ISSN 1023-9855

胸腔醫學

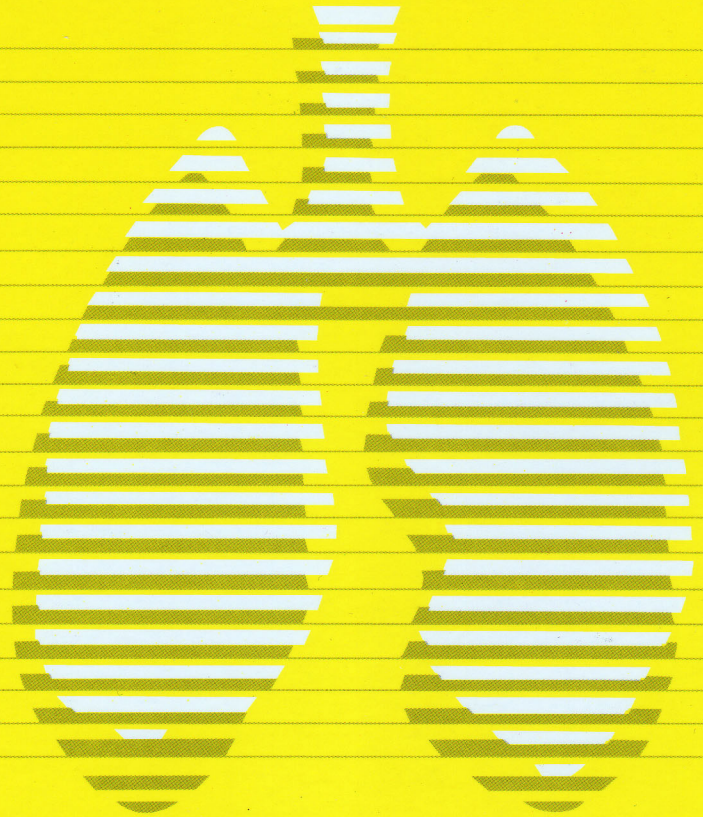
Thoracic Medicine

The Official Journal of Taiwan Society of Pulmonary and Critical Care Medicine

Vol.34 No.4 August 2019

第三十四卷 第四期

中華民國一〇八年八月



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No. 123, Dapi Rd., Niaosong Dist., Kaohsiung City 83301, Taiwan

ISSN 1023-9855

中華民國一〇八年八月　第三十四卷　第四期

ISSN 1023－9855

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原著

病例報告

中華民國一〇八年八月　第三十四卷　第四期

ISSN 1023－9855

Vol.34 No.4 August 2019

胸腔醫學

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The Official Journal of Taiwan Society of Pulmonary and Critical Care Medicine

Orginial Article

Case Reports

Analyzing Characteristics Associated with Symptomatic Sleep Disturbance in COPD Patients

Shan-Fon Tsai, Shew-Meei Sheu*, Ching-Fang Tsai*, Ming-Shian Lin, Wei-Chen, Yi-Jen Chen

Introduction: Sleep disturbance, characterized by difficulty of falling asleep, interrupted sleep, and feeling unrefreshed upon waking, may compromise a patient's quality of life and survival rate. Cough and shortness of breath are the most frequent symptoms in chronic obstructive pulmonary disease (COPD) patients. However, symptomatic sleep disturbance is not clearly defined. Our study aimed to identify characteristics that correlate with symptomatic sleep disturbance in COPD patients in Taiwan.

Methods: This was a cross-sectional study conducted between 2011 and 2012. We successfully recruited 180 COPD patients over 40 years of age. Each participant had to fill out a questionnaire to determine whether they had symptomatic sleep disruption due to cough and difficulty breathing. Analysis parameters included the participants' demographics, acute exacerbation (AE), comorbidities, COPD Assessment Test (CAT) scores, and lung function test results.

Results: The mean age and body mass index of all patients were 71.7 years and 22.8 kg/m^2, respectively. The prevalence of symptomatic sleep disturbances among the COPD patients was 28.9% (52/180). Those with symptomatic sleep disturbances also had significantly higher CAT scores (15.9 ± 10.5 vs. 9.5 ± 7.0, $p < 0.01$) and AE occurrence (52.0% vs. 29.8%, $p < 0.05$) than those without sleep disturbances. Multivariable analysis revealed that the CAT score (odds ratio, 1.1, 95% confidence interval, 1.1-1.2) was an independent factor significantly associated with symptomatic sleep disturbance.

Conclusions: Symptomatic sleep disturbances occurred in 28.9% of COPD patients. The CAT score was correlated with self-reported symptomatic sleep disturbances in COPD patients and can be used as a predictor for symptomatic sleep disturbance. ***(Thorac Med 2019; 34: 139-147)***

Key words: chronic obstructive pulmonary disease (COPD), sleep disturbance, COPD assessment test (CAT)

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Introduction

Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death among adults worldwide and is expected to become the third leading cause of death by 2020 [1-2]. The estimated prevalence of COPD in the general population aged 40 years and older is 6.1%, and COPD is the seventh leading cause of death in Taiwan [3]. Sleep disturbance among COPD patients is significantly associated with worsening health status and impaired quality of life [4-6].

Sleep disturbance is a common symptom of COPD and affects more than 35% of patients [7-8]. Demographic factors such as age, obesity, pharmacotherapy, disease-specific symptoms (wheezing and cough), or comorbid sleep disorders have been shown to be correlated with sleep disturbance [9]. Early intervention for the main factors that contribute to sleep disturbance may reduce acute exacerbation (AE) events and increase the survival rate.

Sleep disturbance is characterized by difficulty falling asleep, interrupted sleep, and feeling unrefreshed upon waking [10]. Various assessment tools, such as sleep disturbance T-scores and the Jenkins Sleep Evaluation Questionnaire (JSEQ), have been used to evaluate sleep disturbance in COPD patients [4,11]. Symptomatic sleep disturbance has not been distinctly defined. Cough, shortness of breath and wheezing are the most frequent symptoms in COPD patients [8], and productive cough increases the risk of COPD exacerbations [12]. However, COPD patient characteristics associated with symptomatic sleep disturbance have yet to be clarified. In this study, we aimed to investigate the factors that may be associated with symptomatic sleep disturbance among COPD patients using a cross-sectional database collected in the setting of a community hospital chest clinic in Taiwan.

Materials and Methods

Patients and study design

This was a cross-sectional research study conducted between 2011 and 2012 at the outpatient department of the Division of Pulmonary and Critical Care Medicine, Ditmanson Medical Foundation Chia-Yi Christian Hospital, which is a 1,000-bed community-based teaching hospital in Chiayi, Taiwan. Potential participants were male or female COPD patients over 40 years of age who had been seen routinely in pulmonary outpatient clinics. We adopted the 2007 Global Initiatives for Chronic Obstructive Lung Disease (GOLD) classification system to help us classify our COPD patients as stage 1, 2, 3 or 4 [2]. Exclusion criteria were the comorbidities of dementia, a history of bronchial asthma, other structural lung diseases (i.e., lung cancer, bronchiectasis, or fibrotic lung), intolerance of bronchodilator use, and/or unstable cardiovascular diseases. Those who met the inclusion and exclusion criteria and signed an informed consent form were enrolled in the study. To determine whether they had symptomatic sleep disturbance, the patients were asked the question, "Does the patient's cough or breathing problem interfere with his/her night sleep?" Based on their self-reported answers (yes/no), the patients were divided into 2 groups: those with (yes) and those without (no) symptomatic sleep disturbances. This study was approved by the Institutional Review Board of the Ditmanson Medical Foundation Chia-Yi Christian Hospital, Taiwan.

Parameters

The patients' medical profiles were retrospectively reviewed and analyzed, including their basic information regarding age, sex, body mass index (BMI), alcohol consumption and smoking status. Furthermore, information on medical comorbidities (hypertension, hyperlipidemia, heart failure, diabetes, and chronic liver disease), AE events, lung function test results, and COPD Assessment Test (CAT) scores were also collected. BMI was calculated from the subjects' reported weight and height (kg/m^2). Referencing the medical records of the individuals, the number of AE in the preceding 3 months and medical comorbidities were recorded. Each participant's forced expiratory value in the first second (FEV_1) and forced vital capacity (FVC) of predicted values were also recorded during the course of the survey. The CAT score is a quick, validated tool for evaluating the COPD patient's health status. It contains 8 items, including cough, phlegm, chest tightness, breathlessness, activities, confidence, sleep and energy. Each item can be scored from 0 to 5. A total score would range from 0 to 40. Higher CAT scores indicate a more severe impact of COPD on the patient's life.

Statistics

Standard statistical analyses were used to calculate the frequencies, percentages, means, and standard deviations of the descriptive demographic variables (age, sex, smoking and alcohol use), comorbidities and clinical characteristics. Between-group proportions for dichotomous outcomes, such as comorbidities, were compared using the chi-square test. Continuous outcomes was tested by *t*-test. We used a logistic regression model to estimate crude odds ratios (OR) to measure associations between possible correlates and OR, adjusting for confounding effects. All statistical analyses were conducted using SPSS software for Windows, version 21.0 (IBM Corp., Armonk, NY, USA). All tests were 2-sided, and a p value < 0.05 was considered statistically significant.

Results

In all, 180 participants were enrolled in this study. The mean age and BMI of all patients were 71.7 years and 22.8 kg/m^2, respectively. Males and smokers were predominant (176, 97.8%; 171, 95.0%). The mean duration of COPD was 4.5 years. The percentages of patients with GOLD 2007 Stages 1, 2, 3, and 4 were 8.9%, 46.1%, 36.7%, and 8.3%, respectively (Table 1).

The patients were divided into 2 groups based on whether their sleep was disturbed by breathlessness and cough (with, n=52 vs. without, n=128). The prevalence of symptomatic sleep disturbances among the COPD patients was 28.9%. A greater proportion of patients with symptomatic sleep disturbances were in stages 3 and 4, compared to those without sleep disturbances (63.5% vs. 37.5%, $p < 0.01$). Those with symptomatic sleep disturbances had significantly lower FEV_1 predicted values than those without sleep disturbances (44.1 ± 16.2 vs. 53.5 ± 19.0, $p < 0.01$). Other factors, such as sex, BMI, smoking status, alcohol consumption, and comorbidities, did not show a significant correlation with symptomatic sleep disturbances in COPD patients (Table 1).

We found that COPD patients with symptomatic sleep disturbances had significantly higher CAT scores (15.9 ± 10.5 vs. 9.5 ± 7.0, $p < 0.01$) and higher rates of AE (52.0% vs. 29.8%, $p < 0.05$) than those without sleep dis-

Table 1. Demographic Characteristics of the Study Patients (N=180)

			Symptomatic sleep disturbances				
	Total (N=180)		With (N=52)		Without (N=128)		
	N	%	N	%	N	%	*p*-value
Age, years (mean ± SD)	71.7 ± 8.3		69.1 ± 8.3		72.8 ± 8.1		0.01
< 60	18	10.0	8	15.4	10	7.8	0.12
60-69	46	25.6	16	30.8	30	23.4	
≥ 70	116	64.4	28	53.9	88	68.8	
Sex							
Male	176	97.8	50	96.2	126	98.4	0.58
Female	4	2.2	2	3.9	2	1.6	
BMI, kg/m^2 (mean ± SD)	22.8 ± 3.4		22.5 ± 3.3		22.9 ± 3.4		0.49
< 24	121	67.2	39	75.0	82	64.1	0.16
≥ 24	59	32.8	13	25.0	46	35.9	
Smoker							
No	9	5.0	4	7.7	5	3.9	0.29
Yes	171	95.0	48	92.3	123	96.1	
Alcohol use							
No	131	73.2	36	70.6	95	74.2	0.62
Yes	48	26.8	15	29.4	33	25.8	
Duration of COPD, years (mean ± SD)	4.5 ± 7.4		5.9 ± 9.7		3.9 ± 6.2		0.17
2007 GOLD classification							
Stage 1	16	8.9	0	0.0	16	12.5	< 0.01
Stage 2	83	46.1	19	36.5	64	50.0	
Stage 3	66	36.7	25	48.1	41	32.0	
Stage 4	15	8.3	8	15.4	7	5.5	
Comorbidities							
Diabetes	25	13.9	6	11.5	19	14.8	0.56
Hypertension	90	50.0	20	38.5	70	54.7	0.05
Hyperlipidemia	16	8.9	3	5.8	13	10.2	0.35
Heart failure	9	5.0	2	3.9	7	5.5	0.06
Chronic liver diseases	14	7.8	2	3.9	12	9.4	0.20
FVC, predicted %	60.5 ± 16.8		57.2 ± 14.2		61.9 ± 17.6		0.09
FEV_1, predicted %	50.8 ± 18.7		44.1 ± 16.2		53.5 ± 19.0		< 0.01
CAT	11.3 ± 8.6		15.9 ± 10.5		9.5 ± 7.0		< 0.01
AE in the previous 3 months, times							
0	104	63.4	24	48.0	80	70.2	0.01
≥1	60	36.6	26	52.0	34	29.8	

Note: All data are presented as n (%) unless otherwise indicated.

AE, acute exacerbation; BMI, body mass index; CAT, COPD assessment test; FVC, forced vital capacity; FEV_1, forced expiratory volume in the first second; GOLD, Global Initiatives for Chronic Obstructive Lung Disease; SD, standard deviation.

turbances. In the multivariable analysis (Table 2), the CAT score was significantly associated with symptomatic sleep disturbances (OR 1.1, 95% confidence interval [CI], 1.1-1.2). In addition, stage 2 and 3 COPD patients had a lower risk of symptomatic sleep disturbance than stage 4 patients (OR < 0.1-0.1, 95% CI < 0.1-0.9).

Discussion

Sleep disturbance is highly prevalent in patients with COPD: more than 35% of these patients were reported to have experienced sleep disturbance [7-8]. However, symptomatic sleep disturbances is not clearly defined, and to establish the high awareness among clinicians potentially improve long-term outcomes for COPD patients [13]. In our study, COPD patients with symptomatic sleep disturbances exhibited significantly higher CAT scores, lower FEV_1 predicted values, and an increase in AE occurrence compared to those without sleep disturbances. However, multivariable analysis further demonstrated that the CAT score was the only factor significantly associated with symptomatic sleep disturbances. Patients' basic information, such as age, gender, comorbidities, smoking or alcohol use, BMI and duration of COPD, did not correlate with symptomatic sleep disturbances.

Our current study showed that the prevalence of symptomatic sleep disturbances in COPD patients was 28.9%. Chang *et al*. reported that 15.9% of their recruited COPD participants ticked "cough/snore loudly at night" as the reason for sleep disturbances [14]. Stephenson *et al*. also showed that the most frequent symptoms, coughing (72.9%) and shortness of breath (61.4%), strongly interfered with COPD patients' sleep [8]. Sleep disturbances have also been evaluated using different assessment tools, such as the sleep disturbance T-score and the JSEQ [4,11]. These results show that coughing and breathlessness are the 2 main causes of sleep disturbance in most COPD patients, despite the discrepancy in the percentages of sleep disturbance. Such variations may be due to the choice of assessment tools and the patient's self-perception of the symptoms, which may interrupt their sleep.

Our study also investigated other factors that may correlate with sleep disturbance, such as age, BMI, gender, smoking/alcohol use, COPD stage, medical comorbidities, lung function test results, and the number of exacerbations. Multivariable analysis did not reveal a statistical correlation between these parameters and symptomatic sleep disturbance in COPD patients. We found no association between symptomatic sleep disturbance and age, which could possibly be due to the greater mean age of the patients with and without symptomatic sleep disturbances [15]. Verberne *et al*. [16] also found no association between an overweight status and sleep disturbance in mild-to-moderate COPD patients. However, further investigation of the associations of these factors among severe COPD patients would be worthwhile. Furthermore, 95% of the population in the current study smoked; therefore, evaluating the association of smoking with symptomatic sleep disturbances was difficult in this study.

In the multivariable analysis (Table 2), we found that the CAT score was an independent factor associated with symptomatic sleep disturbances. Chang *et al*. concluded that the CAT score is a good predictor of poor sleep quality [14]. Moreover, the CAT score is also good for assessing the presence of insomnia in COPD patients [17]. All of these data support the use

Table 2. Logistic Regression Analysis of Patient Characteristics Associated with Symptomatic Sleep Disturbances

	Univariate analysis		Multivariable analysis	
	OR	95% CI	OR	95% CI
Age, years (mean ± SD)				
< 60	Ref.	--	Ref.	--
60-69	0.5	0.1-1.8	0.3	0.1-2.0
≥ 70	0.3	0.1-0.9	0.1	< 0.1-1.0
Sex				
Male	Ref.	--	Ref.	--
Female	2.6	0.4-18.7	11.7	0.8-181.0
BMI, kg/m^2 (mean ± SD)				
< 24	Ref.	--	Ref.	--
≥ 24	0.6	0.3-1.3	0.6	0.2-1.6
Smoker				
No	Ref.	--	Ref.	--
Yes	0.5	0.1-1.9	2.4	0.3-19.8
Alcohol use				
No	Ref.	--	Ref.	--
Yes	1.3	0.6-2.9	2.7	0.9-8.2
Duration of COPD, years (mean ± SD)	1.0	1.0-1.1	1.0	1.0-1.1
2007 GOLD classification				
Stage 1	< 0.1	< 0.1-> 999.9	< 0.1	< 0.1-> 999.9
Stage 2	0.2	0.1-0.8	< 0.1	< 0.1-0.5
Stage 3	0.4	0.1-1.6	0.1	< 0.1-0.9
Stage 4	Ref.	--	Ref.	--
Comorbidities				
Diabetes	0.9	0.3-2.6	2.0	0.4-11.6
Hypertension	0.4	0.2-0.9	0.4	0.1-1.1
Hyperlipidemia	0.4	0.1-1.8	0.5	0.1-3.5
Heart failure	0.7	0.1-3.5	0.3	< 0.1-2.6
Chronic liver diseases	0.6	0.1-3.0	2.3	0.2-26.7
FVC, predicted %	1.0	0.9-1.0	1.1	0.9-1.1
FEV_1, predicted %	1.0	0.9-1.0	1.0	0.9-1.1
CAT	1.1	1.0-1.1	1.1	1.1-1.2
AE in the previous 3 months, times				
0	Ref.	--	Ref.	--
≥1	2.6	1.2-5.4	2.9	0.9-9.1

Note: The association between patient characteristics and symptomatic sleep disturbances was calculated using a logistic regression model.
AE, acute exacerbation; BMI, body mass index; CAT, COPD assessment test; FVC, forced vital capacity; FEV_1, forced expiratory volume in the first second; GOLD, Global Initiatives for Chronic Obstructive Lung Disease; SD, standard deviation

of the CAT questionnaire to better detect COPD patients with sleep disturbance problems. The CAT is a quick, simple assessment tool that can help clinicians monitor and screen COPD patients with disturbed sleep, so as to improve clinical practice.

A high prevalence of sleep disturbance correlates with a worsening disease-related quality of life status and frequent AE events among COPD patients [4-6]. Sleep disturbance can longitudinally predict COPD exacerbations, respiratory-related emergency room utilization, and poor survival [6]. This information helps us realize the importance of early clinical intervention for COPD-associated sleep disturbance symptoms. Calverley *et al*. reported that the use of tiotropium among COPD patients with sleep disturbances reduced the nighttime awakening score and the usage of rescue medication [18]. Lan *et al*. observed that pulmonary rehabilitation improves COPD patients' exercise capacity and health-related quality of life [19].

Some limitations in this study should be acknowledged. First, the study enrolled a smaller patient cohort. Despite the fact that the FEV1 predicted value was significantly lower in the patients with symptomatic sleep disturbances in the univariate analysis, multivariable analysis did not show a statistical significance related to disturbed sleep. That could be due to some unknown confounding factors. Second, the mean BMI of our subjects was lower than 24. Therefore, they were not suitable for analyzing the correlation between BMI and sleep disturbance among COPD patients. Despite these limitations, this study provides data regarding a good predictor of symptomatic sleep disturbance – the CAT score – among COPD patients in Taiwan.

Conclusions

Our data indicate that the CAT score is a good predictor of symptomatic sleep disturbance for COPD patients in moderate and severe stages. The CAT score assessment provides better detection of symptomatic sleep disturbances, which can help with providing suitable clinical management and practice.

Acknowledgment

The authors thank Ms. Chiu-Wan Liu for her considerable assistance in the collection of data.

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分析 COPD 患者症狀性睡眠障礙相關之病人特徵

蔡尚峯　許淑美 *　蔡青芳 *　林明憲　陳煒　陳弈仁

前言：睡眠障礙的特點是入睡困難，睡眠中斷，醒來後感覺不清醒可能會影響患者其生活品質及存活率。咳嗽和呼吸急促是慢性肺阻塞患者最常見之症狀，而症狀性睡眠障礙未被明確定義。此研究在於探討台灣 COPD 患者之症狀性睡眠障礙相關之病人特徵。

方法：此為 2011-2012 年間進行之橫斷面研究，成功招募 180 名 40 歲以上之慢性肺阻塞患者，其皆填寫是否因咳嗽或呼吸困難而產生睡眠障礙之問卷。分析參數包括參與者之人口學變項、急性發作次數、合併症、慢性肺阻塞評估量表（CAT）與肺功能。

結果：患者之平均年齡和身體質量指數（BMI）分別為 71.7 歲和 22.8 公斤 / 平方公尺。症狀性睡眠障礙之罹患率為 28.9%。症狀性睡眠障礙患者之 CAT 分數與急性發作率顯著高於無症狀性睡眠障礙患者（$p < 0.05$）。多變量分析顯示 CAT 分數為與症狀性睡眠障礙具顯著性相關之獨立因子（OR，1.1；95% 信賴區間，1.1-1.2）。

結論：COPD 患者之症狀性睡眠障礙罹患率為 28.9%，CAT 評分與 COPD 患者自我報告的症狀性睡眠障礙相關，可作為症狀性睡眠障礙的預測因子。*(胸腔醫學 **2019; 34: 139-147**)*

關鍵詞：慢性肺阻塞（COPD），睡眠障礙，慢性肺阻塞評估量表（CAT）

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Nonintubated Thoracoscopic Bullectomy and Pleurodesis for Spontaneous Pneumothorax in a Patient with Duchenne Muscular Dystrophy: A Case Report

Wan-Ting Hung, Po-Ni Hsiao*, Ke-Cheng Chen

Thoracoscopic surgery without tracheal intubation for a patient with Duchenne muscular dystrophy (DMD) has not been reported. We describe a man with DMD who underwent thoracoscopic bullectomy and pleurodesis using a nonintubated anesthetic technique of internal intercostal nerve block, vagal block, and targeted sedation for recurrent spontaneous pneumothorax. The successful results with this patient suggest that nonintubated thoracoscopic bullectomy and pleurodesis is technically feasible and safe for selected patients with DMD. ***(Thorac Med 2019; 34: 148-154)***

Key words: Duchenne muscular dystrophy, nonintubated video-assisted thoracic surgery, pneumothorax

Introduction

The use of nonintubated video-assisted thoracoscopic surgery (VATS) has led to a faster postoperative recovery and a lower complication rate compared to its counterpart of intubated general anesthesia [1]. The use of nonintubated VATS with patients at a high risk when undergoing general anesthesia is seldom reported. Here, we report a patient with Duchenne muscular dystrophy (DMD) that underwent nonintubated thoracoscopic bullectomy and pleurodesis for spontaneous pneumothorax.

Case Report

A 27-year-old, 59.5-kg, 170-cm tall male nonsmoker was referred to our thoracic surgeon for right-side recurrent spontaneous pneumothorax. He was diagnosed with DMD when he was 8 years old, and has been wheelchair-bound because of muscle weakness since he was 9 years old. He was also diagnosed with obstructive sleep apnea 2 years ago and has required night time bi-level positive airway pressure (BiPAP) since then. A pulmonary function test showed a forced vital capacity (FVC) of 1.74 L (37.7% of predicted) and forced expiratory volume in 1 second (FEV_1) of 1.55 L (37.6% of

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predicted), and FEV_1/FVC of 89.1%. He also suffered from moderate mitral regurgitation and DMD-related cardiomyopathy, presenting with severely reduced left ventricular systolic function (left ventricular ejection fraction = 29%).

Prior to this presentation, he had had progressive shortness of breath and general malaise for 2 months. Chest roentgenogram revealed right pneumothorax, and chest computed tomography showed bullae formation at the right upper lobe (RUL) apex and right lower lobe (RLL) base (Figure 1). We considered conservative treatment first because of the high risk of general anesthesia for surgical intervention, so a pigtail catheter was inserted for air drainage. Eleven days later, the drain was successfully removed. Two months later, however, the right pneumothorax recurred (Figure 2). A pigtail catheter was inserted again, but air leakage persisted for days this time. After discussion of the risks and benefits of surgical intervention with the anesthesiologist and surgeon, the patient opted for nonintubated anesthesia for thoracoscopic surgery.

The patient was premedicated with intravenous 50 mg ketamine, 2 mg midazolam, 25 μg fentanyl, and 0.2 mg glycopyrrolate. A bispectral index sensor (BIS Quatro, Aspect Medical System, Norwood, MA, USA) was applied to the forehead of the patient to monitor the level of consciousness. He was then sedated with intravenous propofol (Fresfol 1%, Fresenius Kabi GmbH, Graz, Austria) using a target-controlled infusion method (Injectomat® TIVA Agilia, Fresenius Kabi GmbH, Graz, Austria). During the procedure, the electrocardiogram, arterial blood pressure, blood oxygen saturation, end-tidal carbon dioxide, and bispectral index were monitored while the patient breathed oxygen spontaneously through a high-flow nasal cannula.

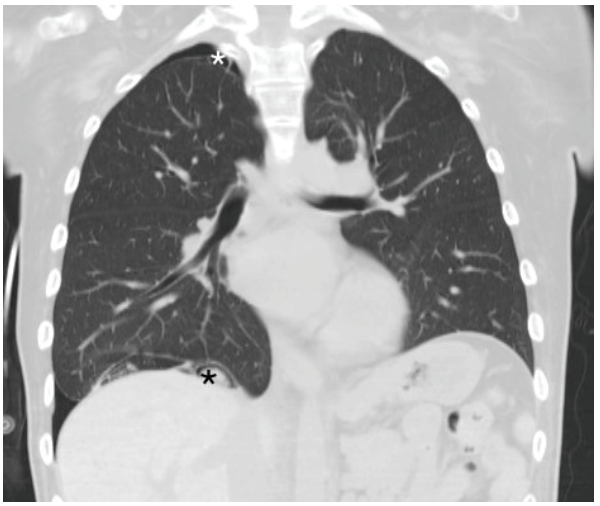

Fig. 1. Preoperative chest computed tomography showed evident bullae (*) at the right upper lobe apex and right lower lobe base.

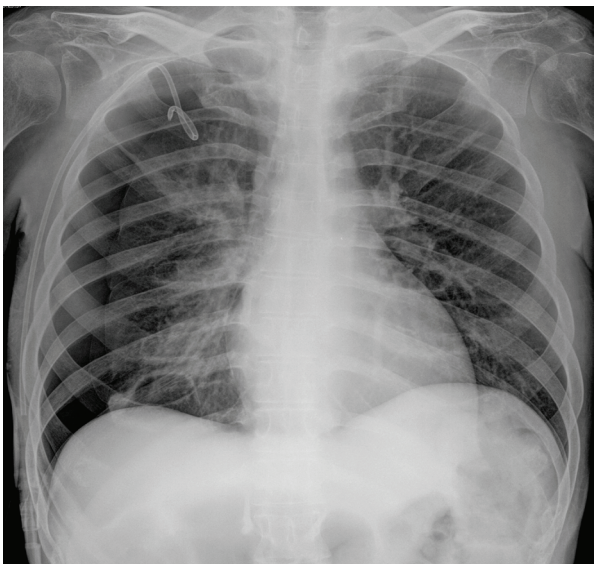

Fig. 2. Chest roentgenogram of recurrent right-side pneumothorax; a pigtail was inserted.

The patient was placed in the left lateral decubitus position, and 3 skin incisions were made. An iatrogenic pneumothorax was made after creating incisions through the chest wall for thoracoscopy, and the lung collapsed gradually. A 5-mm, 30° end-viewing flexible scope

was introduced through the camera port. Blockade of internal intercostal and vagus nerves for pain control and cough suppression was produced by infiltration of 0.25% bupivacaine, as described previously [2]. The pleural adhesion was released with electrocautery. The RUL and RLL bullae were identified and resected with endostaplers. Meanwhile, we applied a vicryl absorbable mesh at the apical lung surface, and performed mechanical abrasion of the pleura for pleurodesis. The hemodynamic status was stable, and oxygen saturation was maintained at 99% to 100%. The end-tidal carbon dioxide level was within normal limits during and after the operation. The total operative time was 67 minutes. After the operation, the patient was transferred to the surgical intensive care unit for observation. Postoperative chest roentgenogram showed complete expansion of the right lung (Figure 3). The pathology report was compatible with bullae of the RUL and RLL. The chest tube was removed on postoperative day 3, and the patient was discharged without incident on postoperative day 4. He was followed for 14 months after the operation, and the plain x-ray film showed good expansion of the right lung. No more recurrence was observed.

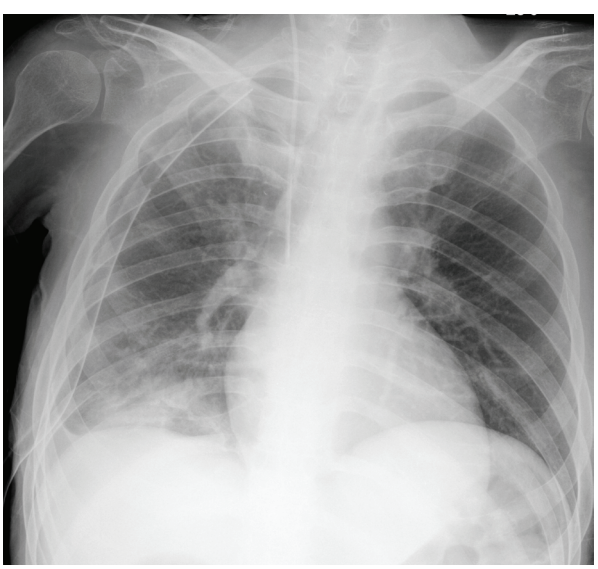

Fig. 3. Chest roentgenogram immediately after operation showed complete lung expansion.

Discussion

Duchenne muscular dystrophy is an X-linked disease affecting primarily skeletal and cardiac muscle. Progressive muscular damage and degeneration occurs in people with DMD, resulting in muscular weakness, associated motor delays, loss of ambulation, respiratory impairment, and cardiomyopathy [3]. Proximal leg weakness makes most patients wheelchair-bound by age 10, and pulmonary function begins to deteriorate between 9 and 11 years of age [4]. Because of advances in the management of DMD, life expectancy has increased and the patient's need to undergo invasive procedures or operations in the future has increased, as well.

Primary spontaneous pneumothorax is a common disease, with a reported incidence of 18-28 cases/100,000 persons per annum for men and 1.2-6 cases/100,000 persons for women [5]. The incidence of pneumothorax among patients with DMD is reported to be even higher (18%) [6]. For those requiring noninvasive positive pressure ventilation, such as our patient, care should be taken with regard to the possibility of pneumothorax occurring. When it occurs, prompt management is necessary to avoid further pulmonary insufficiency. Oxygen therapy and small-bore chest drain comprise the first-line management for pneumothorax. In case of a persistent air leak, surgical intervention should be considered [7]. Chest drainage with a Heimlich valve is also an option to be used over a long term in cases in which air-

leakage is persistent and surgical treatment is excluded, allowing outpatient management for these patients. However, the patient is under a great risk of developing tension pneumothorax if the valve does not function properly or the patient is receiving positive pressure ventilation. The risk of infection of the pleural space is also higher because of the prolonged use of chest tube, and the risk of pneumothorax recurrence is also high [8]. In our case, we could re-expand the patient's lung by simple drainage at the first onset of pneumothorax. But the second episode was refractory to chest drainage. Surgical procedures are more effective for controlling recurrent pneumothorax, and the rate of recurrence is far less than with simple medical-chemical pleurodesis. Therefore, a VATS bullectomy and pleurodesis were preferred for this patient.

Patients with DMD are especially vulnerable to the adverse effects of general anesthesia and procedural sedation, so careful evaluation and adjustment for anesthesia is required. The use of depolarizing muscle relaxants such as succinylcholine is absolutely contraindicated because of the risk of rhabdomyolysis, hyperkalemia, and cardiac arrest [9]. Inhalational anesthetics are associated with the risk of malignant hyperthermia-like reactions in persons with DMD, with the potential for hyperkalemia and sudden death from cardiac arrest [10]. The consensus of the American College of Chest Physicians on management of patients with DMD undergoing general anesthesia or procedural sedation suggests the use of a total IV anesthesia technique for induction and maintenance of general anesthesia. Respiratory support during maintenance of general anesthesia is also of concern [11]. Tracheal intubation with single-lung ventilation traditionally is considered essential for thoracoscopic surgery. To reduce the adverse effects of tracheal intubation and general anesthesia, a nonintubated technique for VATS has been developed recently. Previous experience with the use of this technique in various procedures, including lung volume reduction surgery, pneumothorax, and lung resection [12], has been successful. Nonintubated VATS is also considered a safe therapeutic option in the treatment of primary or secondary spontaneous pneumothorax [13]. However, the use of nonintubated VATS with DMD patients with spontaneous pneumothorax has not been reported yet. The benefits of the nonintubated approach, including faster postoperative recovery, fewer intubation-related complications, prevention of ventilator-related lung injury, avoidance of muscle relaxant use, and minimization of anesthetic side effects [14], may fit the anesthetic needs of patients with DMD. The sedation and analgesia can be done with intravenous propofol infusion and local anesthesia such as xylocaine and bupivacaine only, and the need for muscle relaxants and inhalational anesthetics can be avoided.

Hypoventilation is a concern when using nonintubated VATS. A previous study has shown that impaired respiratory function does not preclude the use of the nonintubated technique, and the level of hypercapnia is tolerable [15]. We used a high-flow nasal cannula (HFNC) for respiratory support with our patient, which improved oxygenation and tachypnea [16], decreased dead space in the upper airway, and provided little positive airway pressure support [17]. Even though the patient required nighttime BiPAP use, during the operation his respiratory pattern was smooth, and the oxygenation and end-tidal carbon dioxide level were within normal range, which may be attributed to the

HFNC support. For patients with compromised lung function, some authors suggest simulating the respiratory condition of the decreased vital capacity and $PaCO_2$ preoperatively; an SpO_2 above 93% and unchanged blood pressure and heart rate after 5 minutes are good signs [13].

Another concern regarding the nonintubated approach is the conditions requiring conversion to tracheal intubation. Our earlier experience revealed that the conditions leading to conversion in lung resection surgery include significant mediastinal movement, persistent hypoxemia, dense pleural adhesions, ineffective epidural anesthesia, bleeding, and tachypnea [12]. Therefore, a simple wedge resection without anatomical vascular dissection and mediastinal dissection is a preferred procedure for the high-risk patient. The even lung collapse on the chest roentgenogram implied that the patient may have had no or just a few localized pleural adhesions. As we expected, the exposure of the target apical bullae was good without evident pleural adhesion, and bullectomy and apical pleurodesis could be performed smoothly. However, if conversion to tracheal intubation is indicated during operation, the procedure may be similar to conversion during a lobectomy. We would insert a single-lumen endotracheal tube with bronchial blocker under the guidance of a bronchoscope, without changing the patient's position, and care should be taken not to use depolarizing muscle relaxants and inhalational anesthetics.

In conclusion, our successful experience showed that nonintubated thoracoscopic bullectomy and pleurodesis can be performed safely in a patient with DMD. The benefits of the nonintubated approach include avoiding the use of depolarizing muscle relaxants and inhalational anesthetics, and faster postoperative recovery. Further studies are required to validate the indications, safety, and efficacy of various nonintubated VATS procedures in patients with a disease involving the respiratory muscles, such as DMD.

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以免插管胸腔鏡肺泡切除術及肋膜沾黏術治療一名氣胸之裘馨氏肌肉失養症病人：病例報告

洪琬婷　蕭柏妮 *　陳克誠

以免插管方式為裘馨氏肌肉失養症病人進行胸腔鏡手術尚未被報告過。在此，我們報告一名裘馨氏肌肉失養症之男性，接受免插管麻醉方式，包括腔內肋間神經阻斷、迷走神經阻斷、及目標導向鎮靜，進行胸腔鏡肺泡切除術及肋膜沾黏術以治療復發自發性氣胸。此成功的案例經驗表示，對裘馨氏肌肉失養症的病人，免插管胸腔鏡肺泡切除術及肋膜沾黏術是技術上可行且安全的手術方式。*(胸腔醫學 **2019; 34: 148-154**)*

關鍵詞：裘馨氏肌肉失養症，免插管胸腔鏡手術，氣胸

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Tuberculous Peritonitis Complicated with Bowel Perforation and Intestinal Obstruction: A Case Report

Yuan-Fu Huang*, Yu-Wung Yeh*,**

Abdominal tuberculosis (TB) is not an uncommon presentation, although severe forms of the disease are rather rare. Young physicians may not be familiar with the presentations of this disease entity. Unfortunately, the proportion of extrapulmonary TB is on the rise, which presents challenges to both the diagnosis and management of advanced abdominal TB. We herein present a case of severe abdominal TB. While infrequently encountered, early identification and diagnosis remain crucial to a favorable outcome. ***(Thorac Med 2019; 34: 155-159)***

Key words: abdominal tuberculosis, tuberculous peritonitis, intestinal obstruction, intestinal perforation

Introduction

Tuberculosis (TB) can involve many organs in the body, including any intra-abdominal organ and the peritoneum. The most common abdominal cases involve the peritoneum, intestine, and/or liver. The incidence rate of pulmonary TB has been steadily decreasing globally, but an increasing proportion of extrapulmonary TB has been reported [1]. This finding may partially be a consequence of the increasing prevalence of acquired immunodeficiency syndrome [2]. Abdominal TB accounts for about 5% of overall extrapulmonary TB. The proportion of extrapulmonary TB among TB diseases increased from 16.4% to 22.4% in Europe during the period 2002-2011 [2]. The diagnosis and management of abdominal TB is an on-going challenge for physicians worldwide. Diagnosis is usually made late due to nonspecific clinical presentations and late use of more advanced or invasive diagnostic tools. Laparoscopic biopsy is often necessary to confirm the diagnosis. If diagnosed in the early stage, abdominal TB is generally responsive to medical treatment.

The use of corticosteroids for the treatment of abdominal TB is controversial. Some have proposed that it may reduce the risk of adhesions, which may later cause intestinal obstruction [3]. Surgery is often necessary for patients with complications, such as perforation, abscess, fistula, bleeding, and/or high-grade obstruction (the most common complication). We herein report a patient with widespread gastrointestinal and peritoneal TB.

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Case Report

A 63-year-old female had a medical history of stage 4 chronic kidney disease and hypertension. The patient presented to the emergency room with abdominal cramps and watery diarrhea. She reported having poor appetite and poor oral intake for an unspecified period of time. On initial examination she appeared malnourished and dehydrated. Computed tomography (CT) scan revealed pneumoperitoneum, skipped intramural air from the ascending colon to the terminal ileum, thickened omentum with numerous tiny nodules, and multifocal peribronchial nodular lesions and patchy consolidations in the bilateral upper lungs. The patient underwent exploratory laparotomy for suspected hollow organ perforation; however, the site of perforation could not be determined. Intraoperative findings included a small amount of turbid ascites, multiple small white nodules all over the small bowel and caking of the omentum with a whitish appearance (Figure 1). Sputum cultures grew *Mycobacterium tuberculosis*, which was sensitive to all 4 first-line anti-TB drugs. Histopathologic examination of the omentum revealed foci of caseous necrosis surrounded by epithelioid histiocytes and Langhan's giant cells (Figure 2). Ziehl-Neelsen staining was negative. The patient was started on treatment with isoniazid, rifampicin, pyrazinamide, and ethambutol. HIV serological testing was negative. HBsAg and anti-HCV antibodies were also negative. Microscopic examination of repeated sputum smears revealed no more acid-fast bacilli after 1 month of the abovementioned treatment. The patient then started hemodialysis for declining renal function. Her hospital course was complicated by difficulty in enteral feeding as she frequently experienced abdomen pain and vomiting. Follow-up CT scanning initially revealed marked improvement of the intra-abdominal and pulmonary lesions after 1 month of anti-TB treatment. However, 2 months later, another CT scan showed deterioration of her intra-abdominal lesions. A small bowel series showed no leakage or obstruction. Second-line IV streptomycin and moxifloxacin were added, but the clinical response was poor. The patient declined repeated laparotomy. The family requested conservative management and signed a

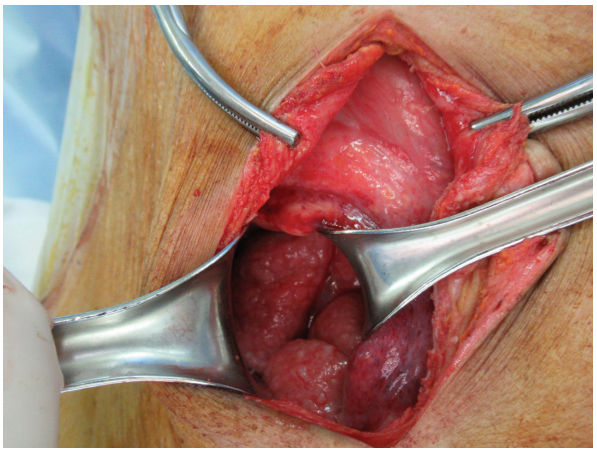

Fig. 1. Operative finding: Multiple fused nodules at the small bowel and thickened solid omentum with a whitish appearance.

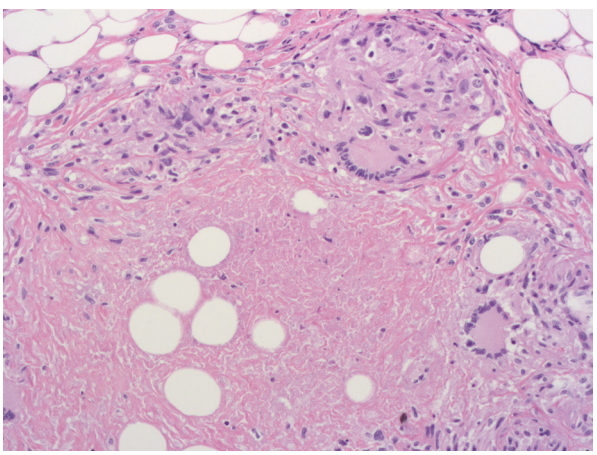

Fig. 2. Histology of an omentum specimen showed caseous necrosis surrounded by epithelioid histiocytes and Langhan's giant cells.

do-not-resuscitate order. Hemodynamics were difficult to maintain after deterioration of her abdominal condition, and the patient died after 3 months of hospitalization.

Discussion

Alcoholic liver disease, cirrhosis, peritoneal dialysis, and diabetes mellitus are all risk factors for abdominal TB [4]. Abdominal TB may have presentations similar to Crohn's disease and intra-abdominal malignancy, including lymphoma [5].

Abdominal TB may result from swallowing infected sputum in patients with advanced pulmonary disease, from hematogenous spread, or from direct spread from adjacent organs or lymph nodes. Peritoneal and intestinal TB can be caused by seeding of bowel mucosal lymphoid tissue, which then undergoes granulomatous change [6]. Mesenteric vascular granulomatous inflammation can lead to mucosa ischemia and ultimately intestinal perforation [7].

Although clinical manifestation, lab data, previous culture results and images may raise a suspicion of abdominal TB, definitive diagnosis should be made based on ascites culture or biopsy via laparoscopy/laparotomy and/or endoscopy. Peritoneal biopsy by laparoscopy is important to rule out lymphoma or carcinomatosis [8-9]. A less invasive procedure with echo-guided biopsy is also helpful since such patients are often poor candidates for surgery because of multiple co-morbidities and poor nutritional status [10].

For most patients with abdominal TB, 6 months of anti-TB therapy is no less effective than 9 months of treatment [11]. Relapse and clinical cure rates are similar for 6 and 9 months of therapy in cases of gastrointestinal tract and peritoneal TB [12]. As abdominal TB may respond well to medical anti-TB therapy, surgery should be reserved for severe complications including bowel perforation, fistula, and severe obstruction. Three types of surgery have been performed for abdominal TB: bypass of involved segments of the bowel, radical resection, and strictureplasty [13].

Although the use of corticosteroids remains controversial for abdominal TB, its main benefit seems to be in reducing abdominal adhesion [3]. In cases similar to that of our patient, enteral feeding may be facilitated if adhesions can be improved through the use of corticosteroids. Repeated surgery may also be beneficial for the same reason. Second line anti-TB drugs can be employed as rescue therapy, as well [14].

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結核性腹膜炎合併腸穿孔和腸阻塞：病例報告

黃元甫 *　葉育雯 *,**

腹部結核（TB）並不罕見。然而，嚴重的疾病形式相當罕見。年輕的醫生可能不熟悉此種疾病的臨床表現。不幸的是，肺外結核的比例正在上升，這對晚期腹部結核病的診斷和治療帶來了挑戰。我們在此提出一例嚴重的腹部結核病。雖然很少遇到，但早期識別和診斷對於有利結果仍然至關重要。*(胸腔醫學 **2019; 34: 155-159**)*

關鍵詞：腹部結核，腹膜結核，腸阻塞，腸穿孔

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Kirschner Wire Migration from the Clavicle into the Left Lung Parenchyma after Trauma – A Case Report

Kuan-Liang Chen, Ming-Cheng Tsao*, Xian-Yuan Guo

Kirschner wires (K-wires) and pins are useful tools in the management of shoulder fractures and dislocations. Migration of broken K-wires after trauma is a rare but serious complication. We describe the case of a 73-year-old woman who underwent open reduction internal fixation for a distal clavicle fracture. Following a second trauma, a broken K-wire migrated into the left lung parenchyma and was successfully retrieved via video-assisted thoracoscopic surgery. Avoiding trauma can be helpful in preventing K- wire migration. ***(Thorac Med 2019; 34: 160-165)***

Key words: broken Kirschner wire migration, clavicle fracture, lung parenchyma, trauma

Introduction

Surgical intervention for repair of a shoulder fracture is indicated in conditions such as unstable Group II fractures (Type IIA, Type IIB, and Type V) and open fractures. Though Kirschner wires (K-wires) and pins are not the first choice of treatment, they are useful tools in the management of some fractures and dislocations, especially when the fracture is transverse [1]. However, the K-wires tend to migrate. Their migration into the thoracic cavity after fixation of a clavicle fracture is a rare but serious complication, and can result in lethal cardiovascular events. A wire from the shoulder region would most commonly migrate to the chest wall, with a chance of invasion into the thoracic cavity [2]. We present the case of a 73-year-old woman who underwent open reduction internal fixation for a distal clavicle fracture with subsequent migration of the K-wire into the left lung parenchyma following a second trauma. The wire was successfully retrieved via video-assisted thoracoscopic surgery (VATS).

Case Report

A 73-year-old woman fractured her left distal clavicle in a traffic accident. The radiograph revealed acromioclavicular separation. Open reduction internal fixation with tension band wiring was performed (Figure 1). Magnetic resonance imaging revealed bilateral spondylolysis of the L4 pars interarticularis with grade 2 listhesis, attributed to a previous trauma. After discharge, she had continuous follow-up as an

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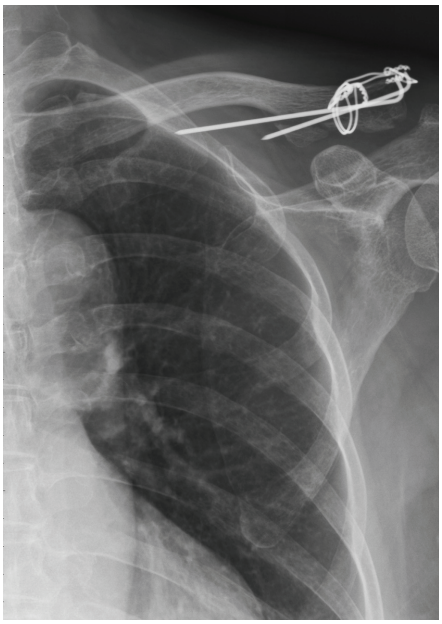

Fig. 1. Radiograph showing internal fixation of the left distal clavicle fracture with acromioclavicular separation using tension band wiring.

outpatient. Three years after the repair of the clavicle, she was involved in a motorcycle accident and subsequently experienced left chest pain that persisted for 1 month. Physical examination revealed local tenderness of the left shoulder and left chest wall. A chest radiograph (posteroanterior view) and computed tomography (CT) images of the chest showed retention of a linear foreign body in the left apex of the lung (Figure 2) that was suspected to be a migrated broken K-wire. The object had penetrated the left apical zone of the lung with no evidence of pneumothorax; the mediastinum showed no evidence of an abnormal mass or enlarged lymph nodes. The diaphragmatic domes, subdiaphragmatic spaces, and visible portion of the liver were normal in appearance. The implant was removed from the left clavicle, and the foreign body was extracted by wedge resection of the left upper lobe using VATS. Pneumonolysis and left tube thoracostomy were also performed, and no remaining foreign bodies were detected in the postoperative chest radiograph (Figure 3). The patient had no further symptoms or hemopneumothorax, and was discharged 4 days after surgery. After detailed explanation to the patient, informed consent was obtained from her legal guardian (due to illiteracy of the patient) to publish the information, including her photographs.

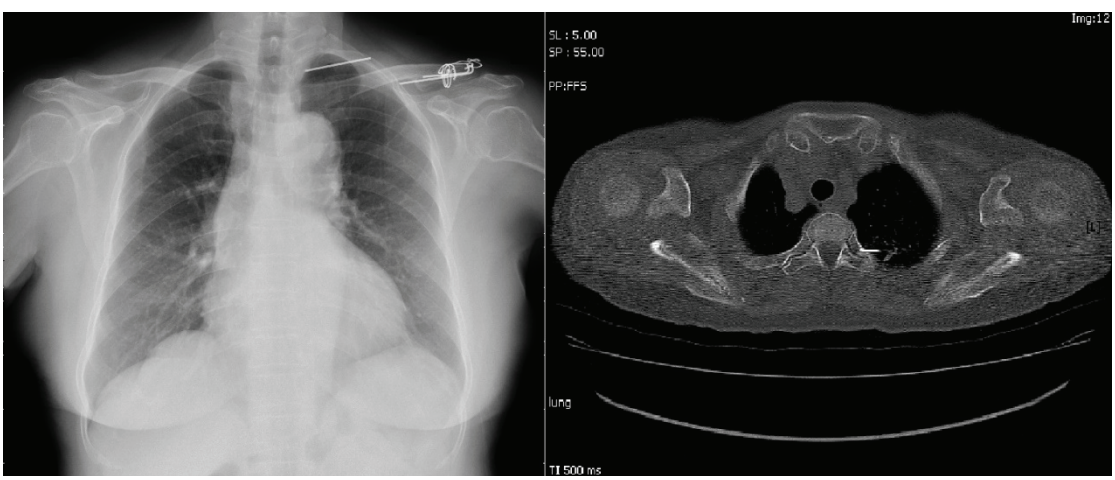

Fig. 2. After a second trauma that resulted in chest pain, the chest radiograph (posteroanterior view) and chest computed tomography images showed retention of a linear foreign body in the left apex of the lung.

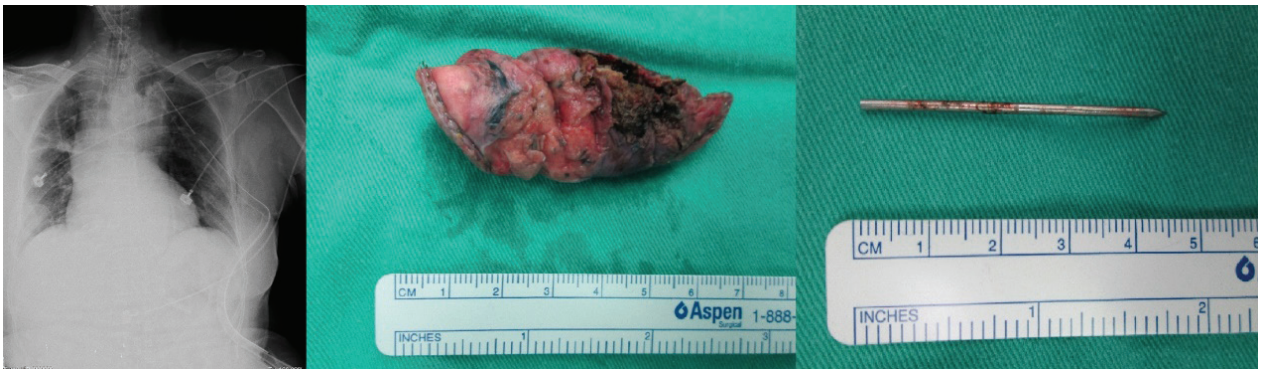

Fig. 3. Radiograph following the second surgery, resected lung tissue, and the K-wire after removal (left to right).

Discussion

Clavicle fractures are common and most orthopedic surgeons adopt a conservative approach. However, not all fractures of this type will bond appropriately using conservative measures [3]. It has been observed that segmental and problematic fractures may require surgery [4].

Symptoms

Zacharia et al reported chest pain and shortness of breath when an implant migrated to the thoracic cavity [5]. Sarper *et al* reported that back pain could be another symptom [6].

Detection

Diagnosis requires a thorough physical examination, complete neurologic examination, and chest imaging using radiographs and CT [2]. Sternotomy, thoracotomy, and video-assisted thoracoscopy are beneficial in the identification of a foreign body [7]. The time between implantation and detection of a migrated orthopedic implant varies widely: 56% of wires that migrated were observed within 3 months, and 74% were detected within 8 months of implant.

Complications

Migration of implants used for internal fixation within the chest – and particularly those from the shoulder – is a rare but known complication [8]. There are reports in the literature about pins and wires that migrated from the shoulder region to the spinal canal, trachea, spleen, pulmonary artery, heart, mediastinum, lung, subclavian artery, and ascending and abdominal aortas [2].

Mortality

Tan *et al* reported 11 deaths from catastrophic cardiovascular events caused by the migration of orthopedic wires; only 1 case was in the lung. The patient died due to multiple organ failure [9].

Mechanisms of migration

One of the mechanisms for the migration of K-wires is loosening of the implant caused by movement of the shoulder girdle over the pin ends. Such movement may be attributed to muscle action [8,10]. Short-term migration of K-wires in unstable orthopedic implants may occur due to excessive range of motion of the shoulder joint, and may be exacerbated by respiratory motion, intrathoracic depression, and

gravity [11]. K-wire migration may also be related to inadequate engagement of the orthopedic wire into the bone cortex [12]. Long-term migration seems to be due to muscle movement, inducing migration along the arteriovenous circuit in contact with the muscles, and under the effect of gravity, thereby shifting the implant to other anatomic regions [13]. Therefore, trauma to a surgical site could cause K-wire migration.

Our experience

In our case, the K-wire was used for fixation of a fracture of the left clavicle. After a second injury to the shoulder, the wire migrated into the chest cavity. Our patient developed left chest pain as a result. Migration of the K-wire was determined on radiography and CT chest imaging. There was no hemothorax or hemomediastinum, but a left tube thoracostomy was done for safety reasons. After removal of the clavicular implant and retrieval of the intrathoracic K-wire by VATS, there were no further complications, and the chest tube was removed.

Management

The free end of the K-wire should be curved at its extremity to prevent its migration [11]. Alternatively, threaded pins, such as the Schanz screw, have an increased ability to remain anchored in the site and prevent migration [14].

Thoracoscopic removal of intrathoracic foreign bodies can be very safe if the object can be withdrawn through a port site, if it does not go beyond the mediastinum, and if the patient can tolerate single-lung ventilation. Otherwise, thoracotomy and sternotomy are safe and could be used to remove migrated wires. Sternotomy may be considered more appropriate in the presence of injury to the heart or great vessels [15].

Conclusion

As the migration of wires and pins following orthopedic surgery can cause potentially fatal complications, we should give more consideration to the possibility of percutaneous treatment of shoulder girdle fractures. The number of implants used during surgery should be recorded in the surgical report. The free end of the wire should be curved at its extremity. The patient should have routine follow-up and revisit the hospital if any associated symptoms and/or signs appear. If it is determined that a wire has migrated, it should be removed immediately. Considering the excessive range of motion of the shoulder joint and muscle movement related to implant migration, the K-wire should be removed as soon as the old fracture is stable. Finally, if the migrated K-wire invades the thoracic cavity, then, for safety reasons, VATS should be performed without any contraindication. Otherwise, thoracotomy and sternotomy are safe and could be used to remove migrated wires.

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創傷後克氏鋼針自鎖骨移入左側肺部

陳冠良　曹明正 *　郭獻源

克氏鋼針是治療肩關節骨折和脫位的工具。創傷後斷裂的克氏鋼針的移行是一種罕見但嚴重的併發症。我們描述了一名 73 歲女性的病例，她為鎖骨遠端骨折進行了開放性復位併內固定術。在第二次創傷後，其中一根克氏鋼針移入左肺實質，並通過胸腔內視鏡輔助手術成功移除。避免創傷有助於防止克氏針移位。*(胸腔醫學 **2019; 34: 160-165**)*

關鍵詞：克氏鋼針斷裂，鎖骨骨折，肺實質，外傷

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索取抽印本請聯絡：郭獻源醫師，國軍高雄總醫院左營分院　外科部　胸腔外科，高雄市左營區軍校路 553 號

Surgical Enucleation of a Huge Esophageal Schwannoma Causing Dysphagia and Exertional Dyspnea

Wei-Yi Lee, Jiun-Yi Hsia*

Benign esophageal tumors are not common, and most of them are leiomyomas; schwannomas are rarely seen. Symptoms worsen as the tumor increases in size. A preoperative diagnosis is difficult, and the definitive diagnosis is often established by histological features and immunohistochemical stain after surgery. An 82-year-old woman had dysphagia for 2 years and exertional dyspnea for 1 year. She had a huge esophageal submucosal tumor with nearly total obstruction of the middle esophagus and compression of the left main bronchus. Tumor enucleation followed with primary suture of the mucosal defect through a right mini-thoracotomy under video-assistance was performed successfully. To our knowledge, this is the first report of an elderly woman with a huge schwannoma located in the middle esophagus that was successfully treated with surgical enucleation instead of total or subtotal esophagectomy. ***(Thorac Med 2019; 34: 166-171)***

Key words: esophageal schwannoma, dysphagia, dyspnea, enucleation

Introduction

Esophageal schwannoma is a rare submucosal tumor and is usually located in the upper esophagus. Most patients are middle-aged women. We present the case of an elderly woman with a giant schwannoma in the middle esophagus that was treated with surgical enucleation instead of esophagectomy. Mucosal repair with interrupted absorbable sutures is feasible.

Case Presentation

An 82-year-old woman presented with a 2-year history of dysphagia that had progressively worsened. She could tolerate only a liquid diet prior to her presentation. Exertional dyspnea during the most recent year was also noted. Upper gastrointestinal endoscopy revealed a protruding submucosal tumor with mucosal ulceration located 23 to 32 cm from the incisors (Figure 1). Endoscopic ultrasound showed a heterogeneous hypoechoic mass at the submucosal layer of the esophagus, with

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an intact fourth layer of the muscularis propria. Biopsy was done and the report revealed an ulcer. Computed tomography (CT) of the chest showed a huge mass in the middle to lower thoracic esophagus, around 10 cm in size (Figure 2). The heterogeneous mass was compressing the left main bronchus. No regional lymphadenopathy was seen. The barium esophagogram revealed a filling defect at the middle thoracic esophagus with proximal dilation (Figure 3). Bronchoscopy revealed external compression at the membranous portion of the distal trachea

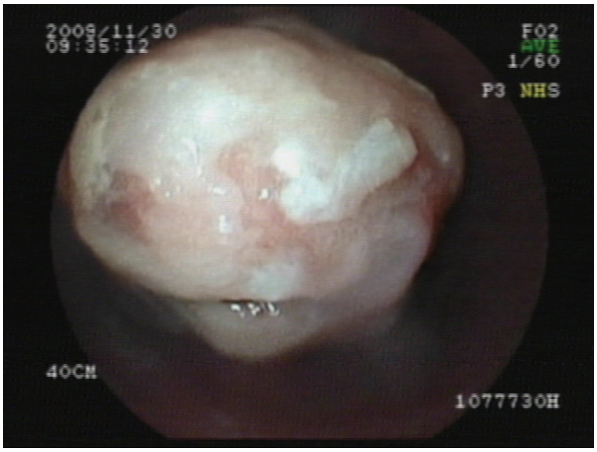

Fig. 1. Upper gastrointestinal panendoscopy revealed a protruding submucosal tumor with nearly obstruction.

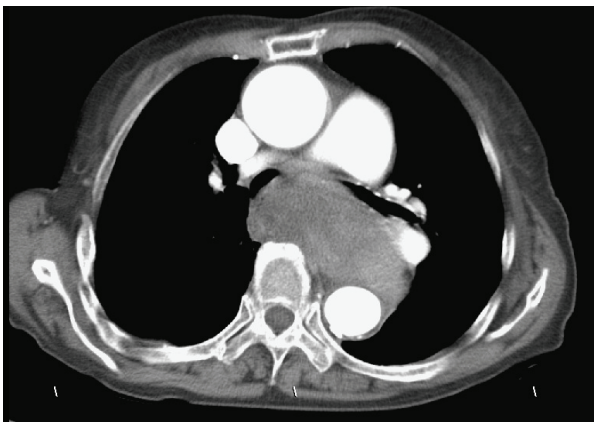

Fig. 2. Chest computed tomography showed a heterogeneous mass in the middle thoracic esophagus with left main bronchus compression.

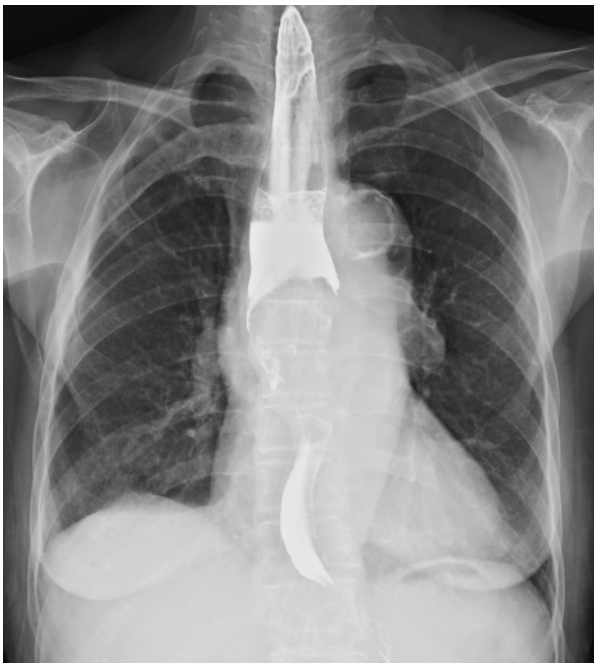

Fig. 3. Esophagogram showed a tumor in the middle thoracic esophagus.

with left deviation. In addition, the orifice of the left main bronchus was torturous, with mild stenosis. The serum tumor markers, including CEA and SCC, were within normal limits.

In consideration of the low incidence rate of malignant esophageal submucosal tumor and the patient's age, we decided to perform tumor enucleation. Thus, the patient underwent a video-assisted right mini-thoracotomy. A well-encapsulated, elastic, firm, and irregularly shaped tumor was found in the muscular layer of the esophageal wall, with a clear margin (Figure 4A, 4B). The frozen section showed a spindle cell tumor, and malignancy was not likely. Enucleation of the tumor was performed, revealing it to be about 10x7x4.5 cm in size. Then, we did several interrupted absorbable sutures for repair of the approximately 10 cm mucosal defect. Pathology of the resected specimen revealed interlacing fascicles of spindle cells. The nuclei

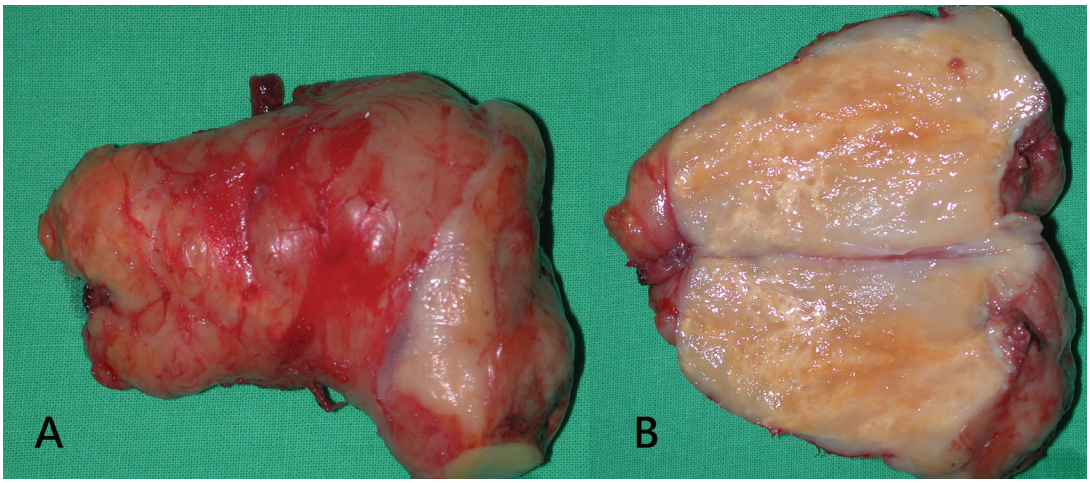

Fig. 4. A, B. A hard, well-defined, and irregular-shaped tumor measuring about 10x7x4.5 cm in size.

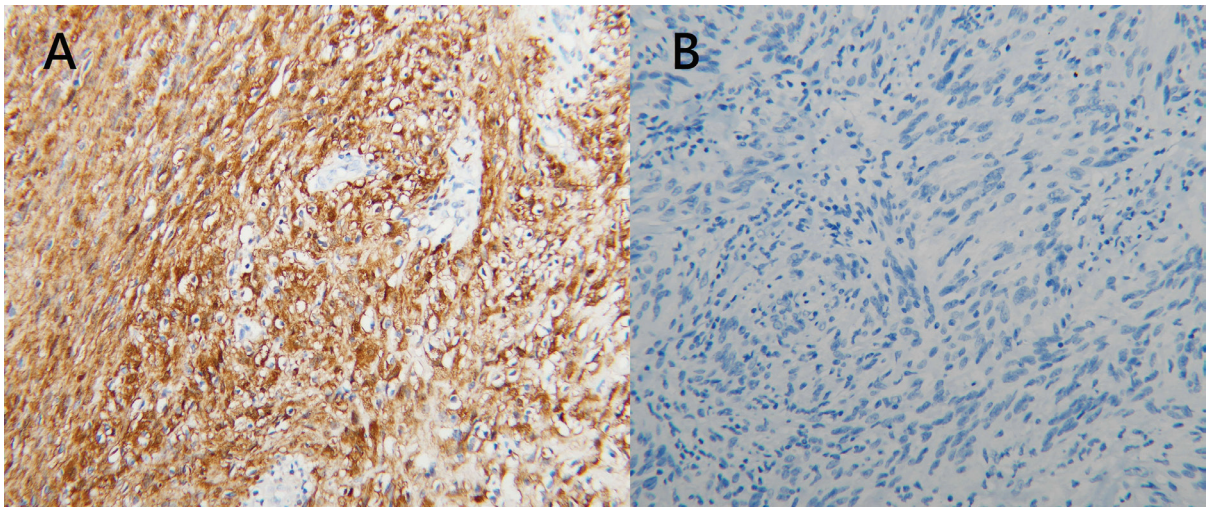

Fig. 5. A. Schwannoma with strong immunoreactivity for S100. B. Schwannoma with a negative stain for desmin.

of the tumor cells varied in size and shape, but the chromatin was distributed uniformly. Very little mitosis was observed. The findings were consistent with an esophageal schwannoma. The diagnosis was confirmed by additional immunohistochemical staining, which was positive for S-100 and negative for desmin, CD34, CD117, and c-kit (Figure 5A, 5B). The patient recovered well after surgery and was discharged 1 week later. During outpatient department follow-up, the patient could tolerate regular food with no difficulty. All the examinations revealed no evidence of tumor recurrence up to 2 years after operation. The patient gave her informed consent regarding the use of her case in a journal article.

Discussion

Only a few cases of esophageal schwannoma have been reported in the medical literature [1-3]. Previous reports found that esophageal

schwannomas were usually located in the upper esophagus, in middle-aged women [4]. They usually originate in the submucosal layer and grow slowly. The most common symptoms are dysphagia and sometimes dyspnea caused by airway compression. In our case, the patient was older and the tumor was located at the middle esophagus. When esophageal submucosal tumors are found, leiomyoma is most commonly suspected, followed by gastrointestinal stromal tumor (GIST), cyst, and lipoma: schwannomas are rare.

Establishing an accurate diagnosis from conventional radiological studies is difficult. However, CT may be helpful. Esophageal schwannoma tends to be an enhanced homogeneous mass; this distinguishes it from a leiomyoma, which shows calcification, and from a leiomyosarcoma, which is more heterogeneous. Barium esophagogram reveals a smooth, polypoid-filled defect, which does not distinguish it. Endoscopic ultrasonography shows a submucosal tumor covered with normal mucosa, which is also non-specific. This technique can guide a fine needle aspiration or histologic needle biopsy, thus providing samples for cytology or histological analysis. However, it is difficult to obtain appropriate tissue due to the location of the tumor beneath the mucosa. A correct diagnosis depends on histopathological and immunohistochemical studies. A histopathological study with hematoxylin and eosin stain reveals a fascicular arrangement of spindle cell and palisading cell nuclei. On immunohistochemical examination, positive for S-100 protein and negative for smooth muscle markers such as actin, desmin, CD117, and CD34 indicate the Schwann cell origin of the tumor. Differentiating schwannoma from GISTs is important because GISTs have a greater malignant potential and require a different treatment strategy. GISTs originate from interstitial cells of Cajal and are positive for c-kit, which is negative for schwannoma. Thus, immunostaining is mandatory to confirm the diagnosis.

In most of the reported literature, management for submucosal tumors is resection, which can be both therapeutic and yield a pathological diagnosis. Thoracotomy with tumor enucleation is usually performed. For tumors less than 2 cm in size, minimally invasive resection by enucleation with video-assisted thoracoscopic surgery (VATS) is possible [5]. For tumors with a high grade on biopsy or greater than 8 cm in size, en bloc esophagectomy with reconstruction is suitable [6-7]. The prognosis of esophageal schwannoma is excellent after surgical intervention. However, a few cases of esophageal schwannoma with malignant potential, lymph node metastasis, or local recurrence have been reported [8-9]. For this reason, all patients with esophageal schwannoma should have long-term follow-up using CT and esophagoscopy. We have summarized and compared the data of the patients who were reported in the above cited literature in Table 1.

Our patient was an elderly woman who suffered from dysphagia and exertional dyspnea due to a huge schwannoma. Esophagectomy is the recommended surgical approach for this kind of huge tumor. However, if the surgical safe margin is adequate and there is no evidence of malignancy by frozen section during operation, tumor enucleation with mucosal repair under a 2-port VATS procedure is applicable.

Table 1. Literature Review of Esophageal Schwannoma Resections

Reference No.	Case	Gender	Age	Tumor maximal length (cm)	Location	Surgical approach	Management
1	1	female	63	7	upper	thoracotomy	enucleation
2	1	female	40	5	upper	sternotomy	enucleation
3	1	female	59	10.9	upper	thoracotomy	subtotal esophagectomy
4	1	female	54	6	upper	abdominocervical approach	subtotal esophagectomy and esophagogastrostomy
6	1	female	55	8	upper	thoracotomy	subtotal esophagectomy and esophagogastrostomy
7	1	female	60	17	upper	unknown	esophagectomy
8	1	female	49	8.2	middle	thoracotomy	enucleation
9	1	male	54	6.4	lower	laparotomy+thoracotomy	esophagectomy

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手術摘除造成吞嚥困難及活動性喘的巨大食道神經鞘瘤

李威億　夏君毅 *

良性食道腫瘤是不常見的，其中最常見的是平滑肌瘤，而神經鞘瘤是相當罕見的，造成的症狀會隨著腫瘤變大而加劇。術前要有確切的診斷是有難度的，通常需要在開刀後，藉由檢體的組織特性和免疫組織化學染色來得到最終診斷。本案例是一位 82 歲女性，有吞嚥困難兩年及活動性喘一年，檢查後發現在食道中段有一巨大的黏膜下腫瘤，造成食道幾乎完全阻塞，左邊主要支氣管也被壓迫到。於是我們為這位病人安排了胸腔鏡輔助下食道腫瘤摘除及黏膜修補手術。經由文獻搜尋，這是第一例成功地以手術摘除巨大中段食道神經鞘瘤，而非全食道或部分食道切除。*(胸腔醫學 **2019; 34: 166-171**)*

關鍵詞：食道神經鞘瘤，吞嚥困難，呼吸困難，手術摘除

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Cyclophosphamide Use in a Young Female with Cryptogenic Organizing Pneumonia and Impending Respiratory Failure: A Case Report

Ho-Sheng Lee*, I-Wei Chang**, Ming-Wei Kao***

A 30-year-old female had productive cough for 1 month, with new fever and dyspnea in the most recent 2 days. Pneumonia was diagnosed, and improved after antibiotic treatment. Recurrent symptoms with severe hypoxia occurred 10 days later, with interstitial infiltration in bilateral lung fields on chest X-ray. There was no response to antibiotics, and the work-up for infection and autoimmune disorders reported negative findings. After strong systemic corticosteroid use, her hypoxia and lung infiltrations improved. The surgical biopsy of the lung revealed organizing pneumonia. Relapse of hypoxia with chylothorax occurred with tapering down of the corticosteroid. Cyclophosphamide was then added. The patient's dyspnea and lung infiltration improved and steroid was discontinued smoothly. Her cryptogenic organizing pneumonia fluctuated when tapering down the dose of cyclophosphamide. Cyclophosphamide was discontinued 2 years later. ***(Thorac Med 2019; 34: 172-177)***

Key words: cryptogenic organizing pneumonia, bronchiolitis obliterans with organizing pneumonia, cyclophosphamide

Introduction

In patients with cough, shortness of breath and pulmonary infiltrations on chest X-ray, pneumonia is often the diagnosis. However, many other diseases need to be ruled out, especially when the patient has poor response to empirical treatment. Here we present a case and hope it can give you some inspiration in clinical practice.

Case Report

A 30-year-old female had productive cough with yellow sputum for 1 month. Fever and shortness of breath were noted during the most recent 2 days. She then went to the emergency room (ER). Her chest X-ray revealed ground-glass interstitial infiltrations at the bilateral lower lung fields (Figure 1). The lab data showed leukocytosis (WBC 12 k/μl). She was admitted to the ward with the diagnosis of atypical pneu-

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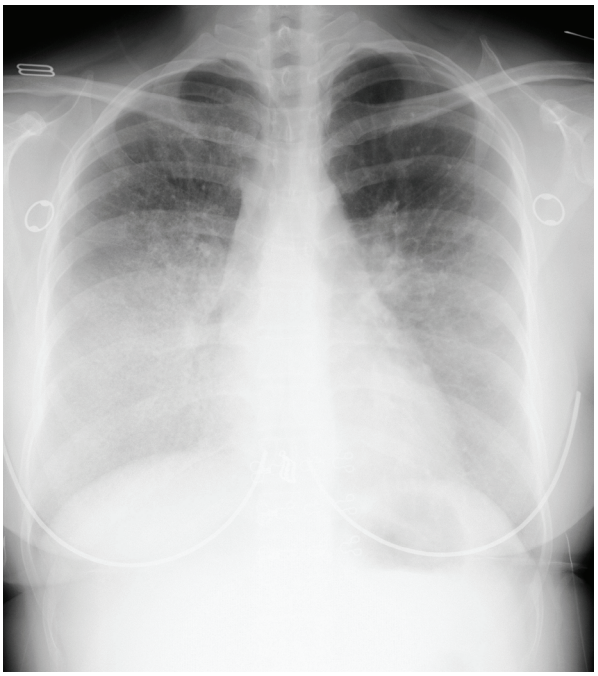

Fig. 1. Ground-glass interstitial infiltrations at bilateral lower lung fields.

monia. The acid-fast stain of the sputum was negative for acid-fast bacilli. Her productive cough and dyspnea improved after levofloxacin treatment for 7 days, and then she was discharged from the hospital.

Ten days later, new onset of low-grade fever was noted. Cough with yellow sputum, chest tightness, and exertional dyspnea were also noted. She went to the ER again, and her SPO_2 was found to be only 90% in room air. Her vital signs showed body temperature of 36.9°C, blood pressure of 130/86 mmHg, tachycardia with a heart rate of 113 beats per minute, and tachypnea with a respiratory rate of 22 breaths per minute. She was fully alert and well-oriented. Inspiratory crackles were heard in the bilateral chest, without wheezing. Lab data showed normal CBC and CRP levels. Chest X-ray showed progression of interstitial infiltrations at the bilateral lower lung fields. Chest high resolution computed tomography showed mixed ground-glass opacities and interlobular septal infiltrations at the right lung zone and basal left lower lobe (Figure 2). At that point, she was hospitalized again.

Ceftazidime, moxifloxacin, and doxycycline were used empirically to cover nosocomial

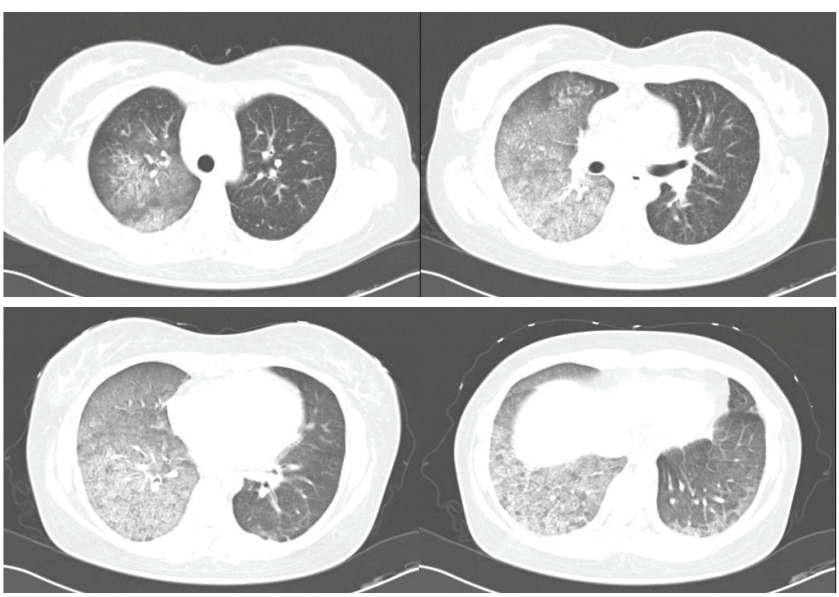

Fig. 2. Mixed ground-glass opacities and interlobular septal infiltrations at the right lung zone and basal left lower lobe.

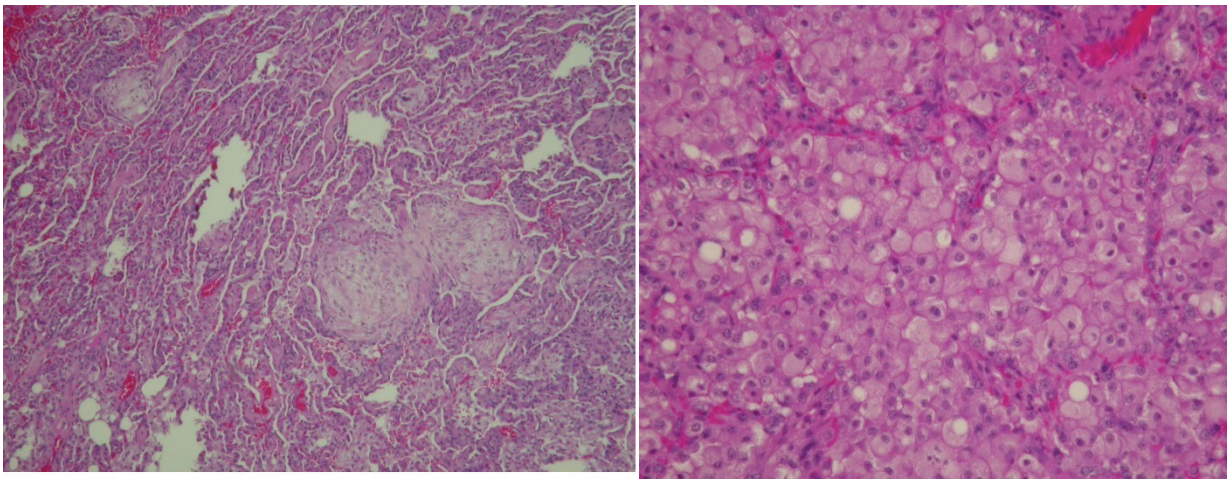

Fig. 3. Microscopic findings of fibrosis of the alveolar wall, lymphocytic infiltration with accumulation of proteinaceous fluid, and aggregation of foamy macrophages in the alveolar space.

and atypical pathogens of pneumonia. Her hypoxia progressed, however, intravenous methylprednisolone 80 mg per day was added for pneumonitis. The follow-up chest X-ray then showed partial improvement. With the response to corticosteroid, interstitial pneumonitis was favored. Bronchoscopy showed swelling of the mucosa at the right bronchial trees with much necrotic material. Bronchial wash fluid cytology was negative for malignancy. Pathology of the transbronchial biopsy from the right lower lobe showed lung and bronchial tissue with some atypical cells, fibrin, and inflammatory cells. We discontinued all antibiotics and arranged surgical wedge resection of the lung for tissue proof. Ceftazidime was used for 14 days, and moxifloxacin and doxycycline for 21 days. Non-intubated single port video-assisted thoracic surgery (VATS) was performed smoothly, and wedge resection of the right lower, middle, and upper lobes was done. Pathology reported cryptogenic organizing pneumonia (COP). Microscopic findings included fibrosis of the alveolar wall, lymphocytic infiltration with accumulation of proteinaceous fluid, and aggregation of foamy macrophages in the alveolar space. Fibroblastic plugs were also noted in the bronchioles, alveolar ducts and alveoli (Figure 3).

Her oxygenation showed improvement. After methylprednisolone use for 14 days, we changed to prednisolone 30 mg per day. She then went home in a stable condition. However, her COP progressed with dyspnea and X-ray showed an increase in lung infiltration. We then changed medications to oral dexamethasone 8 mg/day for COP control.

Despite 2 months of high dose oral-form corticosteroid treatment, mild fever, dyspnea, and progression of lung consolidation recurred. Chylothorax was found in the right chest. An empirical antibiotic, levofloxacin, was prescribed to cover the pneumonia. Intravenous methylprednisolone 80 mg/day was begun, but there was only mild improvement in the hypoxia. She needed an oxygen mask with flow of 10 L/min. However, lung consolidation progressed. Levofloxacin was changed to ceftazidime to cover hospital-acquired pneumonia. Her rheumatoid factor, ANA, ANCA, ENA (Jo-1, Scl-

70, SSA, SSB), C3, C4, and HIV screening test were all negative. We repeated the VATS lung biopsy and lymph node resection, and the pathology once again reported COP.

For severe COP with impending respiratory failure and refractory to strong corticosteroid treatment, we added cyclophosphamide, oral form, 50 mg/day. Her hypoxia and dyspnea then showed improvement. One week later, the oxygen mask was replaced by a nasal cannula. Ceftazidime was used for 1 week. Corticosteroid was tapered down to prednisolone 30 mg/day, and she was discharged home.

She had no cyclophosphamide-related side effects. Therefore, we increased the cyclophosphamide to 100 mg/day, beginning the 12th day, and reduced the prednisolone to 10 mg/day. She was able to breathe well in room air. Cyclophosphamide 100 mg/day was continued and prednisolone was gradually reduced. Prednisolone was completely discontinued 4 months later. The following chest X-ray showed improvement of the pulmonary interstitial infiltration. Then, we tapered the cyclophosphamide dose to 75 mg/day for 2 months, and then 50 mg/day for 6 months, but increased it to 100 mg/day for 1 month due to a flare-up of the COP. After she had stabilized, we tapered the cyclophosphamide to 75 mg/day for 1 month, and then 50 mg/day for 6 months. Another mild flare-up was noted during the course and a combination with prednisolone 20 mg/day was begun. The prednisolone was tapered off in 3 months. Then, cyclophosphamide was tapered to 50 mg every other day for 4 months, and then discontinued. Cyclophosphamide was used for a total of 2 years.

Discussion

Cryptogenic organizing pneumonitis (COP) is an inflammatory disease of the lung, and can be induced by infection or drugs, and other conditions [1]. To reach a diagnosis of COP, we first need to rule out other inflammatory pulmonary diseases, including bacterial and atypical pneumonia, autoimmune disorders, pulmonary fibrosis, tuberculosis, acquired immune deficiency syndrome, and malignancy [2]. In our case, the patient had community-acquired pneumonia, followed by COP. We performed bronchoscopy for bronchial washing and transbronchial biopsy, but collecting bronchoalveolar lavage fluid (BALF) would have been more helpful. BALF has unique findings in cases of COP, such as lymphocytosis, increased mast cell numbers, decreased CD4/CD8 ratios, and neutrophils >5% [3]. We confirmed the diagnosis of COP by VATS biopsy, which gave us the confidence to add cyclophosphamide.

COP usually has a benign course and has a good response to corticosteroid. It usually resolves after a short course of systemic corticosteroid treatment [2,4]. Our patient had rapid worsening of oxygenation, leading to impending respiratory failure, which is uncommon. For steroid-refractory COP, after excluding superimposed infection and autoimmune disorder, the use of a cytotoxic agent while maintaining corticosteroid is supported by case reports [5-6]. The optimal dose of cyclophosphamide for COP is still unknown, but 1-2 mg per day with a maximum of 150 mg/day might be adequate. Successful treatment with adjunctive cyclosporine, and macrolide and steroid has also been reported [7-8].

Our patient had a good response to and tolerance of cyclophosphamide. She could breathe

well in room air and was able to stop corticosteroid after 2 weeks of cyclophosphamide treatment. Discontinuation of cyclophosphamide after use for 6 months has been suggested in reports [5-6]. But our patient's COP fluctuated when tapering down the dose of cyclophosphamide. Airway infection was the most common cause of flare of COP in this patient. We combined treatment with short-term prednisolone to control the flare-up. After her disease had stabilized, we tapered off prednisolone first and then gradually tapered down the cyclophosphamide dose, until it was completely discontinued 2 years later.

Acknowledgements

We thank all colleagues who contributed to this case report. The work is supported by E-DA Hospital, project EDAHP106052. We thank the editors and reviewers for their constructive criticisms.

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Cyclophosphamide 在隱源性器質性肺炎（Cryptogenic Organizing Pneumonia）瀕臨呼吸衰竭的治療—案例報告

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一位三十歲女性咳嗽有痰近一個月，最近兩天因發燒、呼吸困難住院治療，被診斷為肺炎，在抗生素治療後改善並出院。10 天後症狀復發並有嚴重低血氧，胸部 X 光發現兩側肺野有間質性浸潤。再次使用抗生素治療並無改善，而且感染及自體免疫相關的檢查均無特殊發現。在給予高劑量全身性類固醇後，低血氧及肺浸潤開始改善。胸腔鏡肺部切片病理報告為隱源性器質性肺炎（cryptogenic organizing pneumonia, COP）。當減低類固醇劑量時，低血氧再次惡化，並發現有乳糜胸。加入 cyclophosphamide 合併治療後，呼吸困難及肺浸潤改善，並且順利停用類固醇。在後續減量 cyclophosphamide 時，病人 COP 病況起起伏伏，在治療兩年後，在病況穩定的情形下順利停用 cyclophosphamide。*(胸腔醫學 **2019; 34: 172-177**)*

關鍵詞：隱源性器質性肺炎，阻塞性細支氣管炎，環磷醯胺

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