rituximab [anti-CD20]). Plasma exchange is indicated in the acute management of patients with symptoms of hyperviscosity. Other agents have been implicated, including thalidomide, lenalideomide, and high-dose chemoradiotherapy with autologous stem cell transplantation. Novel agents such as oblimersen sodium (BCL-2 antisense oligonucleotide), 131I-tositumomab, imatinib mesylate, and dolastatin are now being evaluated.

In conclusion, PPL is a rare disease, and most manifestations are of B cell lineage. LPL is especially rare within PPLs. It is hard

to diagnose this disease from image studies alone. Combined adequate tissue sampling, immunohistochemical stain, and highly suspicious clinical data will lead to the right diagnosis.

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原發性肺惡性淋巴瘤—淋巴漿細胞惡性淋巴瘤：病例報告及文獻回顧

蔡英明　黃明賢　蔡忠榮　蘇月秋*　劉益昌**　黃吉志

支氣管肺癌是肺腫瘤中最常見，即使科學的進步，創新藥物的發明，支氣管肺癌仍是一個癌症相關死亡率和失能相當高的疾病。然而，除了支氣管肺癌，其他腫瘤亦不能忽略，不論是良性或惡性。胸腔內的惡性淋巴瘤，可分為原發或是續發於其他部位的腫瘤，好發於縱隔腔或是肺門。原發於肺臟惡性淋巴瘤為相當罕見的肺部惡性腫瘤，而文獻中的報導，大多為低惡性B細胞淋巴瘤。而這類的腫瘤，以目前的證據來看，是由支氣管中的黏膜相關類淋巴組織轉型而來。這一位57歲男性抽煙伴有長期咳嗽，體重下降的病人在多種診斷方法下證實為一個原發於肺部惡性淋巴瘤—淋巴漿細胞淋巴瘤，藉此提醒大家這樣一個以長期咳嗽來表現的肺部原發性惡性淋巴癌。*(胸腔醫學* ***2008; 23: 95-102)***

關鍵詞：原發性肺惡性淋巴瘤，淋巴漿細胞惡性淋巴瘤，Waldenstrom大球蛋白血症，黏膜相關類淋巴組織

高雄醫學大學附設中和紀念醫院　胸腔內科　病理科*　血液腫瘤科**
索取抽印本請聯絡：黃吉志醫師，高雄醫學大學附設中和紀念醫院　內科部　胸腔內科，高雄市三民區十全一路100號

Sarcoidosis with a Pulmonary Disseminated Miliary Nodule Presentation: A Case Report and Review

Hung-Jie Chen, Jo-Chi Tseng, Yu-Chih Liu

Sarcoidosis is a systemic disease, and lung involvement is most common. The radiologic patterns of sarcoidosis are usually lymphadenopathy, diffuse lung infiltrations, and multiple nodular lesions. We report a female patient with asymptomatic miliary nodular infiltrations found by routine chest X-ray. The pulmonary function test showed moderately restrictive lung disease. Lung biopsy using video-assisted thoracic surgery (VATS) was performed, and the pathology report revealed non-caseous granulomatous inflammation. All studies for tuberculosis infection were negative, including tuberculin skin test, sputum acid fast stain, and bronchial wash fluid and culture. Under the impression of sarcoidosis, oral corticosteroid treatment was prescribed. After steroid treatment, the patient's lung infiltration and lung function test both improved. ***(Thorac Med 2008; 23: 103-111)***

Key words: sarcoidosis, military nodules, corticosteroid

Introduction

Miliary nodule infiltration is an interstitial pattern in the chest X-ray findings with widespread and well-defined nodules less than 2 mm in diameter. Usually, this infiltration can be seen in metastatic or granulomatous disease. Granulomatous disease can be divided into infectious granulomatous disease, such as miliary tuberculosis and fungal infection, and noninfectious granulomatous disease, such as sarcoidosis, histiocytosis, and hypersensitive pneumonitis, and some pneumoconioses, such as coalworker's pneumoconiosis and primary silicosis.

Sarcoidosis is a systemic, non-caseous granulomatous inflammatory disease. This disease was first described as a cutaneous disease by Jonathon Hutchinson in 1877 [1]. Later, it was found to be a systemic disease involving multiple organs, including the lung, eyes, skin, liver, lymphatic systems, heart, and neurologic system. The clinical symptoms depend on the different organ involvement. Females are more prominent than males. The etiology of sarcoidosis is still unknown, and the exposure of genetically susceptible individuals to specific environmental agents may contribute to the pathogenesis. Clinically, some infections and inorganic agents may induce sarcoidosis. Lung involvement is found in more than 90 % of patients [2], with the presentation of dyspnea, dry cough, or chest pain. The pulmonary func-

Division of Chest Medicine, Department of Internal Medicine, Chang-Gung Memorial Hospital, Keelung
Address reprint requests to: Dr. Hung-Jie Chen, Division of Chest Medicine, Department of Internal Medicine, Chang-Gung Memorial Hospital, Keelung, No. 222, Mai-Chin road, Keelung, Taiwan

tion test can reveal a normal, restrictive or obstructive pattern. Decreased diffusion of carbon monoxide (DLCO) in the lung is frequent. More than 30% of patients with sarcoidosis have restrictive disease [3], which may be related to increased elastic recoil and decreased lung compliance. Obstructive defects have been reported in some studies and might be related to narrowing of the bronchial wall due to granulomatous lesions or fibrotic scarring, compression by enlarged lymph nodes, airway distortion due to fibrosis, small airway disease, and bronchial hypersensitivity [4].

We describe herein a female patient with sarcoidosis with disseminated miliary nodular lesions in the bilateral lung fields and a moderately restrictive ventilatory defect.

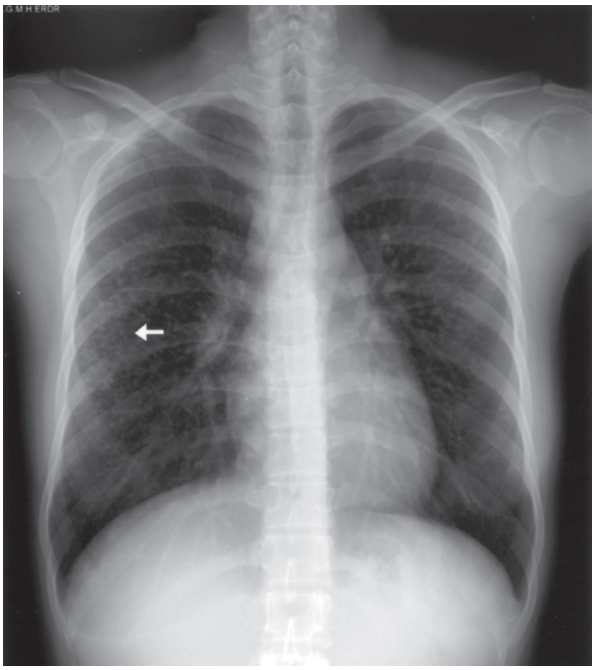

Fig. 1. Chest X-ray film (PA view) showing miliary nodules in the bilateral lung fields. (white arrow) Bilateral CP angle is clear and sparing of miliary nodules.

Care Report

A 25-year-old female patient was a nurse and worked in the medical intensive care unit for more than 2 years. An abnormal chest X-ray (Figure 1) in a routine health examination was noted. She had had no respiratory tract infection, travel, or special contact history with chemicals or animals in recent months. She did not smoke, consume alcohol, or take any medicine or hormonal agents. She had a 1-year-old child. There was no cough, sputum production, fever, chills, shortness of breath, or chest pain prior to this visit. Physical examination revealed no remarkable finding. The vital signs were as follows: blood pressure: 130/71 mmHg; body temperature: 36.2^{o}C; heart rate: 77/min; and respiratory rate: 18/min. Her breathing sounds were clear with no detectable wheezing. Disseminated miliary nodules were found in her chest X-ray, and a pulmonary function test showed a moderatedly restrictive ventilatory defect (FVC = 1.7L, 46.2%, FEV1 = 1.51L, 47.1%, FEV1/FVC = 88.89%). The blood test data showed: WBC: 5900/uL; segment: 61%; lymphocytes: 29.4%; Hb: 14.3 g/dL; creatinine: 0.6 mg/dL; ALT: 17 U/L; AST: 19 U/L; calcium: 9.1 mg/dL; sodium: 137.9 meq/L; potassium: 4.33 meq/L; and albumin/globulin: 4.7/3.5 g/dL. Urine analysis was normal. High-resolution computed tomography (HRCT) (Figure 2) revealed disseminated miliary nodular lesions less than 5mm in diameter with perilymphatic and subpleural spreading, but generally random distribution to the bilateral lungs. Mediastinal lymph node enlargement was also noted. She was admitted to the ward for further evaluation.

The tuberculin skin test was negative. Bronchoscopy was performed and no visible endobronchial lesion was found. The bronchial wash for tuberculosis culture and the cytological

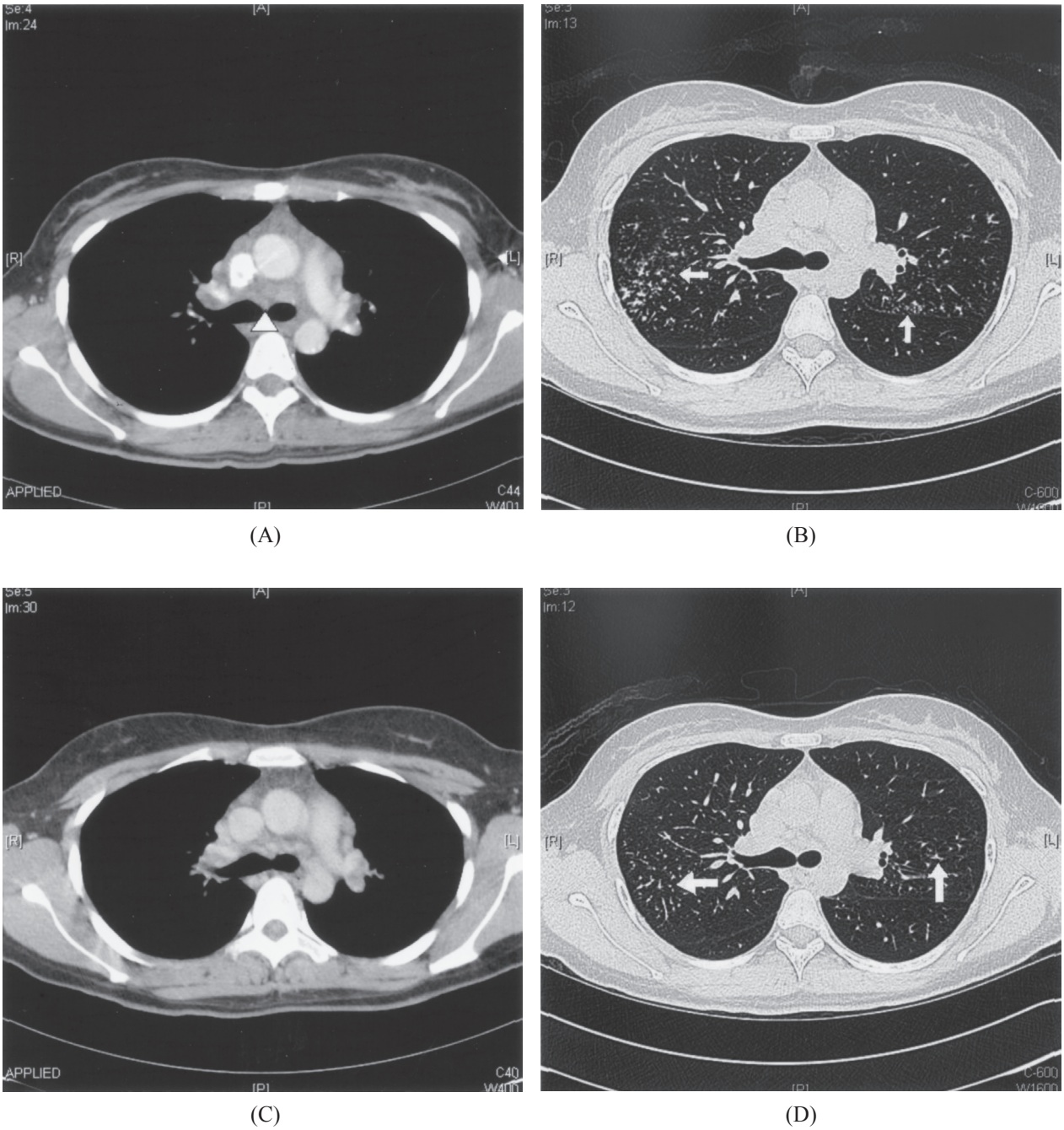

Fig. 2. High resolution computed tomography (HRCT) of the lung with contrast. (Panel A) The image shows mediastinal lymphadenopathy. (triangle) (Panel B) Multiple bronchovascular bundle-disseminated military nodular lesions were found. (white arrow) These nodules are prominent in the right middle and lower lung fields and their sizes vary from 1 mm to 5 mm. After treatment (Panel C), the mediastinal lymphadenopathy showed improvement. (Panel D) Multiple disseminated miliary nodular lesions persist. (white arrow) Better pulmonary miliary nodules are found after treatment.

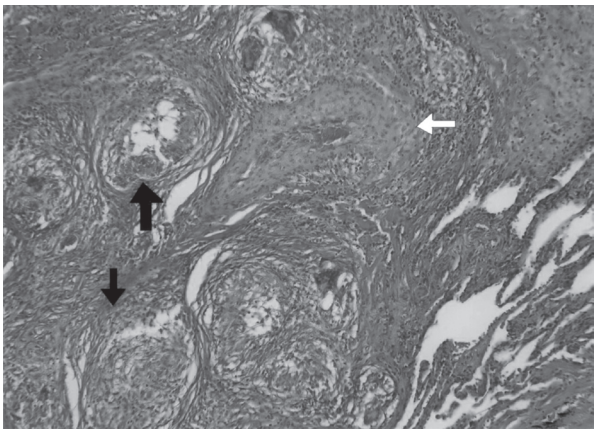

Fig. 3. Lung biopsy, low-power field. Non-caseating granulomas (black arrow) of differing sizes are found in a scattered distribution around the arteriole (white arrow). X100

study were both negative. Open lung biopsy by video-assisted thoracic surgery (VATS) was performed and wedge resection of the right middle lobe was done. The pathologic report revealed non-caseous granulomatous inflammation with multiple-nucleased Langerhans giant cells. (Figure 3) Tissue tuberculosis PCR was done and was negative. Sarcoidosis was diagnosed based on the series of study results and she began taking oral prednisolone 40 mg per day. After a 2-month month treatment, we arranged for her to undergo pulmonary function test follow up; the result showed that the pulmonary function had markedly improved and returned to a normal range (FVC = 3.28L, 89.2%, FEV1 = 3.12L, 97%, FEV1/FVC = 94.88%). Chest X-ray and HRCT were repeated after steroid treatment for 3 months and showed partial resolution of the miliary nodular lesions and mediastinal lymphadenopathy. Because of her stable disease, prednisolone was tapered gradually to 5 mg per day, and the total treatment course was 1 year. She was quite well at the follow-up. (Figure 2)

Discussion

Sarcoidosis usually appears between the ages of 20 and 40; however, both childhood and geriatric cases occur with some regularity. The incidence and prevalence of sarcoidosis varies with different races and countries: the prevalence in the U.S is 35.5 per 100000 for blacks and 10.9 per 100000 for whites; in Japan, the prevalence is 5.6 per 100000 [5]. The highest prevalence rates have been reported in the Scandinavian countries and in the US African-American population. In the Scandinavian countries, Germany, and Japan, there is a second peak incidence in females more than 50 years old. Several studies suggested that sarcoidosis in Afro-Americans is more severe, while Caucasians are more likely to present with asymptomatic disease. The pathogenesis of sarcodosis is still unknown, but some studies indicate that it may present as a result of person-to-person transmission or shared exposure to an environmental agent. Familiar clustering and seasonal clustering of sarcoidosis, especially in winter and early spring, have been reported. Genetic factors and occupational exposure are important in evaluating patients who are suspected of having sarcoidosis. The human leukocyte antigen (HLA)-type A1/B8/Cw7/DR3 carries a good prognosis and correlates with acute disease. Chronic sarcoidosis correlates with HLA-B13/BW15, HLA-DR17 correlates with better lung function, and HLA-B22 correlates with disseminated systemic disease [6]. Because of the complexity of the different occupational exposures, it is hard to pinpoint which occupation may correlate to sarcoidosis, but people who work in occupations with potential exposure to metals or in workplaces with high humidity may be at an increased risk.

Clinically, exposure to some infections (such as viral, mycobacterium, mycoplasma, Borrelia burgdorferi, and Propionibacterium acnes) and exposure to organic agents (such as pine tree pollen) or inorganic agents (such as Aluminum, Zireonium, clay, and talc) may induce sarcoidosis.

The early sarcoid reaction is characterized by an accumulation of activated CD4+ T-cells of the TH-1 type and macrophages at sites of ongoing inflammation [7]. T cells and macrophages release more cytokines and induce granuloma formation. In the lung, activated macrophages can secrete various fibroblast growth factors, which may contribute to fibroblast proliferation, collagen synthesis, and development of fibrosis in sarcoidosis.

Clinically, sarcoidosis can be divided to acute and chronic presentations. The acute presentation, classically with Löfgren's syndrome, and as described by Sven Löfgren in 1946, is defined by acute erythema nodosum with bilateral hilar lymphadenopathy, fever, and polyarthritis, and has a higher rate of spontaneous resolution. Chronic sarcoidosis with a gradual onset may present lupus pernia, which is a persistent, disfiguring, violaceous rash on the nose, cheeks, and ears. Usually, multiple organ involvement is found at the time of chronic sarcoidosis diagnosis. Chronic eye and bone involvement are more common in chronic sarcoidosis, as is persistence of disease and recurrence after treatment. The prognosis of patients with acute disease is usually better. Fatality involves 1 to 5% of sarcoidosis patients, typically owing to progressive respiratory insufficiency or central nervous system or myocardial involvement [8].

Lymph node enlargement and parenchymal lung involvement are the most common radiologic findings of sarcoidosis. Sarcoidosis lung involvement can be divided to 5 stages, based on the chest X-ray findings; stage 0, normal; stage I, bilateral hilar lymphadenopathy (BHL); stage II, diffuse lung infiltration with BHL; stage III, diffuse lung infiltration without BHL; stage IV, pulmonary fibrosis. The staging system does not correspond to the progression of disease, but does correlate with likelihood of future radiographic and symptomatic disease resolution. Sarcoidosis with parenchymal lung involvement can present with nodular patterns, reticular patterns, a ground-glass appearance, and miliary patterns. The miliary pattern is a kind of nodular pattern, and can be seen only 1% of patients with sarcoidosis [9]. K. Hatzakis also reported a 47-year-old male patient with miliary tuberculosis and recurrent miliary sarcoidosis after appropriate treatment for tuberculosis [10]. The nodular pattern is the most common radiologic parenchymal presentation of sarcoidosis [11], and may vary in size from large to miliary. The nodules are usually in a perilymphatic distribution, but can also be seen in the peribronchovascular regions, fissures and interlobar septa, and subpleural regions [12-14]. The pathologic picture of the nodules is granulomatous with macrophages and Langerhans cells. Microscopic interstitial granulomas would have a ground-glass appearance. Usually, in HRCT imaging, the nodular lesions of sarcoidosis are upper-lung predominant, with a perilymphatic distribution and a resemblance to silicosis and pneumoconiosis. Silicosis and coal worker's pneumoconiosis may present with egg-shell calcification or pulmonary massive fibrosis (PMF). Disseminated military nodules can be seen in miliary tuberculosis and metastatic lesions that are hematogenously spread. Miliary tuberculosis was first considered in Taiwan. Miliary tuber-

culosis usually shows random and discrete nodules with a uniform size (1-2 mm), and has a slight lower-lung predominance which may relate to vascular distribution. Miliary nodules are centrilobular nodules with branching linear opacities (tree-in-bud) which reflect the endobronchial spread of infection. They may also be found in pleural effusion and lymph node enlargement. Less peribronchovascular region involvement is noted. Metastasis is another common condition with a random pulmonary nodule appearance. Usually, nodules in metastasis are found various sizes, have more smooth margins, and are well-defined nodules. Metastasis is usually lower-lung predominant and may present lymphangitis carcinomatosis [15]. Our patient's HRCT showed diffuse miliary nodules with perilymphatic seeding and mild interlobular septal wall thickening, but these miliary nodules were prominently in the right middle and lower lung and associated with enlarged mediastinal lymphadenopathy.

The pulmonary function test is a common examination in respiratory disease. In sarcoidosis patients, the pulmonary function test can be a normal, restrictive, or obstructive pattern. Decreased carbon monoxide diffusing capacity (DLCO) and forced vital capacity (FVC) are usually found; 20% patients with sarcoidosis stage I disease have an abnormal function test, and 40-70% of stage II-IV patients have an abnormal pulmonary function test. A restrictive pattern can be related to increased elastic recoil and decreased lung compliance, and an obstructive pattern can involve a narrowing of the bronchial wall because of sarcoidosis infiltration into the bronchial wall, compression by lymph node enlargement, airway distortion, small airway disease, and bronchial hypersensitivity. The pulmonary function test cannot predict the long-term prognosis of sarcoidosis in most studies, but can provide objective and quantifiable measures of sarcoidosis progression and responsiveness to therapy (a change in FVC > 10% to 15% or DLCO > 20% is usually defined as significant) [16-17].

Granulomatous inflammation can be found in many diseases, including tuberculosis, sarcoidosis, cat-scratch disease, lymphogranuloma inguinale, leprosy, brucellosis, syphilis, some mycotic infections, and berylliosis. Granuloma can be divided to 2 types, based on its pathogenesis. Foreign body granuloma is induced by a foreign body phagocytized by macrophages and encapsulated by giant cells and epitheloid cells. No inflammation or immune response is induced in this process. Immune granuloma is caused by insoluble particles, usually microbes, and the cell-mediated immune response is incited later. The pathologic characteristic of a typical sarcoid lesion is circumscribed granulomas of epithelioid cells with little or no necrosis. The difference between sarcoidosis and tuberculosis can be based on the existence of caseating necrosis and tissue polymerase chain reaction (PCR). Gumma, a soft, tumor-like growth of the tissues, is found in syphilis, and has the characteristics of an enclosing wall of histiocytes, plasma cell infiltrates, and central cell necrosis without loss of cellular outline. In the histologic findings, cat-scratch disease presents rounded or stellate granulomas containing central granular debris and recognizable neutrophils.

Treatment is not necessary for all patients with sarcoidosis, and depends on the symptoms and different organ involvement. Spontaneous remission occurs in stage I in 55-90%, stage II in 40-70%, stage III in 10-30%, and stage IV in 0-5% of cases, and often within 3 years. Sarcoidosis with cardiac and neurologic invo-

lvement, hypercalcemia, and ocular disease does not respond to topical therapy need medical treatment. In pulmonary sarcoidosis, about 39% of patients spontaneously resolved within 6 months, and only 22% of patients needed treatment because of symptoms in progress [18]. Systemic steroid is the first drug of choice to treat sarcoidosis. In pulmonary sarcoidosis, progressive disease and poor/worsening lung function tests suggest steroid treatment. This female patient was in stage II disease with a moderately restrictive ventilatory defect.

Treatment with oral steroid usually results in relief of clinical symptoms, and improvement in radiologic findings and lung function tests. Steroid treatment is also suggested for stage IV patients for 8-12 weeks before being labeled as having end-stage fibrosis. The standard dose and duration of steroid treatment is still controversial but usually, the initial dose of steroid is suggested at 20-40 mg/day (prednisolone) for 1-3 months. The dose is adjusted according to clinical response and side effects. Steroid treatment usually persists 1 to 2 years. There are alternative agents, such as methotrexate, azathioprine, cyclophosphamide, and hydroxychloroquine for non-responsiveness or intolerance to steroid treatment.

In summary, sarcoidosis is a systemic disease and presents different patterns on imaging. We reported patient with sarcoidosis who presented with a rare imaging pattern of disseminated miliary nodule lung infiltration and had a moderately restrictive ventilatory defect. She responded well to oral steroid treatment and subsequently recovered. Sarcoidosis should be considered disseminated miliary nodules, excepts in the differentiated diagnosis of tuberculosis and metastasis.

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類肉瘤以肺部散佈性粟狀節結作爲表現

陳宏杰　曾若琦　劉育志

類肉瘤（sarcoidosis）是一種慢性肉芽腫（granuloma）的病變。它可以侵犯肺，心臟，皮膚，神經系統，淋巴系統等。其中以肺部侵犯最為常見。常見的肺部侵犯的臨床症狀包括喘、咳嗽、胸悶、胸痛等。在影像學上，胸部X光片可分為五期。第0期：正常，第1期：雙側肺門淋巴結病變，第2期：瀰漫性肺部浸潤合併雙側肺門淋巴結病變，第3期：瀰漫性肺部浸潤，第4期：肺纖維化。但以尚多發性粟粒狀節結作為表現，是甚為少見。

本病例報告描寫一個年輕女性，在健診中意外發現肺部瀰漫性粟狀節結無合併其他臨床症狀。肺功能呈現中度限制性肺疾病。高解析電腦斷層（high-resolution computed tomography, HRCT）呈現出中下肺葉較明顯的瀰漫性粟粒狀節結。而有關肺結核感染得檢查包括痰液，細菌PCR皆呈現陰性反應。在電視輔助式胸腔鏡手術（Video-assisted thoracoscopic surgery, VATS）的肺生檢切片下，病理學報告是非乾酪性壞死肉芽腫，符合類肉瘤診斷。此病患接受口服類固醇治療，在治療兩個月後，我們追蹤肺功能，並發現肺功能已回到正常值。之後追蹤胸部X光片和高解析電腦斷層之肺部浸潤結節均獲得改善。*(胸腔醫學* ***2008; 23: 103-111)***

關鍵詞：類肉瘤，粟狀結節，類固醇

長庚紀念醫院基隆分院　內科部　胸腔內科
索取抽印本請聯絡：陳宏杰醫師，長庚紀念醫院基隆分院　內科部　胸腔內科，基隆市麥金路222號

Cryptogenic Organizing Pneumonia Associated with Myelodysplastic Syndrome Masking Community Acquired Pneumonia

Kuang-Ming Liao, Han-Yu Chang, Tzuen-Ren Hsiue

Cryptogenic organizing pneumonia (COP) is defined as granulation tissue plugs within the lumens of the small airways. The etiology of COP may be viral-related, or the result of connective tissue disorders, focal cocaine abuse, a drug reaction, HIV infection, myelodysplastic syndrome (MDS), or radiation therapy. Some cases have been idiopathic. Clinical features of COP individually may be nonspecific and with varying presentations, including a single nodule, multiple nodules, and a cavity lesion, rapidly progressing to acute respiratory failure or mimicking pneumonia. Herein, we describe a case of COP with initial presentations similar to pneumonia and with chest radiography findings of right lower lobe consolidation with symptoms of fever and cough, but which failed treatment with antibiotics; the diagnosis was reached by aggressive lung biopsy. The patient's bone marrow microscopic examination showed MDS after COP was diagnosed. The symptoms and chest radiography improved after steroid treatment and the patient was discharged after recovering from fever and cough. ***(Thorac Med 2008; 23: 112-117)***

Key words: cryptogenic organizing pneumonia (COP), myelodysplastic syndrome (MDS), bronchiolitis obliterans organizing pneumonia (BOOP)

Introduction

Cryptogenic organizing pneumonia (COP), also called idiopathic bronchiolitis obliterans organizing pneumonia (BOOP), is defined as granulation tissue plugs within the lumens of the small airways, sometimes with complete obstruction of the small airways and granulation tissue extending into the alveolar ducts and alveoli [1]. The etiology of COP may be viral-related, or the result of connective tissue disorders, focal cocaine abuse, a drug reaction, HIV infection, myelodysplastic syndrome (MDS), or radiation therapy. Some cases have been idiopathic [2].

A more aggressive variant of BOOP, termed rapidly-progressive BOOP, has been described. This variant follows a fulminant course, leading to respiratory failure, and is associated with high mortality [3]. We describe a case of COP masking pneumonia presentations and associated with MDS, that was managed aggressive-

Department of Internal Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan
Address reprint requests to: Dr. Han-Yu Chang, Department of Internal Medicine, National Cheng Kung University Hospital, No. 138, Sheng-Li Rd., Tainan, 704, Taiwan

ly with early lung and bone marrow biopsy to reach the diagnosis, and was successfully treated with steroids [4].

Case Report

An 88-year-old man was admitted to the hospital because of fever and cough. The patient had a history of gouty arthritis and benign prostate hypertrophy. He had no smoking history. He was in his usual state of health until 1 month prior to hospital admission when he developed a nonproductive cough and fever, and the X-ray taken showed no obvious patch (Figure 1). He was then admitted to another hospital and treated for 10 days with oral amoxicillin/clavulanic acid without complete resolution of his symptoms.

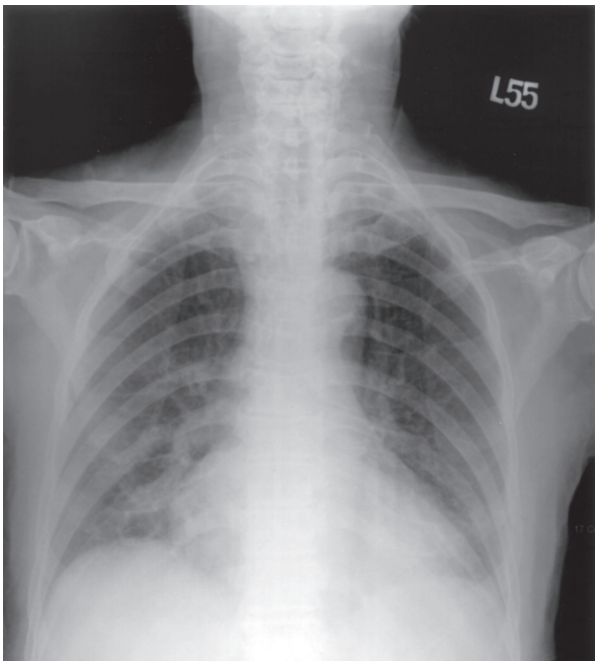

Fig. 1. Chest radiograph without obvious pneumonia patch when symptoms occurred.

The patient was transferred to our hospital and showed a white-cell count (per mm^3) of 8900, a differential count (%) of band forms: 1, neutrophils: 77, lymphocytes: 8, monocytes: 6, eosinophils:6, and platelets (per mm^3) 976000, and a mean corpuscular volume (μm^3) of 116.3. Under the impression of right lower lobe pneumonia, the patient received a complete course of ceftriaxione and moxifloxacin, and visits to the outpatient department for follow-up was arranged. However, he reported subjective fever, dry cough and chills accompanied with lethargy, poor appetite and dyspnea during exertion, but denied chest pain or sweats after being discharged. He was a retiree without known occupational exposure. He had no allergies and no history of pulmonary disease.

Vital signs on hospital admission showed a temperature of 37.6°C, heart rate of 88 beats/min, respiratory rate of 24 breaths/min, and blood pressure of 142/75 mmHg. The physical examination results were remarkable for mild pale conjunctiva and right basilar inspiratory crackles on lung auscultation.

After admission, the hemogram showed a white-cell count (per mm^3) of 4200, a differential count (%) of band forms: 13, neutrophils: 54, lymphocytes: 9, monocytes: 16, eosinophils: 2, and platelets (per mm^3) 595000, and a mean corpuscular volume (μm^3) of 107.2. The levels of electrolytes, aspartate aminotransferase, alanine aminotransferase, and creatine kinase were normal, except hypokalemia (K: 3.3 mmol/liter). Arterial blood gas analysis on nasal prong 2 liter/min showed a pH of 7.510, PCO_2 of 35.9 mmHg, PO_2 of 96 mmHg, HCO_3 of 29 mmHg, and saturation of 98.2%. A chest radiograph (Figure 2) disclosed right lower field consolidation and small pleural effusions. Thoracentesis showed transudative pleural effusion and no bacteria, fungus, or mycobacteria isolation after culture. The patient

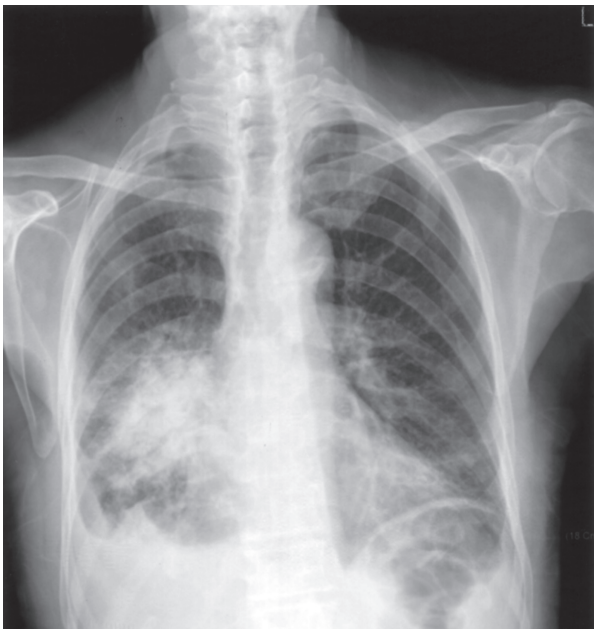

Fig. 2. Chest radiograph showing right lower lung field consolidation with air-bronchogram and pleural effusion.

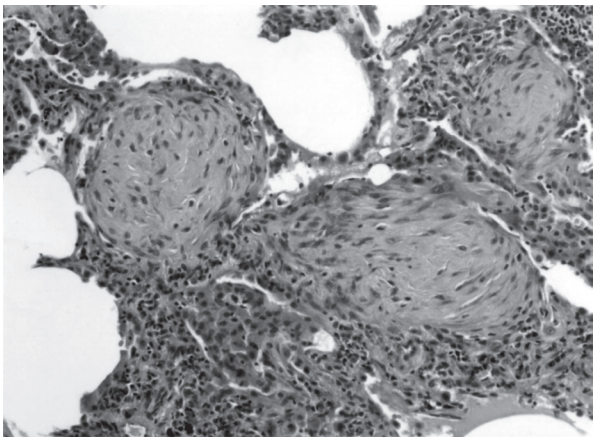

Fig. 3. Microscopic examination shows lung parenchyma composed of fibroblastic plugs filling the air space.

still ran a spiking fever under piperacillin/tazobactam and amikacin treatment. A non-contrast CT of the thorax showed right lung consolidation with air-bronchogram, and left lingula segment atelectasis, with no mass lesions or adenopathy identified.

Tests for serum Cryptococcus antigen, urine Pneumococcus antigen, throat virus screen, urine Legionella antigen, serum antinuclear antibody, and rheumatoid factor were all negative. The culture for blood was sterile, and sputum was mixed normal flora. Due to persistent fever, SpO_2: 98% under the 2L/min nasal prong, and radiography without improvement, the patient underwent right lung biopsy with a video-assisted thoracoscopy procedure on hospital day 4. Surgical pathologic findings were characteristic of an organization of lung parenchyma composed of fibroblastic plugs filling the air space. The PAS, AFS, and GMS stain failed to reveal a microorganism, and there was no evidence of malignancy under microscopic examination (Figure 3).

Methylprednisolone 160 mg per day was prescribed and patient had no further episodes of fever after medication. Neutropenia was noted during the treatment course, and the history of macrocytic anemia without a deficiency of folate and cobalamin, and an absence of hypothyroidism and liver disease led to the suspicion of MDS. Bone marrow biopsy was performed and there were increased megakaryocytes, blast cells, abnormal mononuclear cells and prominent dysplastic changes in the myeloid and erythroid lineage; MDS was favored. Neutropenia improved after using G-CSF for 2 days. The radiographic abnormality gradually resolved (Figure 4) and the patient was discharged from the hospital on day 15, after tapering steroid to prednisolone 30 mg per day in 2 divided doses.

Discussion

Mean age at onset for COP patients is 55 years, with a short course (median of less than

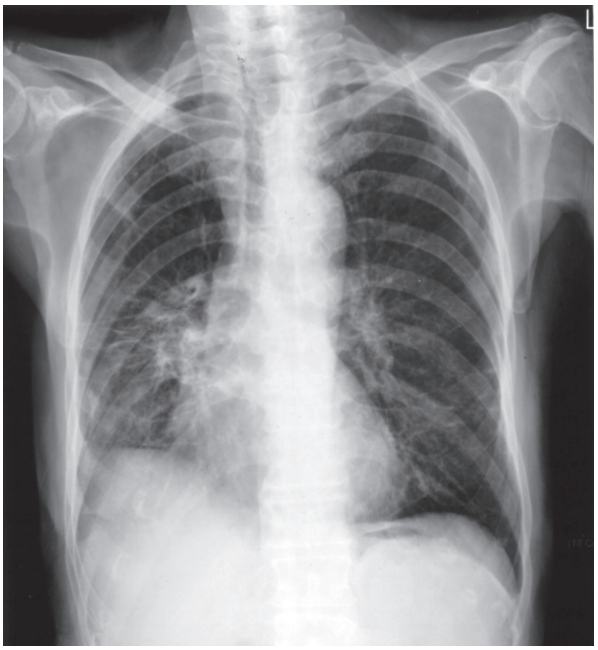

Fig. 4. Chest radiograph showing improved right lower lung consolidation after steroid treatment.

3 months) [6]. The typical patient presents with nonspecific symptoms of dyspnea, cough without sputum, and fever, as did our patient. There is no definite relationship with smoking, but those who do not smoke outnumber those who smoke by a ratio of 2:1. Sometimes, the illness may occur after a lower respiratory tract infection, which is often treated with 1 or more courses of antibiotics [7]. Our patient underwent 2 courses of antibiotics with no clinical improvement.

The clinical features of COP individually may be nonspecific, but when combined in a pattern of a flu-like illness, crackles, patchy infiltrates, and abnormal gas exchange, the possibility of COP increases substantially [2]. Chest radiographs show bilateral basal ground-glass and reticular opacities that have a peripheral distribution, and single or multiple alveolar opacities for which an infectious or neoplastic etiology cannot be found [7-8]. CT scan findings include consolidation, ground-glass attenuation, irregular linear opacities, and nodules [9]. In this report, we described a case of COP with an initial presentation similar to pneumonia, in which chest radiography showed right lower lobe consolidation with a patchy area, and treatment with antibiotics failed; the patient was diagnosed by aggressive lung biopsy. Step sectioning of transbronchial biopsy specimens in patients may support the diagnosis of COP [10], but does not provide adequate specimens to confirm other disorders. Open lung biopsy or video-assisted thoracoscopic surgery may be necessary to reach a definite diagnosis. In our case, bronchoscopy was not performed due to unstable saturation and dyspnea. Since the most common manifestations are nonspecific, diagnosis is often delayed and more invasive procedures for definite tissue proof should not be delayed.

Since the illness shows an excellent response to steroids, it should be differentiated from bacteria infection, and prolonged treatment with steroids is advisable to avoid relapses. But, the clinical scenario is sometimes difficult to distinguish. Initial doses vary from 0.75-1.5 mg/kg per day, with further boluses of methylprednisolone in the first few days and a progressive decrease of dosage over the following weeks [11]. The duration of treatment is not established, but 1 year is often proposed.

After COP is diagnosed, there should be further surveys to exclude infective disease, connective disease, HIV, MDS, and a drug-related reaction. The patient had macrocytic anemia that was ignored for a long time, and the bone marrow microscopic examination showed MDS. Two cases of organizing pneumonia associated with MDS were reported in Japan; 1 was diagnosed by video-assisted thoracoscopic

lung biopsy and the other by transbronchial lung biopsy (TBLB) [12-13]. One case of BOOP in association with MDS reported in Taiwan 12 years ago [14], and this is the second one.

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骨髓化生不良症候群（MDS）造成的原因不明器質化肺炎（COP）與社區性肺炎相似

廖光明　張漢煜　薛尊仁

原因不明器質化肺炎定義為小支氣管管腔內的肉芽組織栓子，造成的原因可以是病毒相關的，結締組織的疾病，古柯鹼濫用，藥物的反應，愛滋病毒相關的，骨髓化生不良症候群，放射線治療造成的，或是原發性的。臨床上細小支氣管阻塞機化性肺炎的個別表現並無特定，包含單一結節，多發性結節，開洞的病灶，迅速進展為呼吸衰竭或類似肺炎。在這裡，我們描述一個細小支氣管阻塞機化性肺炎一開始類似肺炎的表現，胸部X光呈現右下葉的實質化，並且伴隨發燒和咳嗽的症狀，但在抗生素治療失敗後積極的做肺部切片。病人在細小支氣管阻塞機化性肺炎診斷後，其骨髓在顯微鏡檢查下為骨髓化生不良症候群。在類固醇的治療下，症狀和胸部X光片都獲得改善，病人也在無發燒和咳嗽後出院。*(胸腔醫學* ***2008; 23: 112-117)***

關鍵詞：原因不明器質化肺炎，骨髓化生不良症候群，細小支氣管阻塞機化性肺炎

成大醫學院　內科部　胸腔內科
索取抽印本請聯絡：張漢煜醫師，成功大學附設醫院　內科部　胸腔內科，台南市勝利路138號

Diffuse Alveolar-Septal Form of Isolated Pulmonary Amyloidosis Mimicking Lymphangitic Carcinomatosis: A Case Report

Sheng-Jun Lee*, Chin-Pyng Wu, Chin-Feng Giian, Giian-Wen Chen, Wann-Cherng Perng

Pulmonary amyloidosis may be isolated or a part of systemic amyloidosis. It appears in 3 patterns: tracheobronchial, parenchymal nodular, and a diffuse alveolar-septal form. A 64-year-old man presented complaining of a chronic dry cough and dyspnea that had persisted for 2 months. Chest radiographs and a high-resolution computed tomography (HRCT) scan revealed patchy areas of air-space consolidative lesions in the right middle and left lingual lobes of his lungs. There were also diffuse thickening of bronchovascular bundles, intralobular and interlobular septa, and centrilobular opacities in both lungs, mimicking lymphangitic carcinomatosis. Histopathology of a transbronchial biopsy showed some amorphous eosinophilic depositions, and Congo red staining revealed apple-green birefringence under polarized light. After a series of examinations, the deposition of amyloid was found to be limited to the lungs. The final diagnosis was a rare, isolated pulmonary diffuse alveolar-septal form of amyloidosis. ***(Thorac Med 2008; 23: 118-124)***

Key words: pulmonary amyloidosis, alveolar-septal, lymphangitic carcinomatosis

Introduction

Amyloidosis encompasses a heterogeneous group of diseases associated with the extracellular deposition of insoluble protein fibrils called amyloid. On specific staining with Congo red dye, the amyloid presents apple-green birefringence when examined using polarized light microscopy [1]. Deposition of amyloid within the lungs has 3 different presentations. Isolated pulmonary amyloidosis is associated with light chain amyloid (AL) in the majority of cases, and diffuse alveolar-septal form involvement has been reported only rarely [2-3].

Case Report

A 64-year-old man, a printing press worker, had smoked 1 pack per day for 13 years. He visited our outpatient chest department and complained of having had a dry cough for 2 months. He did not pay attention to it until he experi-

Division of Pulmonary Medicine, Department of Medicine, Tri-Service General Hospital, Taipei, Taiwan
*Department of Medicine, Hualien Armed Forces General Hospital, Hualien, Taiwan
Address reprint requests to: Dr. Wann-Cherng Perng, Division of Pulmonary Medicine, Department of Medicine, Tri-Service General Hospital, No. 325, Section 2, Cheng-Kung Road, Nei-Hu, Taipei, Taiwan, Republic of China

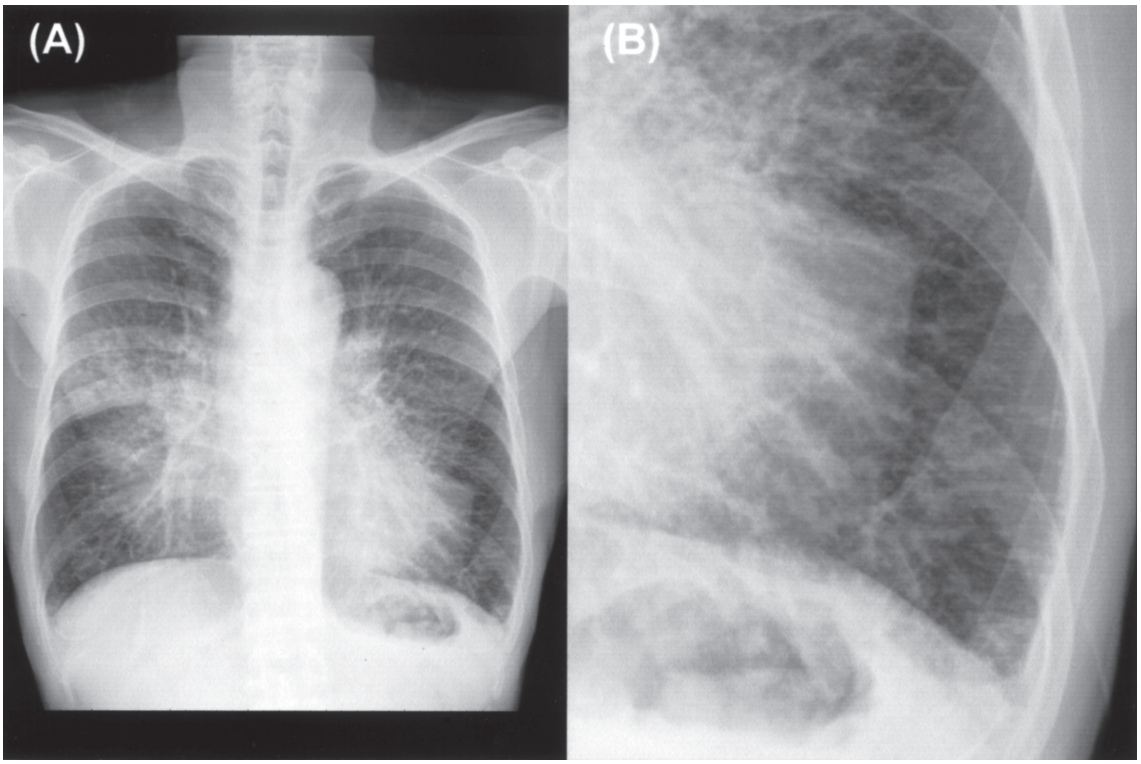

Fig. 1. Chest radiographs (A) revealing patchy consolidation in the right middle and left lingual lobes of the lungs and diffuse interstitial line thickening of both lung zones, (B) Kerley's B lines are seen in the magnified image.

enced shortness of breath and mild chest tightness. His respiratory rate was 20/min and body temperature 37°C. Physical examination showed bilateral dry crackly breathing sounds, no obvious palpable lymphadenopathy, no peripheral pitting edema and no peripheral numbness. Chest radiographs revealed patchy consolidation in the right middle lobe and left lingual lobe of the lungs, diffuse interstitial line thickening of both lung zones, and positive Kerley's B lines (Figure 1). High-resolution computed tomography (HRCT) scans of the patient's chest revealed patchy areas of air-space consolidating lesions in the right middle and left lingual lobes of the lungs, diffuse thickening of bronchovascular bundles, intralobular and interlobular septa, and centrilobular opacities in both lungs. There was 1 enlarged node (about 1.5 cm in diameter) in the mediastinum (Figure 2). He was admitted to our ward under the suspicion of lung cancer with lymphangitic carcinomatosis, and acute pulmonary edema or pneumonia in the right middle and left lingual lobes.

After admission, we prescribed empirical antibiotic treatment with levofloxacin 500 mg per day and collected blood and sputum for the culture of atypical pathogens, bacteria, and tuberculosis, and for virus isolation studies. These examinations were all negative. Hematology revealed a leukocyte count of 7700/μL with a differential count of 64.4% neutrophils and 20.8% lymphocytes; the hemoglobin level was 11.4 g/dL, hematocrit 33%, and platelet count 359000/μL. The C-reactive protein (CRP)

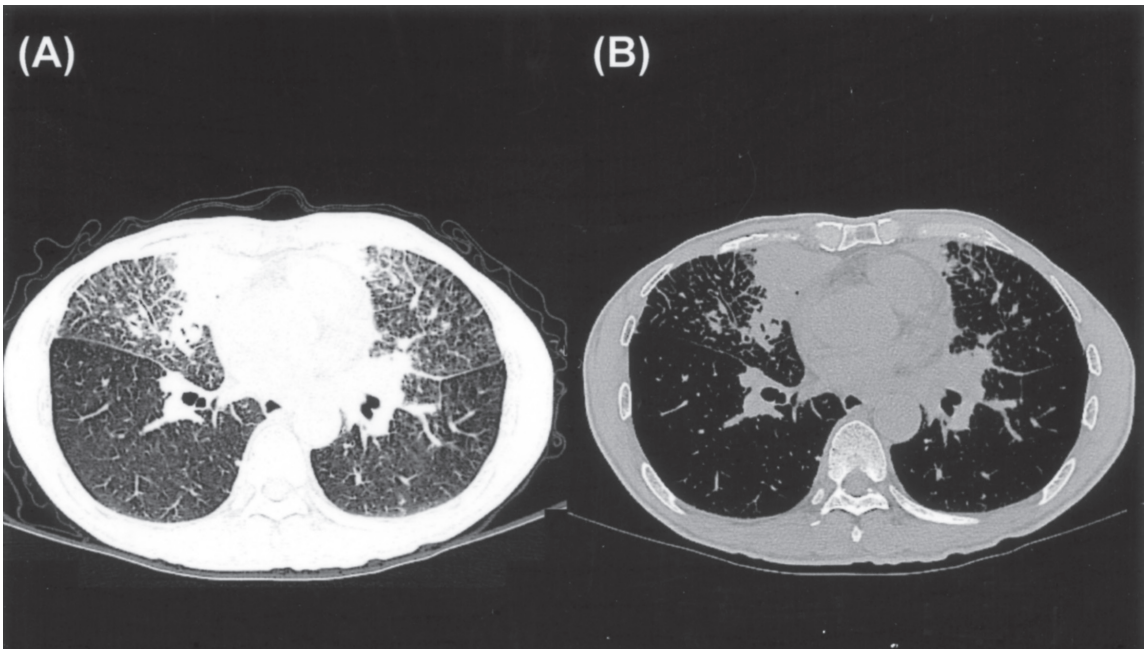

Fig. 2. High-resolution computed tomography of the patient's chest. (A) lung window and (B) mediastinum window. These revealed patchy areas of air-space consolidating lesions in the right middle and left lingual lobes of the lungs, diffuse thickening of bronchovascular bundles, intralobular and interlobular septa, and centrilobular opacities in both lungs.

level was 2.21 mg/dL, and tumor markers, including the CEA and SCC levels, were within normal ranges. Echocardiography showed an estimated 73% left ventricular ejection fraction, no valve dysfunction and no interventricular septum or left ventricular wall thickening.

We performed bronchoscopy, which revealed only mild erythematous mucosal changes in both main bronchi. A transbronchial biopsy was done. Histopathology showed some amorphous eosinophilic material deposited in the submucosa with a few chronic inflammatory cell infiltrations and some multinucleated giant cells. The deposition was weakly PAS-positive and displayed lambda monoclonal restriction, as did the infiltrating plasma cells in the submucosa. Congo red staining showed apple-green bi-refringence under polarized light (Figure 3).

Based on the results of the above examinations, AL-type pulmonary amyloidosis was diagnosed. Later, we arranged further tests for systemic amyloidosis. An electrocardiogram showed a normal sinus rhythm without low voltage. Abdominal sonography showed no significant abnormal findings. Excisional biopsy of the patient's abdominal fat was negative for Congo red staining. Bone marrow examinations showed normal cellularity for the patient's age (40%), no excess blast cells, a normal distribution of the myeloid series, and 3.0% plasma cells. Congo red staining was negative. Urinary kappa and lambda light chain levels were within normal ranges, Bence Jones protein was negative, and proteinuria was 77 mg/day (normal <150 mg/day). Serum immunoglobulins were: IgG 23.20 g/L (normal range 7.51-15.60); IgA 1.62 g/L (normal range, 0.82-

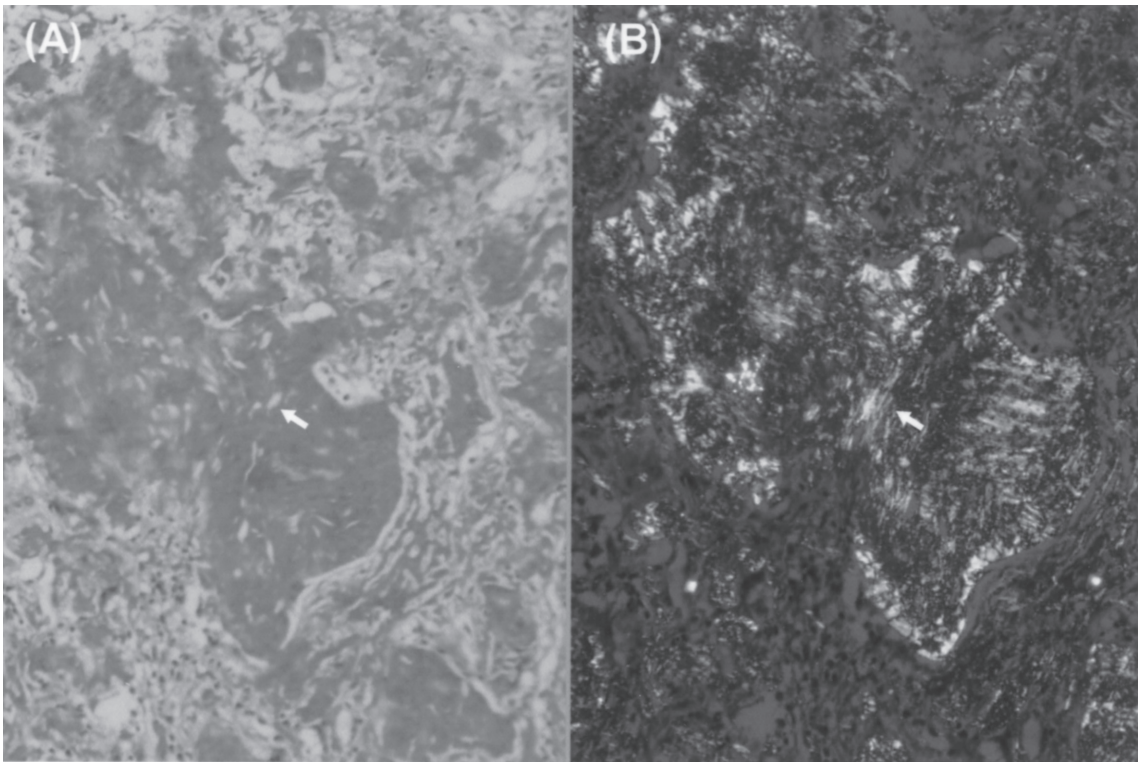

Fig. 3. Histopathology of a transbronchial biopsy revealed (A) the deposition of orange-colored, dense amorphous materials stained with Congo red (arrow); (B) apple-green bi-refringence viewed under polarized light microscopy (400 x) (arrow).

4.53); IgM 1.18 g/L (normal range, 0.46-3.04); IgD <48 IU/mL (normal range, 0-100); IgE <30 IU/mL (normal range, <103); and RF 17.7 IU/mL (normal range, <20). The ANA titer was negative. Serum kappa was 6.22 g/L (normal range, 6.29-13.50), and lambda was 15.90 g/L (normal range, 3.13-7.23). Pulmonary function testing showed normal ventilatory function and normal lung diffusing capacity for carbon monoxide (DLCO) value (FEV1 2.74L, 87.1% predicted; FEV1/FVC 77.32%; TLC 6.14L, 92.7% predicted; DLCO 17.7 mL/min per mmHg, 96% predicted).

According to the results of the above examinations, the final diagnosis was isolated pulmonary alveolar-septal-form amyloidosis. The patient has visited our outpatient department regularly and has been in a stable condition for more than 1 year.

Discussion

The deposition of amyloid may be systemic, involving multiple organs, or it may be isolated and limited to a single organ, such as the lung. Clinically, the systemic patterns are mainly subclassified into (1) primary amyloidosis, when it is associated with plasma cell dyscrasia; (2) secondary amyloidosis as a complication of underlying chronic inflammation diseases; (3) hereditary, or (4) familial [4].

Primary amyloidosis, deriving from the deposition of immunoglobulins or light chains, is often associated with multiple myelomas or

monoclonal gammopathy of unknown significance. Therefore, it is a light chain-related amyloidosis (AL), the most common form. The major organs involved by AL amyloidosis are the kidney, heart, liver and peripheral nerves. Isolated pulmonary involvement, as in this case, is particularly rare, but the AL type is still the most commonly diagnosed form when amyloidosis occurs in the lung [5].

Pulmonary amyloidosis may be isolated or as a part of systemic amyloidosis. It appears in 3 patterns: tracheobronchial, parenchymal nodular and a diffuse alveolar-septal form. Diffuse alveolar-septal amyloidosis is usually reported in association with systemic AL amyloidosis, but is rare in isolated pulmonary amyloidosis. Nodular pulmonary amyloidosis is generally isolated and is usually an incidental finding that needs to be distinguished from neoplasm. Tracheobronchial amyloidosis, most often presenting as multifocal submucosal plaques, is an organ-limited type of amyloidosis [5].

The clinical manifestations of pulmonary amyloidosis, based on the forms and severity of deposition, may present in a variety of ways: asymptomatic, dry cough, airway obstruction, hemoptysis, or increasing dyspnea [6]. Our patient presented with a dry cough, progressively increasing exercise dyspnea, and some pulmonary crackles on physical examination. Determining the relative contribution of symptoms in pulmonary amyloidosis can be difficult, because diffuse pulmonary alveolar-septal involvement can be associated with cardiac amyloidosis and may contribute to cardiopulmonary failure. In a case report, diffuse alveolar-septal amyloidosis developed persistent undetermined exudative pleural effusion presenting as heart failure [11].

The radiological appearances in our case included diffuse septal line thickening and positive Kerley's B lines, and could be confused with pulmonary edema, viral or mycoplasma pneumonia, chronic interstitial inflammatory disease, lymphangitic carcinomatosis, and idiopathic diseases such as idiopathic pulmonary fibrosis and diffuse alveolar-septal amyloidosis.

Pulmonary edema and viral or mycoplasma infection were eliminated in our case because of the long duration of the disease, the lack of fever, and that the echocardiogram and some infection-related laboratory examinations within normal ranges. The other diseases were difficult to exclude without histopathology. Thus, we performed bronchoscopy and biopsy.

The diagnosis of amyloid deposition is confirmed by histopathology of tissue specimens stained with Congo red, with further birefringence under polarized microscopy. Immunohistochemistry with anti-kappa and anti-lambda light chain anti-sera confirms the immunoglobulin origin of the amyloid protein. Pulmonary specimens may be obtained by surgical biopsy (preferentially video-assisted) or by transbronchial biopsy [5]. Screening of blood and urine for a monoclonal component, a monoclonal intact immunoglobulin or light chain and monoclonal urinary free light chains (i.e., Bence Jones protein) is necessary [7, 9]. Once the diagnosis of amyloidosis with a clonal immunoglobulin component is made, hematology is necessary to determine if a myeloma or any other systemic lymphoproliferative disorder is present [1]. In this case, no malignancy was noted and the amyloidosis in our patient was restricted to the pulmonary system. It was a rare, diffuse, alveolar-septal form of isolated pulmonary amyloidosis.

Pulmonary function tests in patients with

pulmonary amyloidosis may show a restrictive ventilatory defect with markedly reduced DLCO and hypoxemia deteriorating on exercise [5]. This patient had a normal ventilatory function and a normal DLCO value, although he had experienced dyspnea for 2 months.

Diffuse, alveolar-septal-form pulmonary amyloidosis usually has a poor prognosis, and 2 reports indicated that the median survival of patients is only about 16 months [1, 7]. The various choices of treatment for amyloid deposits within the pulmonary system include simple observation with supportive care while symptoms are limited [8], local intervention such as endoscopic excision or stenting when airway obstruction occurs, and systemic chemotherapy if diffuse deposition presents in the parenchyma [5, 9-10].

Our patient was followed at the outpatient department with supportive care after discharge, because there was no airway obstruction, no ventilatory impairment and no abnormal gas exchange. He was in a stable condition 1 year later.

In conclusion, the diagnosis of amyloid in the respiratory tract may be difficult. It can mimic carcinoma, pulmonary edema, heart failure with pleural effusion, diffuse lung fibrosis, lymphangitic carcinomatosis, and many other cardiothoracic diseases. Therefore, pulmonary amyloidosis should be thought of when a clinical diagnosis is not easy to confirm on initial investigation, although it is a rare condition.

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侷限性肺部肺泡間隔型類澱粉沈著症以癌性淋巴管炎影像表現—病例報告

李昇駿* 吳清平 簡志峰 陳健文 彭萬誠

肺部類澱粉沈著症可以是侷限性或是全身性類澱粉沈著症所影響之其中一個器官。它可以三種型態來表現：氣管支氣管型，肺實質結節型與廣泛肺泡間隔型。在此我們報告一位64歲男性因持續乾咳與呼吸急促長達兩個月時間來本院就診。胸腔影像檢查呈現局部肺泡浸潤與廣泛性肺間隔紋路增厚疑似癌性淋巴管炎，經氣管肺切片檢查，病理結果發現切片組織呈現一些無定形嗜伊紅性物質沈積於細胞外，並用剛果紅染色再以偏光鏡下檢查呈現特異性蘋果綠的顏色，隨後再作骨髓穿刺切片並無此發現，其他器官在相關檢查亦無受侵犯。最後診斷為少見之“侷限性肺部肺泡間隔型類澱粉沈著症”。*(胸腔醫學* ***2008; 23: 118-124)***

關鍵詞：肺部類澱粉沈著症，肺泡間隔型，癌性淋巴管炎

三軍總醫院 胸腔內科，*國軍花蓮總醫院 內科
索取抽印本請聯絡：彭萬誠醫師，三軍總醫院 胸腔內科，臺北市內湖區成功路二段325號

Non-invasive Management of Chylothorax Secondary to Liver Cirrhosis -- Report of a Case

Chang-Sheng Lin, Meng-Jer Hsieh*, Ying-Huang Tsai*

Chylothorax is a rare event that occurs when milk-like lymphatic fluid accumulates in the pleural space. The common causes of chylothorax are tumors, trauma, or other unknown etiologies. Liver cirrhosis has been classified as one of the uncommon etiologies of chylothorax with a worse prognosis than other etiologies. Patients often die from malnutrition or an immunocompromised status. This report describes a patient who suffered from chylothorax with initial presentations of dyspnea and generalized edema. After a series of work-ups, decompensated liver cirrhosis was found to be the only possible etiology. Generally, chylothorax secondary to liver cirrhosis is hard to manage and the prognosis is poor. Many invasive or expensive therapies have been introduced to manage chylothorax secondary to liver cirrhosis, but successful management with noninvasive conservative therapy has not been reported. Our patient was successfully treated with diuretics, and the chylothorax did not recur during the following 12 months under a sodium-restricted diet. ***(Thorac Med 2008; 23: 125-131)***

Key words: chylothorax, pleural effusion, thoracic duct, triglyceride

Introduction

Chylothorax is a rare condition that involves the accumulation of milk-like lymphatic fluid in the pleural space. Chylomicrons, formed from long-chain triglycerides, enter the intestinal lacteal vessels and are transported to the cisterna chili. The thoracic duct leaves the cisterna chili and ascends to the thorax. Finally, it terminates in the left jugular and subclavian veins. Chylothorax develops when the thoracic duct or one of its major divisions is obstructed or disturbed. It is usually caused by tumors, trauma, including surgery, or idiopathy, including congenital anomalies [1]. However, other rare etiologies of chylothorax exist, including pulmonary lymphangiomyomatosis, intestinal lymphangiectasis, superior vena cava thrombosis, filariasis, mediastinal tuberculosis, congestive heart failure, nephrotic syndrome, liver cirrhosis, and others [1]. These rare etiologies accounted for 8% of all chylothoraces, with only 1% caused by liver cirrhosis, in one study [2].

Chylothorax secondary to liver cirrhosis is

Department of Pulmonary Medicine, Show Chwan Memorial Hospital, Changhua, Taiwan
*Department of Pulmonary and Critical Care Medicine, Chang Gung Memorial Hospital, Taoyuan, Taiwan
Address reprint requests to: Dr. Chang-Sheng Lin, Department of Pulmonary Medicine, Show Chwan Memorial Hospital, No. 542, Sec. 1, Chung-Shan Rd., Changhua 500, Taiwan

hard to manage and the prognosis is poor [3-5]. These patients usually succumb to malnutrition or sepsis due to compromised immunity caused by the massive loss of protein and immunoglobulin after drainage. This report presents a case of chylothorax caused by liver cirrhosis successfully managed by noninvasive conservative treatment.

Case Report

A 45-year-old man was a patient with chronic hepatitis C and decompensated liver cirrhosis, Child's criteria C. He had no history of other systemic disease, such as diabetes, hypertension or congestive heart failure. He had suffered from progressive dyspnea and cough with scanty sputum 2 days before he was admitted. At the Emergency Department (ED), physical examination revealed generalized edema without fever. In addition, no lymphadenopathy or jugular vein engorgement was detected in the neck, and no lymphadenopathy was palpable in the axillary or inguinal area. On auscultation, crackles were identified in the bilateral lower lung fields, and a decreasing breathing sound was heard in the right lower lung field. Chest radiography revealed pulmonary congestion with a moderate amount right side pleural effusion (Figure 1A). Liver echogram showed liver cirrhosis and splenomegaly without ascites. Echocardiography revealed a normal cardiac chamber size without regional wall motion abnormality and an ejection fraction of 78.8%. A total blood cell count showed hemoglobin of 8.5 g/dL, a leukocyte count of 16.9×10^9/L (82% granulocytes, 17% lymphocytes, and 1% eosinophils), and a platelet count of 130×10^9/L. A biochemical study showed blood glucose of 96 mg/dL, aspartate aminotransferase of 43 U/L, total bilirubin of 5.6 mg/dL (direct forms 0.8 mg/dL), total serum protein of 8.1 g/dL (albumin 3.5 g/dL), triglyceride of 144 mg/dL, lactic dehydrogenase (LDH) of 472 U/L, and prothrombin time prolongation of 5.4 seconds. Thoracentesis yielded a milk-like fluid, and chylothorax was confirmed by analysis of the fluid (Table 1). Biopsy of the right pleura revealed neither granulomatous inflammation nor malignancy. A chest and abdominal computed tomography (CT) scan was performed later which excluded the existence of lymphadenopathy or a solid tumor (Figure 1D). A lymphangiogram was performed 3 days after admission and showed no obstruction or leakage from the thoracic duct.

Once chylothorax caused by liver cirrhosis was suspected, the patient received therapy with furosemide at 40 mg/day and spironolactone at 75 mg/day. The patient felt less breathless on the 7th day of hospitalization. After 14 days of treatment, the body weight had declined from 68 kg to 55 kg. Chest radiography taken after 2 weeks' diuretic treatment revealed clear lung fields with only minimal pleural effusions in the bilateral costophrenic angles (Figure 1B). Chest radiography taken at the outpatient clinic 1 week after discharge revealed clear lung fields with sharp bilateral costophrenic angles and a normal cardiothoracic ratio (Figure 1C). He was regularly followed up with a sodium-restricted diet. The chylothorax did not recur during a period of more than 12 months' follow-up.

Discussion

Chylothorax is a relatively uncommon event. Light classified the etiologies of chylothorax into 4 major categories - tumor, trauma

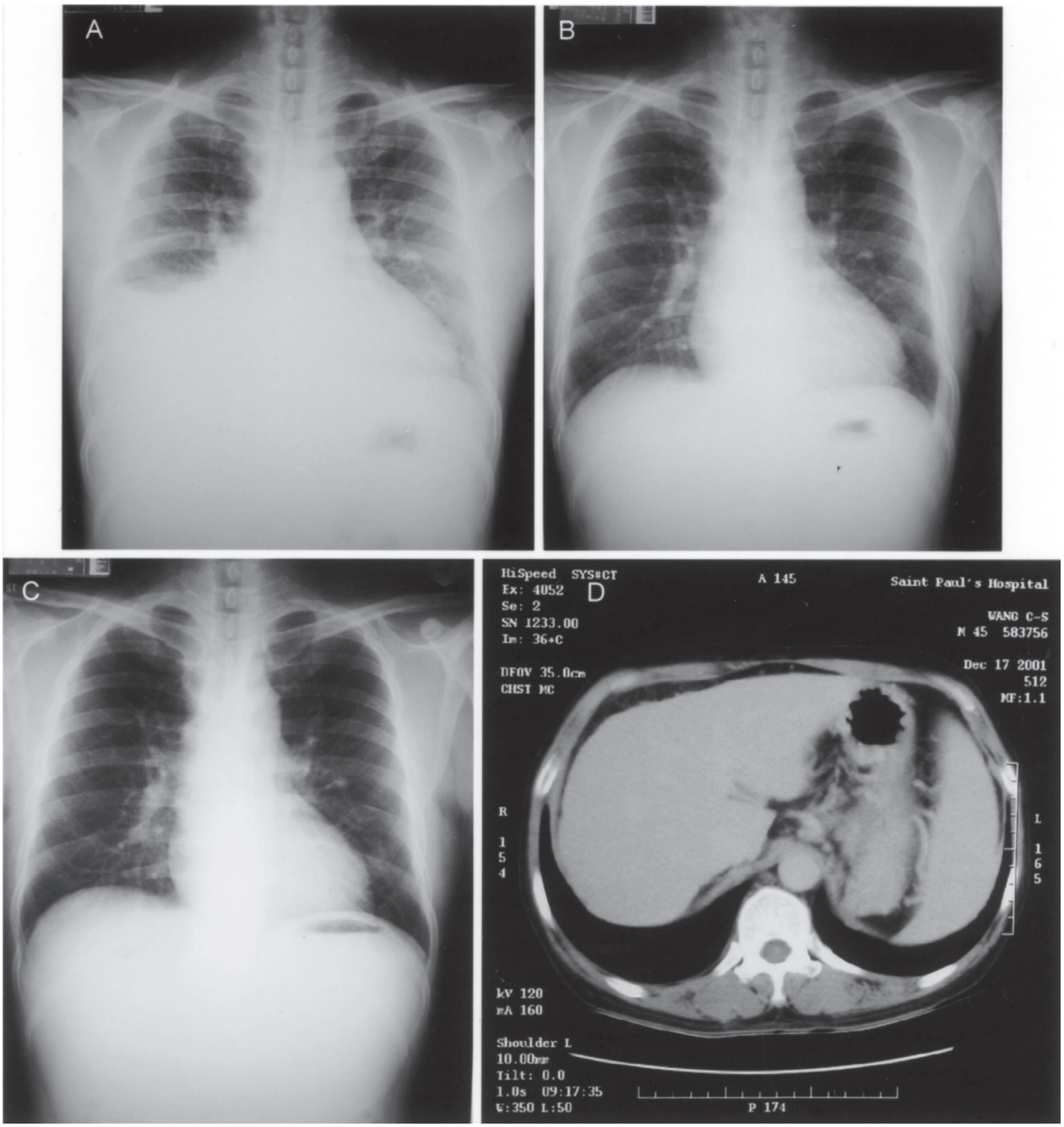

Fig. 1. Chest radiography (A) pulmonary congestion with a moderate amount of right side pleural effusion (B) clear lung fields with only minimal pleural effusions in the bilateral costophrenic angles and a normal cardiothoracic ratio after 2 weeks' diuretic treatment (C) clear lung fields with sharp bilateral costophrenic angles and a normal cardiothoracic ratio 1 week after discharge (D) computed tomography showed no lymphadenopathy or solid tumor.

including surgery, idiopathic including congenital, and miscellaneous [1]. Over 50% of chylothoraces are induced by tumors, especially lymphoma. Trauma due to surgery, most fre-

Table 1. Characteristics of pleural effusions

	Pleural effusion		Plasma
Appearance	Milky		
Odor	None		
Leukocytes (mm^{-3})	430		
Lymphocytes (%)	99		
Culture	No growth		
Cytology	Negative finding		
Glucose (mg/dL)	158		96
Total protein (g/dL)	4		8.1
Total protein E/P		0.49	
LDH (U/L)	253		472
LDH E/P		0.54	
Triglyceride (mg/dL)	216		144
Triglyceride E/P		1.5	
Cholesterol (mg/dL)	38		

E/P = the concentration ratio of effusion to plasma; LDH = lactic dehydrogenase

quently following cardiovascular or thoracic surgery, is the 2nd leading cause of chylothorax. Idiopathic chylothorax is the most common type of neonatal pleural effusion and may be due to thoracic duct trauma during delivery, or to a developmentally abnormal thoracic duct. The incidence of miscellaneous chylothorax is less than 10%, and liver cirrhosis is one of these rare etiologies [1]. Chest and abdominal CT scan and history-taking helped to rule out tumor and trauma-induced chylothorax in this case. Although general edema was found and the ED chest radiography revealed pulmonary congestion, congestive heart failure-induced chylothorax was excluded by echocardiography and the follow-up chest radiographies. Tracing the patient's past history, the most likely cause was liver cirrhosis induced by chronic hepatitis C.

The pathophysiology of chylothorax secondary to liver cirrhosis is not very clear. Liver cirrhosis may increase hepatic capillary pressure and proportionately increase lymph flow in the liver and the thoracic duct. Increased pressure in hepatic lymph vessels and the thoracic duct increases the risk of extravasation of chyle and promotes the development of chylous ascites [6]. However, microscopic anatomical defects are present in the diaphragm and a negative pressure is found in the pleural space. Chylous ascites may move from the peritoneum into the thorax, across these defects of the diaphragm, and accumulate in the pleural space [7]. Accordingly, chylothorax forms with or without chylous ascites.

The effusion in this case was a milk-like fluid. The possibility of empyema was excluded because lymphocytes were predominant in the effusions, the level of glucose in the effusion was 158 g/dL, and culture for bacteria or Mycobacterium tuberculosis was negative. The ratio of the concentration of effusion protein to that of plasma (E/P) was less than 50% (4/8.1), and the E/P of the lactic dehydrogenase was less

than 60% (253/472), indicating a transudative effusion according to Light's criteria [1]. However, the triglyceride level in the effusion was greater than 110 mg/dL with an E/P of greater than 1 (216/144), and the cholesterol levels in the effusions were low (Table 1). Thus, the diagnosis of chylothorax was confirmed not to be a false-positive chylothorax in patients with hypertriglyceridemia or pseudochylus. Theoretically, chylothorax should be exudative in nature [2], but our patient's data showed transudative, and were slightly below the criteria for exudates (protein E/P 49%; LDH E/P 54%), perhaps because of the diluting effect of the transudative ascites due to liver cirrhosis.

The management of chylothorax depends on its etiology or the underlying disease. No large, randomized, controlled studies have addressed the management of chylothorax induced by liver cirrhosis, because of the low incidence. Several ways of managing chylothorax or chyloperitoneum induced by liver cirrhosis have been introduced. These include a modified diet with medium-chain triglycerides that are directly absorbed into the portal vein to reduce lymphatic leakage of chyle, total parenteral nutrition with resting of the bowels, tubal thoracotomy, or returning chylous ascites to systemic circulation by peritoneovenous shunting. However, responses to these kinds of management have been poor [4-5, 7-8]. Successful management by transjugular intrahepatic portosystemic shunt has been reported [9], but it was too invasive. Fortunately, in our case, soon after conservative management with 40 mg/day of furosemide and 75 mg/day of spironolactone, the patient felt less breathless, and chest radiography revealed improvement after 2 weeks' medical treatment. The body weight decreased by 13 kg and the edema improved, indicating a decline in the pleural effusion and general tissue edema.

Chylothorax secondary to liver cirrhosis has had a worse prognosis than common causes of chylothorax secondary to malignancy or trauma, or hydrothorax secondary to liver cirrhosis without chylothorax or chyloperitoneum [5, 8]. Early conservative intervention with diuretics for chyloperitoneum induced by liver cirrhosis might yield a good response [8]. To our knowledge, no previous study has reported the successful conservative management of chylothorax secondary to liver cirrhosis. However, we suspected that early intervention might yield a response as effective as that to chylous ascites, because the chylous pleural effusion secondary to liver cirrhosis had moved from the chyloperitoneum. For our patient, management introduced before malnutrition developed might have been a factor for a better prognosis.

In summary, chylothorax is a rare event, and liver cirrhosis is an uncommon etiology of chylothorax. Generally, chylothorax secondary to liver cirrhosis has an unfavorable prognosis. However, in our case, early management by diuretics might have yielded a good response. Therefore, all patients with chylothorax caused by liver cirrhosis should be treated conservatively before invasive or expensive management is performed.

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肝硬化併發乳糜胸的非侵入性治療

林昌生　謝孟哲*　蔡熒煌*

乳糜胸是肋膜腔內聚積乳狀淋巴液的一種罕見疾病，常見的致病因有腫瘤、外傷及其他未知或少見的因素。肝硬化被歸類為罕見的病因之一，並有較差的預後，病患常因營養不良或免疫力差而死亡。本篇病例報告敘述一位乳糜胸的患者，最初以呼吸困難和水腫來表現，經進一步檢查得知肝硬化是其致病因。一般而言，肝硬化併發乳糜胸通常是難以處理且預後不佳。以往，有許多侵入性或昂貴的治療曾被提出，但未曾有過以非侵入性方式成功治療肝硬化併發乳糜胸的病例。此病患成功地以利尿劑治療且合併低鈉飲食的控制下，經一年的追蹤，乳糜胸並未再發生。*(胸腔醫學 **2008; 23: 125-131**)*

關鍵詞：乳糜胸，肋膜積水，胸管，三甘油脂

秀傳紀念醫院　胸腔內科，*長庚紀念醫院　胸腔內科
索取抽印本請聯絡：林昌生醫師，秀傳紀念醫院　胸腔內科，500彰化市中山路一段542號

Synovial Sarcoma of the Mediastinum: A Case Report

Chia-Hung Sun*, Shinn-Liang Lai**, ***, Reury-Perng Perng**, ***

Synovial sarcoma is an extremely rare tumor of the mediastinum. Although it occurs predominantly in the soft tissues of the extremities, this neoplasm has been described in a wide variety of other locations. We report a case of synovial sarcoma occurring in the mediastinum. This 24-year-old male patient presented with dry cough and chest pain. Imaging studies revealed a huge mass lesion originating from the right lower mediastinum with right lower lung invasion and right rib destruction. Computed tomography-guided biopsy confirmed the diagnosis of synovial sarcoma. He underwent surgery and post-operative irradiation therapy. His condition was stable 1 month after the operation. ***(Thorac Med 2008; 23: 132-137)***

Key words: synovial sarcoma, mediastinum, surgery, irradiation therapy, chemotherapy

Introduction

Synovial sarcoma is a malignant mesenchymal neoplasm occurring most commonly in the joints of the extremities. This tumor has been reported in a wide variety of other locations, including the head, neck, esophagus, tongue, and retroperitoneum [1-5]. Although it may occur at any age, synovial sarcoma is typically a disease of adolescents and young adults. Classically, it is a biphasic tumor consisting of epithelial and spindle cell components. Its monophasic types, composed solely of spindle cells or epithelial cells, and a poorly differentiated variant, have been recognized. The monophasic spindle cell type is now the most common type [6-7]. Herein, we report the case of a young man with synovial sarcoma of the mediastinum. The tumor invaded the right lower lung and the adjacent rib. He received surgery and radiotherapy. Molecular analysis of the neoplasm disclosed a monophasic spindle cell type.

Case Report

This 24-year-old man was an athlete and a hepatitis B virus carrier, and smoked occasionally. He was referred to our hospital in March 2006 due to dry cough and right chest pain for 1 month. The chest X-ray showed total opacity in the right-side lung field associated with a massive amount of right-side pleural effusion (Figure 1). The chest computed tomography scan revealed a 13.4 x 11.0 cm soft tissue mass

*Department of Internal Medicine, Taipei City Hospital, Taiwan; **Chest Department, Taipei Veterans General Hospital, Taiwan; ***School of Medicine, National Yang-Ming University, Taipei, Taiwan
Address reprint requests to: Dr. Shinn-Liang Lai, Chest Department, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan

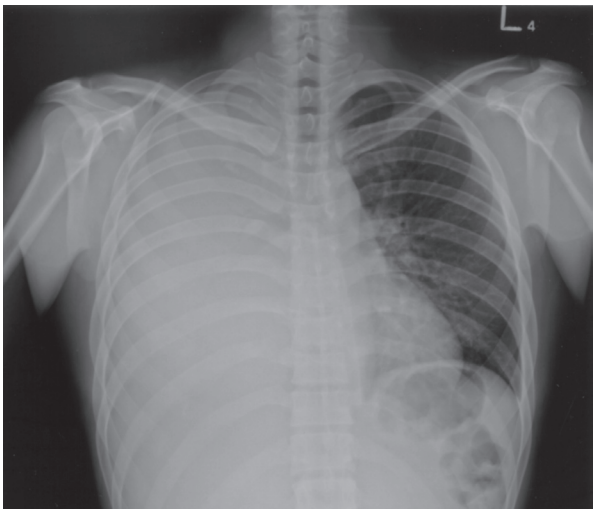

Fig. 1. Chest X-ray showing total opacification in the right-side lung field and a massive amount of right-side pleural effusion.

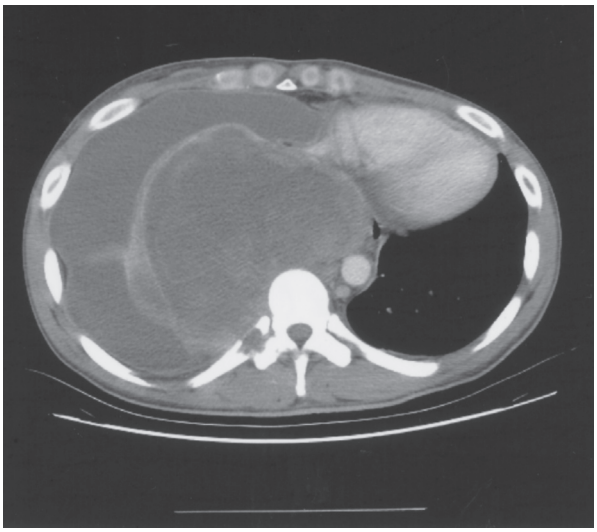

Fig. 2. Chest computed tomography scan reveals a 13.4 x 11.0 cm heterogenous soft tissue mass at the right posterior mediastinum. The tumor invaded the right lung and pleura, compressed the right heart and esophagus, and destroyed the posterior part of right 10th rib and 10th vertebra.

with heterogenous density and a necrotic area at the right posterior mediastinum; tumor invasion to the right lung and pleura with compression of the right heart, esophagus, and inferior vena cava, and destruction of the posterior of the right 10th rib were also observed (Figure 2). Thoracocentesis yielded reddish exudative pleural effusion that was negative for malignant cells. CT-guided biopsy of the tumor showed synovial sarcoma with a spindle cell component. Whole body bone scan revealed 2 foci of increased MDP uptake in the posterior 9th and 10th costovertebral junctions. The patient underwent explorative thoracotomy, and the operative findings showed a huge mass measuring about 20 x 20 x 12 cm originating from the right posterior mediastinum with invasion to the right lower lobe, pericardium, right hemidiaphragm, the posterior of the 9th-10th rib, and the 10th vertebra. Palliative surgery by partial resection of the tumor, right lower lobe lobectomy, and debulking of involved ribs and vertebra were performed. The residual tumor was at the 10th rib end and the 10th vertebral body. Pathology of the neoplasm disclosed infiltrative synovial sarcoma with extensive necrosis. The tumor cells were immunoreactive for bcl-2, CD99, and vimentin, and negative for cytokeratin and epithelial membrane antigen (EMA) (Figure 3, 4). However, the polymerase chain reaction (PCR) result for t (X; 18) and SYT-SSX of the synovial sarcoma was negative. This patient received post-operative irradiation therapy for the residual tumor with a total dose of 1800 cGy in 9 fractions. His condition was stable 1 month after operation.

Discussion

Synovial sarcoma is a rare soft tissue neoplasm that was first described nearly a century ago [8]. This tumor accounts for 5.6%-10.0% of all soft tissue tumors; about 72% of patients are younger than 40 years old [9]. Although

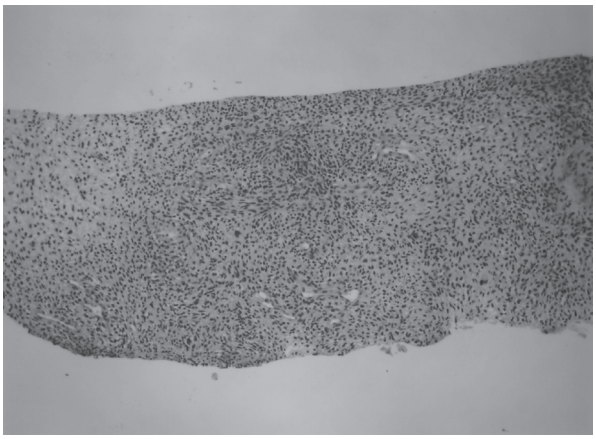

Fig. 3. The tumor was composed of monophasic spindle cells with scant cytoplasm and frequent mitotic figures (H&E stain, 200X).

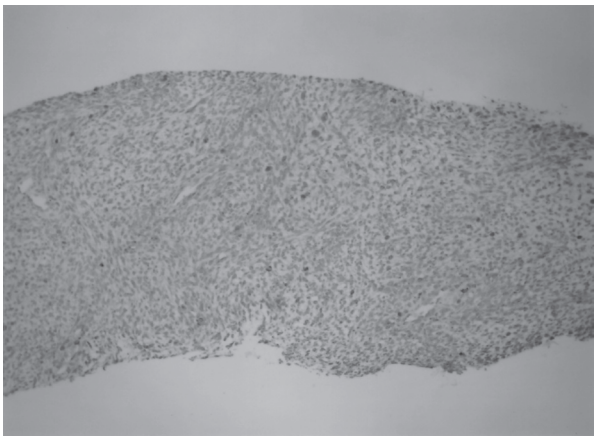

Fig. 4. Both nuclear and cytoplasmic staining of the tumor cells was immunoreactive with bcl-2 (200X).

the most common location for this tumor is the joints of the extremities, it has now been recognized in a variety of locations including the head, neck, chest wall, lung, heart, pleura, esophagus, mesentery, retroperitoneum, vulva, and intracranial regions [10-13]. The mediastinal synovial sarcoma is really a rare and aggressive mesenchymal neoplasm.

Synovial sarcoma is composed of 2 types of cells that form a characteristic biphasic pattern: spindle cells, and epithelial cells. Based on the relative prominence of these 2 elements, synovial sarcoma can be classified into 4 subtypes: (1) biphasic, (2) monophasic spindle, (3) monophasic epithelial and (4) poorly differentiated. Biphasic synovial sarcoma has a relatively limited differential diagnosis when it arises from the extremities. However, the differential diagnosis is more extensive when this tumor arises in atypical sites such as the mediastinum [14]. With a diagnosis of primary synovial sarcoma of the mediastinum, the histology of our case was monophasic spindle cell type.

Molecular techniques are particularly useful in the diagnosis of synovial sarcoma. Biomarkers like vimentin, EMA and cytokeratin are usually tested during immunohistochemical examinations; however, these studies may not be sufficient to diagnose all cases [7, 15-16]. In a study of 15 patients with synovial sarcoma of the mediastinum, 5 cases were biphasic and 10 were monophasic. These tumor cells were immunoreactive for EMA, vimentin, bcl-2, and CD99. This characteristic was typically expressed in synovial sarcoma of the mediastinum, but not in any other tumors [17]. The SYT-SSX fusion transcripts in the chromosomal translocation (X;18) were specifically expressed in more than 95% of synovial sarcomas originating from the limbs, but the percentage of this tumor from the mediastinum was not clear due to limited data [15]. Although the detection of the chromosomal abnormalities t (X; 18) and SYT-SSX by PCR was also considered useful for the differential diagnosis of mediastinal neoplasm, this investigation in our patient showed negative results [7, 15].

The differential diagnosis for these tumors arising from the mediastinum might be difficult, especially in distinguishing the monophasic

spindle cell type of synovial sarcoma from other spindle cell neoplasms encountered at this location. A lot of spindle cell neoplasms present as a primary tumor in the mediastinum, including sarcomatoid carcinoma, sarcomatoid methothelioma, spindle cell thymoma or thymic carcinoma, blastoma, solitary fibrous tumor, leiomyosarcoma, malignant fibrous histiocytoma, and malignant peripheral nerve sheath tumor. To distinguish these types of mediastinal tumors, clinical history, radiographic patterns, histological features, immunohistochemical staining, and molecular studies must be analyzed [15-17]. In our patient, the positive immunochemical staining findings for bcl-2, CD99, and vimentin would favor a diagnosis of synovial sarcoma over sarcomatoid carcinoma [17]. However, the negative cytokeratin, EMA, and SYT-SSX gene transcript results might lead to including solitary fibrous tumor in the differential diagnosis. Contrary to synovial sarcoma, solitary fibrous tumor always stains positively for CD34, though this immuohistochemical staining was not investigated in our study. The morphological features of solitary fibrous tumor would be characterized by fibroblast-like cells and connective tissue in varying proportions, findings which might be useful in distinguishing solitary fibrous tumor from synovial sarcoma [17-18].

Synovial sarcoma is a highly malignant soft tissue tumor. The mainstream treatment is primary radical surgery, as the tumor exhibits little sensitivity to radiotherapy or chemotherapy [16]. Radiation therapy had been suggested to treat unresectable or recurrent synovial sarcoma. Some reports showed that post-operative adjuvant chemotherapy was effective against synovial sarcoma, but others demonstrated the opposite results. So, the efficacy of adjuvant chemotherapy remains controversial [19-20]. The 5-year survival rate of patients with synovial sarcoma of the extremities ranges from approximately 36% to 64%, with the poor prognostic indicators including: age over 20 years old, tumor size greater than 5 cm in diameter, proximal origin, and a monophasic type [9, 21]. The previously reported synovial sarcomas of the mediastinum were large and tended to recur. According to these published reports, the prognosis of synovial sarcoma of the mediastinum was even poorer than that of synovial sarcoma of the extremities. In a study of 4 cases of mediastinal synovial sarcoma; 3 patients survived 10 months to 4 years after diagnosis [22]. It was impossible to completely resect the synovial sarcoma in our patient because the tumor was huge with extensive involvement in the neighboring organs. Only palliative resection of the neoplasm and post-operative irradiation therapy of the residual tumor could be performed to achieve some relief of symptoms. His outcome was followed up after surgery and irradiation therapy.

In summary, synovial sarcoma of the mediastinum is a rare and aggressive neoplasm. The characteristics of this tumor are the histological pattern and molecular analysis. Although surgery, irradiation therapy and chemotherapy have been used previously, the poor prognosis results from local recurrence and metastasis.

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縱隔腔的滑膜肉瘤：病例報告

孫嘉宏* 賴信良**,*** 彭瑞鵬**,***

縱隔腔的滑膜肉瘤是一個相當罕見的腫瘤。此腫瘤雖然好發於肢體的軟組織，但是也曾在其他部位被描述過。本篇文章中，我們報告一位發生於縱隔腔的滑膜肉瘤的病例。這是一個24歲的男性病患，因為乾咳和胸痛而就診。影像學檢查發現一個原發於右下後縱隔腔的巨大腫瘤病灶，同時侵犯右下肺和破壞右側肋骨。經過電腦斷層導引的切片檢查，確定診斷為滑膜肉瘤。他接受手術及之後的放射治療，在手術後一個月其病情穩定。*(胸腔醫學 **2008; 23: 132-137**)*

關鍵詞：滑膜肉瘤，縱隔腔，手術，放射治療，化學治療

*台北市立醫院 內科部，**台北榮民總醫院 胸腔部，***國立陽明大學醫學院
索取抽印本請聯絡：賴信良醫師，台北榮民總醫院 胸腔部，112台北市北投區石牌路二段201號14樓

Pneumocystis Jiroveci Pneumonia with Adult Respiratory Distress Syndrome in an Immunocompetent Patient -- A Case Report

Kok-Khun Yong, Tzu-Ching Wu, Yu-Jen Lee*, Chih-Pin Chen, Thomas Chang Yao Tsao

Pneumocystis jiroveci pneumonia (PJP) is a life-threatening opportunistic infection which occurs in immunocompromised hosts, especially in patients with acquired immunodeficiency syndrome (AIDS), and increases in frequency in other immunocompromised patients, but it is very unusual in healthy people. We report a 49 -year-old woman who had been healthy until 2 weeks before admission. She suffered from productive cough with exertional dyspnea. The above symptoms progressed and respiratory failure developed after admission. Her chest radiographs revealed diffuse uniform nodular infiltration in both lungs. High resolution computed tomography (HRCT) showed diffuse alveolar densities and interstitial changes in both lower lungs. PJP was confirmed by Giemsa's stain of the bronchoalveolar lavage fluid retrieved via a bronchoscope. The symptoms improved and the patient was successfully weaned from the ventilator after treatment with trimethoprim- sulfamethoxazole. The chest radiographic infiltrations almost completely resolved 2 months after the treatment. ***(Thorac Med 2008; 23: 138-143)***

Key words: *Pneumocystis jiroveci* pneumonia (PJP), immunocompetent

Introduction

Pneumocystis jiroveci (*PJ*) was first identified as a protozoan nearly 100 years ago, and reclassified as a fungus in 1988. It causes a life-threatening opportunistic pulmonary infection which occurs in immunocompromised hosts, especially in patients with acquired immunodeficiency syndrome (AIDS). *Pneumocystis jiroveci* pneumonia (PJP) is increasing in frequency in other immunocompromised patients, including organ transplant recipients, patients treated with high-dose corticosteroids, and patients treated with chemotherapeutic regimens for malignancy. However, PJP is very unusual in healthy people. Herein, we report a case of PJP which occurred in an immunocompetent patient.

Division of Thoracic Medicine, Chung Shan University Hospital and Chung Shan Medical University, Taichung, Taiwan; *Division of Thoracic Medicine, Cathay General Hospital, Hsinchu, Taiwan
Address reprint requests to: Dr. Thomas Chang Yao Tsao, Vice Superintendent, Chung Shan Medical University Hospital and Dean, School of Medicine, Chung Shan Medical University, Taichung, Taiwan, 110 Sec. 1, Chien-Kuo N. Road, Taichung, 402, Taiwan

Case Report

This 49-year-old woman had been very healthy until 2 weeks before admission. She then began suffering from fever, cough with whitish sputum and exertional dyspnea. Although she visited a general practitioner and took medicine, the symptoms worsened. Therefore, she was admitted to a local hospital for 2 days. She denied symptoms such as poor appetite, diarrhea, abdominal pain, or body weight loss.

In our emergency room, the patient had fever, cough with blood-tinged sputum, and severe dyspnea on resting. The laboratory examinations revealed mild leukocytosis (10,100/mm^3) and a high level of CRP (25.7 mg/dl). The chest radiograph showed diffuse uniform nodular infiltrations in both lungs (Figure 1). The chest high resolution computed tomography (HRCT), which was done at a local hospital, showed diffuse alveolar densities and interstitial changes in both lower lungs (data not shown because we have only copy films). She was then admitted to the chest ward at our hospital. The differential diagnosis included pneumonia, pulmonary tuberculosis, PJP, or lung alveolar cell carcinoma. The dyspnea progressed and she was transferred to the ICU due to impending respiratory failure on hospital day 2. The arterial blood gas analysis demonstrated both hypoxemia and hypercapnia (ABG analysis: FiO_2 = 40%, pH = 7.32, $PaCO_2$ = 61 mmHg, PaO_2 = 63 mmHg, HCO_3^-= 31.4 mmol/L, SaO_2 = 90%). On the same day, she was intubated and mechanical ventilation was implemented. The blood cultures, sputum examinations for bacterial and tuberculous infection, as well as sputum cytology showed negative findings. Bronchoscopy with bronchoalveolar lavage (BAL) was performed for the infectious pathogen studies. The bacterial, tuberculous and cytological BAL results were negative, but the smears with Giemsa's stain revealed *PJ* (Figure 2).

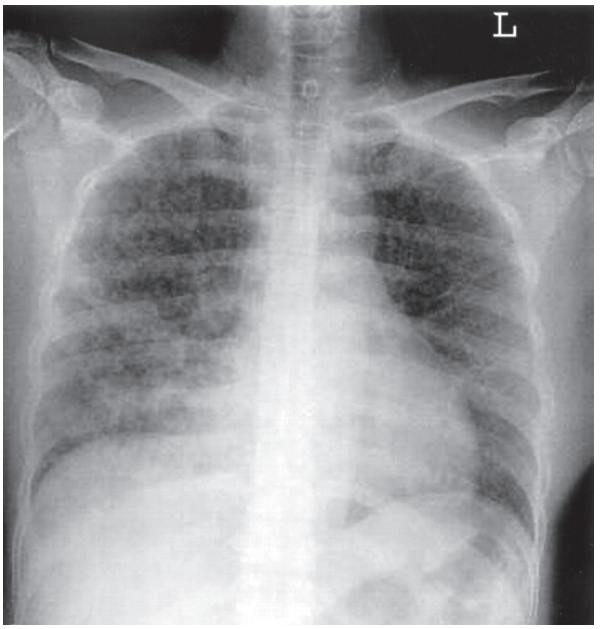

Fig. 1. The chest radiograph shows diffuse uniform nodular infiltration in both lungs.

Trimethoprim sulfamethoxazole antibacterial treatment was given from that time. Corticosteroids were also prescribed for the diffuse, severe lung injuries with respiratory failure, and the symptoms improved gradually. The patient was successfully weaned from the ventilator and extubated on day 12 after the start of antibacterial treatment. All of the studies for autoimmune diseases, virus infections and HIV showed negative results. The chest HRCT (Figure 3) performed on hospital day 21 and chest radiograph performed on hospital day 34 (Figure 4) after antibacterial treatment demonstrated much improvement. The pulmonary function tests showed moderately restrictive lung impairments with total lung capacity of 3.82 L (80% predicted). The patient had no respiratory

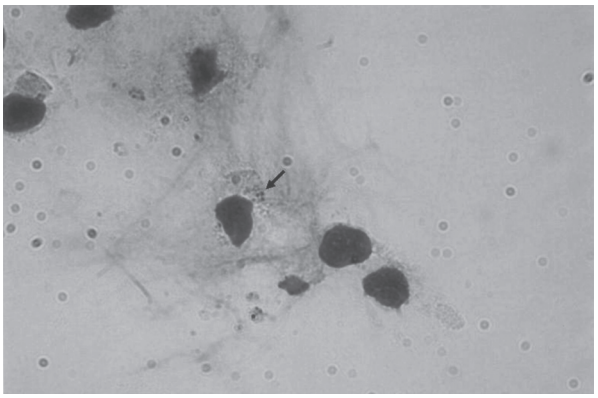

Fig. 2. Giemsa's stain showing typical findings of *Pneumocystis jiroveci* (↙).

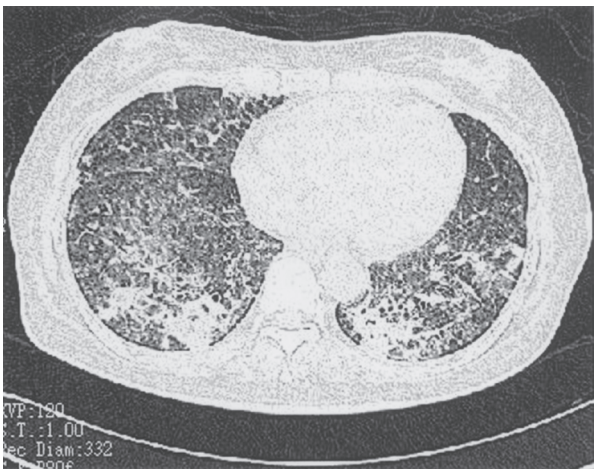

Fig. 3. Chest HRCT showing diffuse alveolar densities and interstitial changes in both lower lungs.

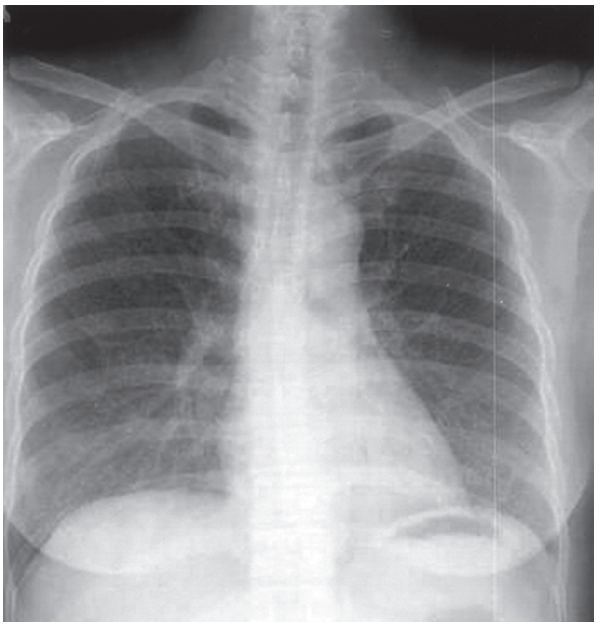

Fig. 4. Chest radiograph at week 4, showing dramatic improvement.

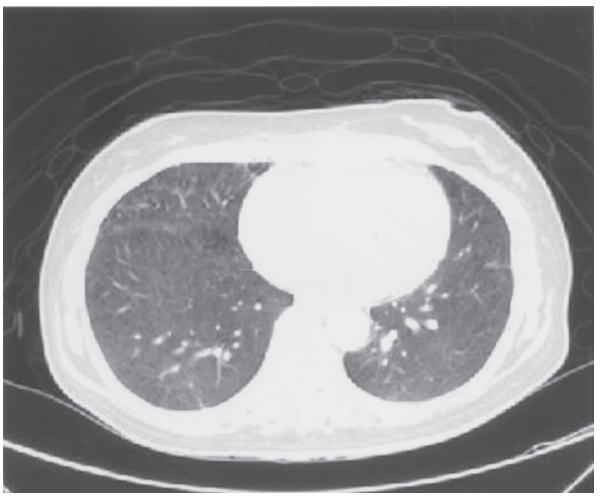

Fig. 5. HRCT still showed bilateral diffuse ground-glass opacities after 4 weeks, but improved as compared with the previous film.

symptoms, including cough and dyspnea, 3 months later; however, her chest HRCT still showed bilateral diffuse ground-glass opacities. (Figure 5) The HIV marker follow-up 3 months later still showed negative.

Discussion

The method of transmission of *PJ* is not fully understood, but it can be transmitted via air-droplets from person to person [1]. *PJ* can be a normal flora in the lungs in healthy people, but may shift to a lethal pathogen when the immune defenses break down, especially in HIV-infected patients and other immunocompromised hosts. In HIV-infected patients, total $CD4^+$ T cell counts provide a major criterion

for initiation and discontinuation of primary prophylaxis against *PJ* infection. [2] We did not check the $CD4^+$ cell count of this patient because her HIV marker showed negative. Throughout the course, as an immunocompetent person, the patient's white blood cell count showed a typical response to the infection. The severity of the inflammatory process depends on the immune defense of the infected host. Inflammatory responses control infection, but may promote pulmonary injury. Neutrophilic lung inflammation may cause diffuse alveolar damage, impaired gas exchange, and respiratory failure [3]. The normal immune response with severe inflammatory processes might account for the acute lung injuries with respiratory failure in this patient after *PJ* infection. Hanano *et al*. [4-5] demonstrated that first-line anti-Pneumocystis defense mechanisms appear to be mainly executed by macrophages in the roles of IFN-γ, TNF-α and IL-1. Pathological processes are induced by *PJ* which attach to type I pneumocytes and mediate the damage to the alveolar-capillary boundary.

PJP was associated with respiratory failure in 5-30% of cases and had been reported to be the most common cause of acute respiratory failure and of admission to the ICU among HIV-seropositive patients. Soub *et al*. [6] found that at presentation, patients with AIDS had a longer median duration of symptoms, lower median respiratory rate and higher median room air arterial oxygen tension, and demonstrated a higher mortality in non-HIV-related PJP compared with AIDS-related PJP (50% vs. 20%).

The treatment of choice for PJP is trimethoprim-sulfamethoxazole, and corticosteroids may be indicated for severe inflammation of the lung [7]. The duration of trimethoprim-sulfamethoxazole treatment depends on host immunity; this patient was treated i.v. for 14 days, followed by orally for 10 days. Dramatic improvements in the clinical symptoms and chest radiographic findings were found after treatment. High-dose corticosteroids were given intravenously in the beginning and were tapered gradually, for a total 7 weeks. Although there were no respiratory symptoms, the chest HRCT still demonstrated residual bilateral diffuse ground-glass opacities. Post-inflammatory pulmonary fibrosis was considered.

In conclusion, although PJP is most common in immunocompromised hosts, it still can occur in immunocompetent patients. Since these patients have a normal immune response to such infection, the neutrophilic pulmonary immune reaction may occur vigorously and cause severe lung injuries. An early intervention for the diagnosis of opportunistic infection in an immunocompetent patient, such as with the use of bronchoscopy with BAL, should be considered.

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肺囊蟲肺炎感染併發急性呼吸迫症候群發生在免疫健全者一病例報告

楊國坤　吳子卿　李友仁*　陳世彬　曹昌堯

肺囊蟲肺炎（PJP）主要是發生在免疫不全的病人，而且是一種威脅生命的傳染病，它常常發生在後天性免疫不全症候群（愛滋病）的病人身上，也可以發生在其他免疫不全的病人身上，但是不常發生於健康的人身上。在此，我們報告一名健康的49歲婦女在住院前兩週發生咳嗽有痰以及活動性呼吸急促的症狀。住院後上述症狀逐漸惡化並且進展到呼吸衰竭。她的胸部X光片揭示兩側肺葉擴散性的結節性浸潤。同樣的，在高解析度胸部電腦斷層（HRCT）也顯示彌漫性肺泡型浸潤。後來進行支氣管鏡及肺泡灌洗檢查，肺泡灌洗液抹片經由Giemsa's染色法証實是肺囊蟲的感染。病患在使用Trimethoprim-sulfamethoxazole治療之後症狀改進並且成功脫離呼吸器。在治療完成兩個月後追蹤的胸部X光已接近正常。*(胸腔醫學* ***2008; 23: 138-143)***

關鍵詞：肺囊蟲肺炎，免疫健全

中山醫學大學附設醫院　胸腔內科，國泰綜合醫院　胸腔內科*
索取抽印本請聯絡：曹昌堯醫師，中山醫學大學附設醫院　胸腔內科，台中市南區建國北路一段110號

Cardiovocal Syndrome: Aortic Dissecting Aneurysm Presenting as Hoarseness

Yu-Te Lai, Chih-Hung Chen, Cheng-Hsien Wu*, Jaw-Ji Chu**, How-Wen Ko, Ying-Huang Tsai

Hoarseness is a common clinical problem which may also imply an initial manifestation of serious disease. Lesions affecting the recurrent laryngeal nerve will result in vocal cord paralysis and hoarseness. Malignancy accounts for most of the extralaryngeal causes of vocal cord paralysis, but other causes could include even cardiovascular disease. Cardiovocal syndrome is a left recurrent laryngeal nerve palsy caused by cardiovascular disease. Hoarseness may be the only presentation of thoracic aortic aneurysm or painless dissection. Vocal cord function can return after successful repair. We report a 72 year-old man who had hoarseness for 1 month. Dissecting aneurysms of the aortic arch and thoracic aorta were found. An operation was performed, but the patient had difficulty weaning from the ventilator and died of sepsis. ***(Thorac Med 2008; 23: 144-149)***

Key words: cardiovocal syndrome, hoarseness, left vocal cord palsy, aortic dissecting aneurysm

Introduction

Cardiovocal syndrome was first described by Ortner in a patient with mitral stenosis in 1897 [1]. It is a clinical entity with the presentations of hoarseness and left vocal cord palsy secondary to cardiovascular disease. Because of its specific anatomic character, the left-side recurrent laryngeal nerve is usually involved. Thoracic aortic aneurysm or dissection is a cause of cardiovocal syndrome. Chest and back pain is the most common symptom of aortic dissection, but sometimes hoarseness is the only clue to painless aortic dissection [2-3]. We herein report a case of left vocal cord paralysis associated with dissecting aneurysm of the aortic arch and thoracic aorta.

Case Report

In December 2005, a 72-year-old man presented to chest and ENT doctors in a small local hospital in Taiwan with the symptom of progressive hoarseness of 1 month's duration. His medical history included chronic arterial hypertension for 9 years without regular control. An old cerebrovascular accident occurred in 1997 without sequela. He was a heavy smoker,

Department of Chest Medicine; *Department of Radiology; **Division of Cardiovascular Surgery, Chang Gung Memorial Hospital, Taoyuan, Taiwan
Address reprint requests to: Dr. How-Wen Ko, Department of Chest Medicine, Chang Gung Memorial Hospital, 5, Fu-Hsin St. Kweishan, Taoyuan, Taiwan

at 40 pack-years, but had quit smoking for 10 years. He had never undergone surgery, including the head, neck and chest. Cardiomegaly was revealed by previous chest X-ray in May 1997, but no evidence of aortic aneurysm was found. The fiberoptic laryngoscope showed left-side vocal cord paralysis, and chest radiography (Figure 1) revealed a widening mediastinum, suggesting a thoracic aortic aneurysm. Cardiovocal syndrome was highly suspected. Thoracic aortic dissection could not be excluded by 2-dimensional echocardiography. Thereafter, he was referred to our regional research hospital.

At his visit, hoarseness was still noticed. He denied experiencing neck swelling, dysphagia, cough, shortness of breath, or chest pain. Vital signs were: body temperature, 37.0ºC; pulse rate, 87/min; respiratory rate, 20/min; blood pressure, 158/84 mmHg. His physical examination was unremarkable. No cardiac murmur, carotid or abdominal bruit was heard. Pulse was symmetric in the 4 extremities. Chest computed tomography (CT) disclosed aneurysmal dilatation of the aortic arch and descending segment of the thoracic aorta. The presence of an intimal flap (Figure 2) was seen from the aortic arch to the distal thoracic aorta, with thrombosis. Since it was dissecting the aneurysm at the thoracic aorta, type B was favored. Meanwhile, 2-dimensional echocardiography and cardiac catheterization revealed only a huge thoracic aortic aneurysm with intramural hematoma. It was supposed that the left recurrent laryngeal nerve was compressed by the thoracic dissecting aneurysm. Owing to high risk and possible mortality from thoracic aortic dissection, surgical intervention for thoracic aneurysm was strongly suggested. Resection of the descending thoracic aortic aneurysm was performed on 4 January 2006. The operative finding revealed a huge aortic aneurysm with many intramural thrombi, which was subsequently confirmed by pathological report. Em-

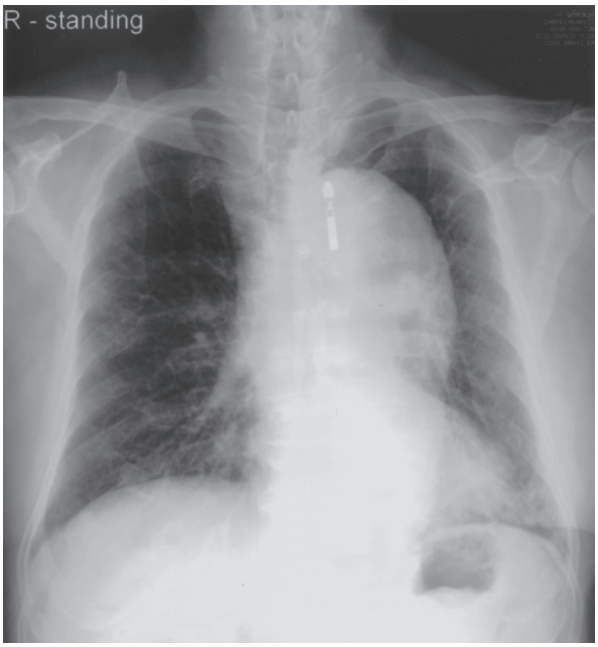

Fig. 1. Chest radiography showing widening of the mediastinum, suggesting thoracic aortic aneurysm

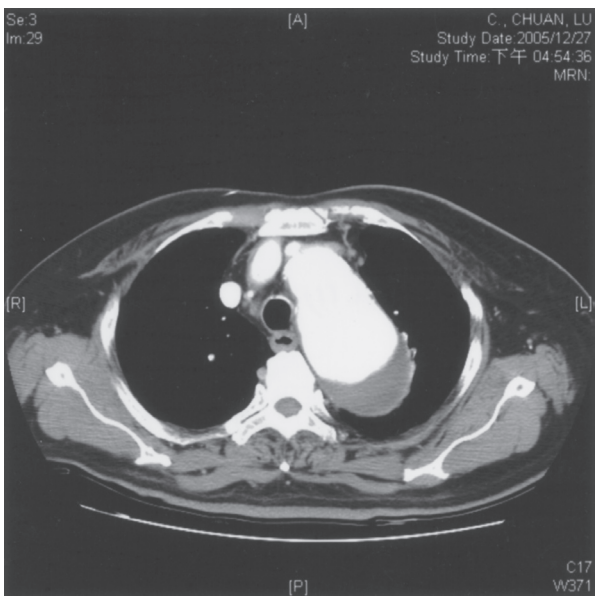

Fig. 2. Chest computed tomography reveals aneurysmal dilation of the aorta with thrombosis of the false lumen

physematous lung and severe pleural adhesions were found as well. After the operation, the patient experienced difficulty weaning from the mechanical ventilator due to poor lung function. Unfortunately, he died of *A. baumannii* pneumonia and sepsis on 4 March 2006.

Discussion

Hoarseness is a common clinical presentation in the otolaryngology clinic. A variety of voice changes could be described as hoarseness by patients, including voice tremor, or a low pitched, breathy, or strained voice quality. A thorough history and physical examination are vital for determining the origin of this complaint. Several benign lesions and etiologies, such as inflammation, surgery, trauma, intubation injury, gastroesophageal reflux disease, vocal cord polyps, and neurological conditions, can lead to voice changes. Vocal cord palsy is an important cause of hoarseness. Patients with hoarseness for more than 2 weeks should have a detailed examination to rule out malignancy. Bronchogenic carcinoma is the most common cause of vocal cord palsy with hoarseness.

Intrathoracic causes of vocal cord dysfunction have been described. Hoarseness from left recurrent laryngeal nerve palsy associated with cardiovascular diseases (cardiovocal or Ortner syndrome) is an unusual condition, and was first described a century ago by Ortner [1]. In his report, a patient with hoarseness had an enlarged left atrium due to mitral valve stenosis. Left vocal cord immobility was found as well, and thought to be due to vocal cord palsy as a result of compression of the left recurrent laryngeal nerve by the dilated left atrium. Accordingly, any nonmalignant cardiac or intrathoracic process that results in a change of either recurrent laryngeal nerve-usually by stretching, pulling, or compression-and causes a vocal cord paralysis, should be considered cardiovocal syndrome [1, 4]. The left recurrent laryngeal nerve, which has a longer course around the aortic arch, is more frequently involved than the right recurrent laryngeal nerve. Hoarseness is correctable after treatment of the underlying cardiovascular disease.

Aortic aneurysms are classified according to location and period of onset. Two different anatomic systems have been used to classify aortic dissection by location. The Stanford system, more widely used, classifies type A as those involving the ascending aorta, regardless of the primary intimal tear; all others are classified as type B. The DeBakey system is based on the site of origin. Type 1 originates in the ascending aorta and propagates to at least the aortic arch, whereas type 2 originates in and is confined to the ascending aorta. Type 3 is defined as a lesion that originates in the descending aorta and extends distally or proximally.

Acute onset dissecting aneurysms are commonly seen with severe blunt trauma, whereas chronic onset is mostly noted in cases of atherosclerosis and aging. In a retrospective review of 168 cases of thoracic aortic aneurysm, 8 (5%) patients manifested hoarseness secondary to recurrent laryngeal nerve palsy, and only 1 patient regained vocal cord function after surgical treatment of the aneurysm [5]. Aortic dissection is 1 of the most catastrophic medical emergencies and requires prompt management. Chest and back pain is the typical presentation, but about 5~10% of patients present with painless aortic dissection [6]. Hoarseness may be the only clue in this clinical setting. In 1999, Khan *et al*. reported a woman with painless aortic dissection and a 2-day history of hoarse-

ness. After surgical repair, she recovered her normal voice within 2 weeks [2]. Charbel *et al*. described a similar case in 2004, but the patient did not have a successful outcome [3]. Our patient presented hoarseness for 1 month without any other symptoms. Aortic dissection was suspected initially at the first hospital, and CT of the chest in our hospital also revealed a thoracic aortic aneurysm with possible dissection. Serial cardiovascular examinations disclosed intramural hematoma, suggesting a dissecting aneurysm. There was no inflammatory process or malignancy shown on the imaging study. It was highly suspected that the dilated aortic arch and dissecting aneurysm of the thoracic aorta were compressing the recurrent laryngeal nerve, causing Ortner's syndrome.

In the literature, other causes of Ortner's syndrome have included atrial septal defect, ventricular septal defect, mitral stenosis [7], patent ductus arteriosus aneurysm [8], mitral valve prolapse [4], primary pulmonary hypertension [9], compression from atheromatous plaque in the aorta, cystic fibrosis [10], mycotic aneurysm of the aorta caused by *S. cholerasuis* [11], and rarely Schistosomal cor pulmonale [12]. Some cases were reported because of iatrogenic complications, including transradial cardiac catheterization [13], transcatheter coil closure of patent ductus arteriosus [14], and post-surgery complication of thoracic aortic aneurysm. One study indicated that surgical repair for thoracic aortic aneurysm is associated with a relatively high incidence of vocal cord paralysis, despite preservation of the recurrent laryngeal nerve [15]. The paralysis did not show spontaneous recovery, even 6 months after surgery.

In conclusion, hoarseness is not just a common presentation, but can be a clue to underlying serious disease. Because the left recurrent laryngeal nerve follows a unique path, intrathoracic disorders account for most causes of vocal cord palsy; lung cancer is the most common, but cardiovocal syndrome, also called Ortner's syndrome, is a rare but important entity. Sometimes hoarseness is the only symptom of cardiovascular disease, such as thoracic aortic aneurysm or aortic dissection. If a patient presents with hoarseness and abnormal CXR findings in cardiovascular structures, cardiovocal syndrome should be considered in the differential diagnosis.

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心因性聲帶麻痺：胸主動脈瘤以聲音沙啞表現

賴祐德　陳志弘　吳政賢*　朱肇基**　柯皓文　蔡熒煌

聲音沙啞在臨床上是很常見的問題，但是有時也意味著嚴重疾病的初期表現。影響返喉神經的病灶常會造成聲帶麻痺和聲音沙啞。因為解剖位置的特殊性，左側返喉神經經常被影響到。心因性聲帶麻痺是因為心血管疾病影響到左側返喉神經麻痺所造成的症狀。聲音沙啞可以是胸主動脈瘤或是無痛性主動脈剝離的唯一表現，聲帶的功能在經過成功的修補後可能可以復原。我們報告一位聲音沙啞已經一個月的72歲的男性，在主動脈弓和胸主動脈被發現有剝離性動脈瘤，雖然進行了手術，最後卻因為呼吸器難以脫離且死於敗血症。*(胸腔醫學 **2008; 23: 144-149**)*

關鍵詞：心因性聲帶麻痺，聲音沙啞，左側聲帶麻痺，主動脈剝離性動脈瘤

林口長庚紀念醫院　呼吸胸腔科　放射科*　心臟血管外科**
索取抽印本請聯絡：柯皓文醫師，林口長庚醫院　呼吸胸腔科，桃園縣龜山鄉復興街5號

A Rare Iatrogenic Bronchial Foreign Body Detected by Routine Bronchoscopy after Percutaneous Tracheostomy: A Case Report

Isaac Chun-Jen Chen*,**, Chien-Sheng Huang*, Pin-Tarng Chen***, Chih-Cheng Hsieh*, Han-Shui Hsu*, Yu-Chung Wu*, Wen-Hu Hsu*

We describe herein a patient with an unusual iatrogenic bronchial foreign body, who was confirmed and treated unexpectedly with the routine use of a bronchoscope in the process of percutaneous dilatational tracheostomy (PDT). Routine use of the fiberoptic bronchoscope in PDT can prevent not only injury to the tracheal posterior wall, but also avoid the associated iatrogenic tracheobronchial foreign body retention in the airway. This unusual iatrogenic bronchial foreign body was identified subsequently as a part of the airway exchange catheter. The airway exchange catheter should be used meticulously during jet ventilation. The differential diagnosis of an unusual pneumothorax, which occurred shortly after the use of the airway exchange catheter with jet ventilation in the same case, is also discussed. ***(Thorac Med 2008; 23: 150-155)***

Key words: bronchial foreign body, bronchoscopy, percutaneous dilatational tracheostomy

Introduction

Few cases of iatrogenic tracheobronchial foreign body are reported. We describe herein a very unusual incident occurring during endotracheal tube replacement using the changing guide wire, in which a plastic tube became dislodged from the airway exchange catheter and inadvertently impacted in the bronchus intermedius. Neither the delayed detection nor the successful endoscopic removal of this endobronchial foreign body were achieved until a scheduled percutaneous dilatational tracheostomy (PDT) was performed with the routine use of a fiberoptic bronchoscope 11 days after reintubation. In addition, an unusual episode of localized pneumothorax occurred shortly after this incident.

Case Report

A 60-year-old man had hemangioblastoma of the left cerebellum. He underwent craniectomy and removal of the cerebellar tumor.

* Division of Thoracic Surgery, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan
** Division of Traumatology, Department of Emergency, Taipei Veterans General Hospital, Taipei, Taiwan
*** Division of Anesthesiology, Taipei Veterans General Hospital, Taipei, Taiwan
Address reprint requests to: Dr. Chien-Sheng Huang, Division of Thoracic Surgery, Department of Surgery, Emergency Department, Taipei Veterans General Hospital, 201, Sec. 2, Shih-Pai Road, Taipei 112, Taiwan

Postoperative weakness of his right extremities and the condition of choking easily, developed thereafter. His neurosurgeons were aware of the lower cranial nerve palsy. Striders and diffuse rhonchi worsened, and he required frequent suctioning for thick excessive secretion. He was reintubated 3 months after the operation and placed on mechanical ventilation during the prolonged postoperative hospital stay. A significant cuff leak occurring on insertion of the endotracheal tube necessitated an immediate tube change using a 14-F, 83-cm, Cook airway exchange catheter (Cook Critical Care, Bloomington, IN, USA), as well as a Rapi-Fit connector (Cook Critical Care, Bloomington, IN, USA) to ventilate the patient with jet ventilation during the exchange. The postintubation chest radiograph (Figure 1A) showed marked collapse of the middle and lower lobes of the right lung, with a deep sulcus sign lateral to the right hemidiaphragm. The upper lobe of the right lung seemed to remain expanded. The findings were consistent with localized pneumothorax. We used chest tube drainage with a 16 French pigtail catheter, (neither the application of the airway exchange catheter nor the plastic tube that had disappeared from it was made known) (Figure 2D). The chest radiograph obtained later that day (Figure 1B) showed reexpansion of the right lung and resolution of the localized pneumothorax. The pigtail catheter was removed 4 days later, and no more pneumothorax occurred. A series of chest radiographs, as in Figures 1A and 1B, failed to demonstrate the foreign body in the bronchus intermedius We performed PDT using a guide wire dilating forceps under fiberoptic bronchoscopic guidance due to neurogenic alveolar hypoventilation 11 days after reintubation. When we performed routine

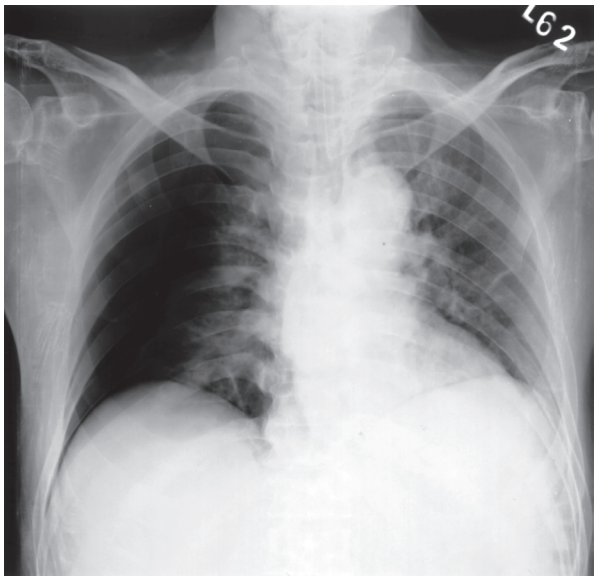

Fig. 1A. The postintubation chest radiograph shows marked collapse of the middle and lower lobes of the right lung with a deep sulcus sign lateral to the right hemidiaphragm. No visible foreign body in the airway could be identified in this radiograph.

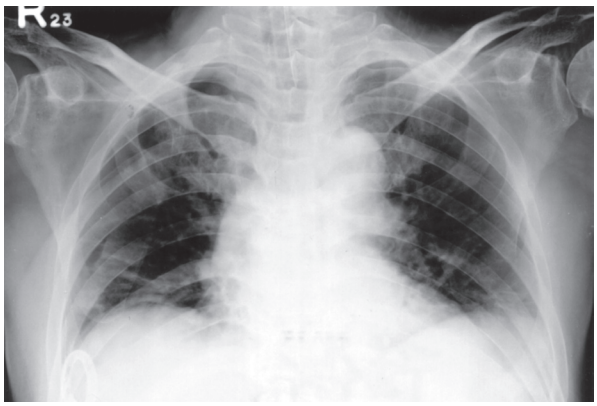

Fig. 1B. The chest radiograph obtained later that day shows reexpansion of the right lung and resolution of the localized pneumothorax. No visible foreign body in the airway could be identified in this radiograph.

fiberoptic bronchoscopy after inserting the tracheostomy tube, the previously dislodged plastic tube was detected unexpectedly in the bronchus intermedius (Figures 2A and 2B). We extracted this endobronchial foreign body smoothly by using fiberoptic bronchoscopic

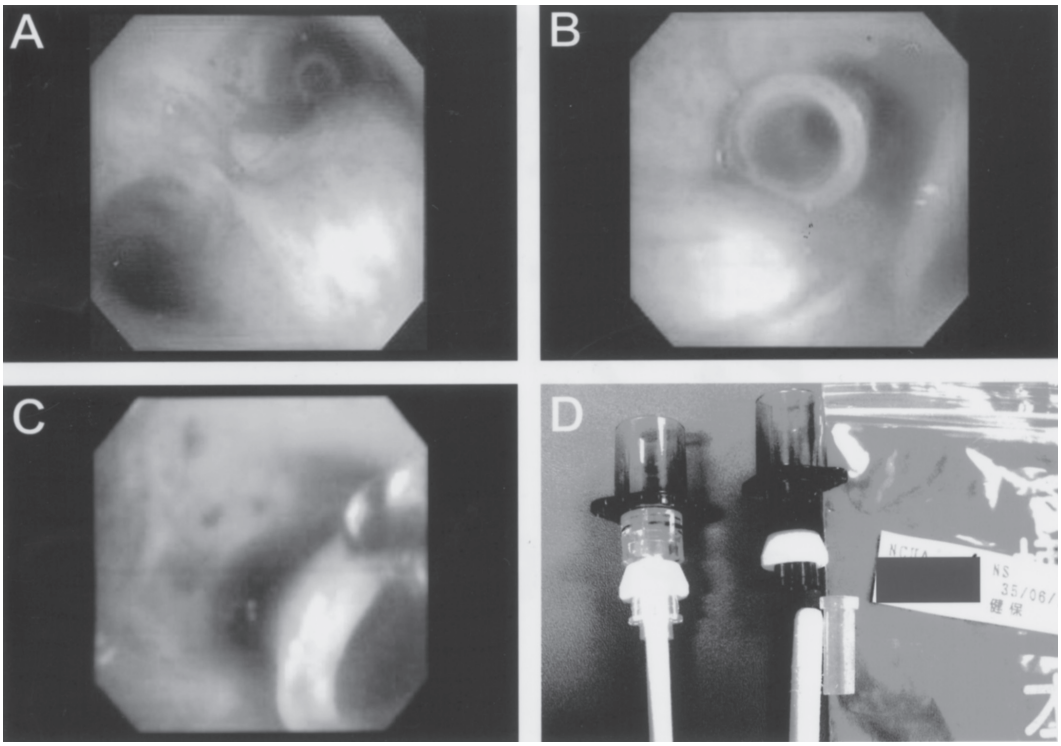

Fig. 2. The plastic tube dislodged from the airway exchange catheter incidentally retained in the bronchus intermedius. (A) The bronchoscopic view is above carina. (B) Another bronchoscopic view in the right mainstem bronchus. (C) The plastic tube was extracted using fiberoptic bronchoscopic alligator forceps. (D) The dissociated assembly composed of the Cook airway exchange catheter and the Rapi-Fit connector is compared with a normal one.

alligator forceps (Figure 2C). Shortly afterwards, we confirmed that the extracted plastic tube was the cap of the airway exchange catheter used to connect to the connector (Figure 2D). The patient was weaned off mechanical ventilation successfully 18 days after PDT, and could self-expectorate favorably via an uncuffed tracheostomy tube at home during a 10-month follow-up.

Discussion

To the best of our knowledge, this is the first report of an unusual iatrogenic bronchial foreign body, which was identified and extracted unexpectedly by routine use of the fiberoptic bronchoscope in the process of performing PDT. There has been little mention of iatrogenic tracheobroncial foreign bodies in the previous English literature. Phukan *et al*. [1] report an unusual complication of PDT in which the guide wire became lodged in the bronchial tree and was removed successfully with the assistance of an expert bronchoscopist. Pinder *et al*. [2], reported an incident that occurred during PDT using the Portex technique, in which a significant cuff leak on insertion of the tracheostomy tube necessitated an immediate tube change--a process similar to our case. Their dislodged guide wire introducer was impacted in the trachea. The endotracheal foreign body was removed via routine fiberoptic bronchoscopy, as well [2]. It has been argued that the use of a fiberoptic bronchoscope to

guide operators in performing PDT makes the procedure safe, and especially avoids injury to the tracheal posterior wall [3], although this is not supported by the results of a recent meta-analysis study [4]. In our case, the series of chest radiographs failed to demonstrate the foreign body in the bronchus intermedius, probably because the foreign body material was not visible in the plain film of the chest radiograph. Thus, the dislodged plastic tube from the airway exchange catheter would not have been identified and removed successfully if we did not use a routine fiberoptic bronchoscope in performing PDT.

The possible cause of the foreign body in our case could be that the airway exchange catheter was used upside down. The plastic tube, dislodged from the airway exchange catheter incidentally, was inadvertently impacted in the bronchus intermedius following insertion of the endotracheal tube. The Difficult Airway Algorithm recommends the airway exchange catheter be used in the management of difficult airway [5], and it is now commonly used as a guide wire in exchanging endotracheal tubes [6]. Recently, a rare complication, bilateral tension pneumothoraces following jet ventilation via an airway exchange catheter, was reported [7]. The airway exchange catheter should be used meticulously during jet ventilation.

There was an unusual episode of localized pneumothorax shortly after the use of the airway exchange catheter with jet ventilation in our case. The pneumothorax likely resulted from the barotrauma related to the jet ventilation. The differential diagnosis should include "ex vacuo" pneumothorax occurring under conditions of acute lobar collapse from acute bronchial obstruction. Berdon and coworkers [8] first reported 3 cases of ex vacuo pneumothorax in children: in 2 patients, acute obstruction of the upper lobe bronchus of the right lung from an aspirated foreign body occurred, and in 1, selective intubation of the bronchus intermedius. Woodring *et al*. [9] later identified 3 cases of ex vacuo pneumothorax which occurred within 1 year; all were teenagers with severe head injury. The researchers suggested that retained secretions or mucous plugs are also a common cause of ex vacuo pneumothorax. The condition was not thought to be rare, but unrecognized [9].

The possible mechanisms of ex vacuo pneumothorax have been discussed in the literature. In acute lobar collapse resulting from acute bronchial obstruction, a marked increase in negative intrapleural pressure around the collapsed lobe is present. As a result, gas is drawn into the pleural space around the collapsed lobe while the seal between the visceral and partial pleura of the adjacent lobe or lobes remains intact [9-10].

Treatment of ex vacuo pneumothorax should be directed toward relieving the bronchial obstruction rather than chest tube drainage. Ex vacuo pneumothorax could occur due to acute collapse of any lobe [9]. One case of selective intubation of the bronchus intermedius involved the middle and lower lobes of the right lung [9]. The findings on the chest radiograph, which were characterized by marked collapse of the middle and lower lobes of the right lung, close approximation of the ribs, and elevation of the right hemidiaphragm, implied volume reduction in the right hemithorax. By comparison, there was similar marked collapse of the middle and lower lobes of the right lung in our case, but the upper lobe of the right lung seemed to remain expanded with neither definitive borders nor signs of volume reduction of the right hemithorax, as in the previous case (Figure

1A). Furthermore, the localized pneumothorax resolved using chest tube drainage in our case, which was not compatible with the treatment of ex vacuo pneumothorax. Nevertheless, the suspicion of ex vacuo pneumothorax could lead to early diagnosis of the foreign body in the bronchus intermedius.

In conclusion, an iatrogenic bronchial foreign body is very rare. Routine use of the fiberoptic bronchoscope in PDT can prevent not only injury to the tracheal posterior wall, but also the retention of an associated iatrogenic tracheobronchial foreign body in the airway. The airway exchange catheter should be used meticulously during jet ventilation.

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經皮氣管切開手術合併例行性支氣管鏡發現一罕見支氣管異物—病例報告

陳俊仁*,** 黃建勝* 陳品堂*** 謝致政* 許瀚水* 吳玉琮* 許文虎*

我們報導一位罹患罕見醫原性支氣管異物之病例，不預期地在經皮擴張性氣管切開手術後，經由例行性使用支氣管鏡證實並治療。在施行經皮擴張性氣管切開術時，例行性使用支氣管鏡不僅可避免氣管後壁之傷害並且可預防異物留滯在呼吸道。此罕見醫原性支氣管異物，最後被確認是在使用呼吸道交換導管並噴射通氣時，從呼吸道交換導管上所掉落之零件。在使用呼吸道交換導管並噴射通氣時，務要謹慎。此同一病例當時在使用呼吸道交換導管並噴射通氣後，亦併發一不尋常之氣胸，其鑑別診斷予一併討論。*(胸腔醫學* ***2008; 23: 150-155)***

關鍵詞：支氣管異物，支氣管鏡，經皮擴張性氣管切開術

*臺北榮民總醫院 外科部 胸腔外科，**臺北榮民總醫院 急診部 創傷科，***臺北榮民總醫院 麻醉部
索取抽印本請聯絡：黃建勝醫師，臺北榮民總醫院 外科部 胸腔外科，11217台北市北投區石牌路二段201號