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83301 高雄市鳥松區大埤路 123 號
No. 123, Dapi Rd., Niaosong Dist.,
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原著

- 台灣肺阻塞的病人有較高睡眠呼吸中止症的風險 178~189
郭家佑，蔡明儒，李瑞英，許超群，洪仁宇，鍾飲文

病例報告

- 肺癌的少見遠端轉移：病例系列報告及文獻探討 190~196
吳昱蔚，阮筠婷，陳建維，蘇柏嵐，林建中
- 雞尾酒療法下人體免疫不全病毒感染者的Afatinib相關重症肺炎：病例報告 197~204
邱華彥，江起陸，陳沛谷，柯信國，李毓芹
- 非小細胞肺癌心臟轉移引起之血流動力不穩—案例報告 205~212
沈佳儀，江起陸，胡栢璋，吳元宏，邱昭華，陳育民，李毓芹
- 慢性嗜伊紅性白血球肺炎—病例報告 213~220
吳珈潤，徐國軒
- 肋膜肺實質彈性纖維增生合併尋常性間質性肺炎之影像學/病理學變化的個案：
案例報告及文獻回顧 221~229
李奕嫻，謝明書，郭炳宏



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Original Article

- Increased Risk of Sleep Apnea in Taiwanese Patients with Chronic Obstructive Pulmonary Disease 178~189
Chia-Yu Kuo, Ming-Ju Tsai, Jui-Ying Lee, Chau-Chyun Sheu, Jen-Yu Hung, Inn-Wen Chong

Case Reports

- Uncommon Metastasis from Lung Cancer: A Case Series and Literature Review 190~196
Yu-Wei Wu, Yun-Ting Juan, Chian-Wei Chen, Po-Lan Su, Chien-Chung Lin
- Afatinib-Related Severe Pneumonitis in a Patient with HIV under Anti-Retroviral Therapy:
A Case Report 197~204
Hwa-Yen Chiu, Chi-Lu Chiang, Pei-Ku Chen, Hsin-Kuo Ko, Yu-Chin Lee
- Hemodynamic Instability Caused by Cardiac Metastases of Non-small Cell Lung Cancer –
Case Studies 205~212
Chia-I Shen, Chi-Lu Chiang, Bo-Wei Hu, Yuan-Hung Wu, Chao-Hua Chiu, Yuh-Min Chen, Yu-Chin Lee
- Idiopathic Chronic Eosinophilic Pneumonia Successfully Treated with Corticosteroids:
A Case Report 213~220
Jia-Jun Wu, Kuo-Hsuan Hsu
- A Case of Pleuroparenchymal Fibroelastosis with Coexisting Features of Usual Interstitial Pneumonia 221~229
I-Hsien Lee, Min-Shu Hsieh, Ping-Hung Kuo

Increased Risk of Sleep Apnea in Taiwanese Patients with Chronic Obstructive Pulmonary Disease

Chia-Yu Kuo*, Ming-Ju Tsai*, **, Jui-Ying Lee***, Chau-Chyun Sheu*, **,
Jen-Yu Hung*, **, Inn-Wen Chong*, **

Objective: The potential association between chronic obstructive pulmonary disease (COPD) and sleep apnea has been previously studied; however, the study results are contradictory. Therefore, we designed a nationwide population-based cohort study to determine the association between COPD and sleep apnea in Taiwan.

Methods: Using the Taiwan National Health Insurance Research Database, adult patients with a diagnosis of COPD were enrolled; those with a sleep apnea diagnosis prior to their COPD onset were excluded. The date of each patient's first COPD diagnosis was defined as the index date. Each COPD patient was matched with 5 randomly selected control subjects without a COPD diagnosis. The control subjects were assigned the same index dates as their corresponding COPD patient, and we ensured that they had no sleep apnea diagnosis prior to their index date.

Results: A total of 35,095 COPD patients were matched with 175,475 control subjects. The incidence rate of sleep apnea was significantly higher among the COPD patients than among the control subjects (0.5 vs. 1.0 per 1,000 patient-years; $p<0.0001$). Multivariable Cox regression analysis revealed COPD to be a significant risk factor for sleep apnea ($p<0.0001$). Factors associated with incident sleep apnea among COPD patients in this study included male, resident of northern Taiwan, higher income, heart disease, connective tissue disease and cancer.

Conclusion: COPD patients had a significantly higher risk of developing sleep apnea than non-COPD patients. When caring for patients with COPD in any context, clinicians need to pay special attention to the risk of incident sleep apnea, especially among male patients, and those with heart disease, connective tissue disease and cancer. (*Thorac Med 2019; 34: 178-189*)

Key words: sleep apnea, sleep disordered breathing, chronic obstructive pulmonary disease

*Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Kaohsiung Medical University Hospital; **College of Medicine, Kaohsiung Medical University; ***Division of Chest Surgery, Department of Surgery, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan
Address reprint requests to: Dr. Jui-Ying Lee, Division of Chest Surgery, Department of Surgery, Kaohsiung Medical University Hospital, No. 100, Tz-You 1st Road, 807 Kaohsiung, Taiwan

台灣肺阻塞的病人有較高睡眠呼吸中止症的風險

郭家佑 * 蔡明儒 ** 李瑞英 *** 許超群 *,** 洪仁宇 *,** 鍾飲文 *,**

目的：肺阻塞（COPD）和睡眠呼吸中止症（SA）兩者之間的關係一直有所爭議。因此，我們進行了一個以全國性的人口為基礎的研究來探討 COPD 與 SA 間的關聯性。

方法：從台灣全民健康保險研究資料庫中，我們收錄了成人 COPD 的病人，並排除了在診斷 COPD 前即確診 SA 的病人。以病人第一次診斷 COPD 的日期為指標日期。每個 COPD 患者與 5 個隨機選擇之無 COPD 診斷的對照者配對。對照組在指標日期前確定沒有 SA 的診斷。

結果：本研究共收錄 35,095 位 COPD 患者與 175,475 位對照者進行分析。SA 在 COPD 的病人比起對照組有較高的發生率。以多變項 Cox 迴歸分析校正後，COPD 仍然是發生 SA 的獨立危險因子。在 COPD 的病人當中，男性、居住於北台灣、較高收入、合併心血管疾病、結締組織疾病及癌症與較高的 SA 發生率有關。

結論：COPD 病人有明顯較高的風險罹患 SA。因此，臨床醫師針對 COPD 的病人需花費更多的注意力在 SA 的發生，尤其是針對男性、居住於北台灣、較高收入、合併心血管疾病、結締組織疾病及癌症的病人。（*胸腔醫學 2019; 34: 178-189*）

關鍵詞：睡眠呼吸中止，睡眠呼吸障礙，肺阻塞

高雄醫學大學附設中和紀念醫院 內科部 胸腔內科 *，醫學院 **，高雄醫學大學附設中和紀念醫院 外科部 胸腔外科 ***
索取抽印本請聯絡：李瑞英醫師，高雄醫學大學附設中和紀念醫院 外科部 胸腔外科，高雄市 807 自由一路 100 號

Uncommon Metastasis from Lung Cancer: A Case Series and Literature Review

Yu-Wei Wu, Yun-Ting Juan*, Chian-Wei Chen, Po-Lan Su, Chien-Chung Lin

The most common sites of lung cancer metastasis include the brain, bone, liver, adrenal glands, contralateral lung, and distant lymph nodes. Metastasis of lung cancer to other organs is relatively rare and may not be identified by routine chest computed tomography for lung cancer staging or by checking tumor markers.

We report 3 cases of advanced lung carcinoma with uncommon metastasis at a southern medical center in Taiwan. These uncommon distal metastases included ovary metastasis, intestinal metastasis, and kidney metastasis. All of the metastases were adenocarcinomas. One presented as abdominal pain, the second as flank pain, and the third as an abdominal mass.

Lung cancer patients with uncommon metastases are rare, and the prognosis of this group is relatively poor, according to the literature review. When a patient presents with atypical symptoms including abdominal pain or flank pain, additional images should be taken to identify whether there is an uncommon metastasis. Local treatment and re-biopsy may be beneficial for these patients. (*Thorac Med 2019; 34: 190-196*)

Key words: lung cancer, uncommon metastasis, ovary metastasis, intestine metastasis, kidney metastasis

Division of Chest Medicine, *Department of Internal Medicine, National Cheng Kung University Hospital, Tainan, Taiwan

Address reprint requests to: Dr. Chien-Chung Lin, Division of Chest Medicine, Department of Internal Medicine, National Cheng Kung University Hospital, #138, Sheng-Li Road, Tainan 704, Taiwan

肺癌的少見遠端轉移：病例系列報告及文獻探討

吳昱蔚 阮筠婷 * 陳建維 蘇柏嵐 林建中

肺癌常見的遠端轉移包含腦部、骨頭、肝臟、腎上腺、淋巴結，而其他器官的轉移相對來說少見，並且無法藉由常規的胸部斷層掃描或腫瘤指數察覺。

在此我們提出三位在南台灣醫學中心被診斷肺腺癌的個案，分別有卵巢、小腸、腎臟的轉移。兩位以疼痛來表現，另一位則是發現腹部的腫塊。

經文獻回顧，這些少見的轉移預後較差，當病人有不典型的症狀時，可能需要更進一步的影像檢查。
(*胸腔醫學* 2019; 34: 190-196)

關鍵詞：肺癌，遠端轉移，卵巢轉移，小腸轉移，腎臟轉移

Afatinib-Related Severe Pneumonitis in a Patient with HIV under Anti-Retroviral Therapy: A Case Report

Hwa-Yen Chiu*, Chi-Lu Chiang*, **, Pei-Ku Chen*, Hsin-Kuo Ko*, **, Yu-Chin Lee*, ***

Afatinib, a second-generation epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI), improved progression-free survival and time-to-treatment failure as a first-line treatment in non-small cell lung cancer (NSCLC) patients. Use of combination antiretroviral therapy (cART) for human immunodeficiency virus (HIV) infection poses a potential risk of drug-drug interaction in HIV-infected patients simultaneously receiving EGFR-TKI treatment for NSCLC. EGFR-TKI-related pneumonitis is known as a serious drug toxicity. Previous research on EGFR-TKI-related pneumonitis mainly focused on gefitinib and erlotinib. We presented the first case of afatinib-related severe pneumonitis in a patient with NSCLC and HIV under cART. This study emphasizes the critical issue of drug-drug interaction between cART and afatinib. The patient's severe drug-related pneumonitis resolved after steroid pulse therapy. (*Thorac Med 2019; 34: 197-204*)

Key words: drug-related pneumonitis, human immunodeficiency virus (HIV), afatinib, EGFR-TKI, tyrosine kinase inhibitor (TKI), NSCLC

*Department of Chest Medicine, Taipei Veterans General Hospital, Taipei, Taiwan; **Faculty of Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan; ***Department of Respiratory Therapy & Chest Medicine, Sijhih Cathay General Hospital

Address reprint requests to: Dr. Yu-Chin Lee, Department of Respiratory Therapy & Chest Medicine, Sijhih Cathay General Hospital, No. 2, Lane 59, Jiancheng Rd., Sijhih District, New Taipei City, Taiwan

雞尾酒療法下人體免疫不全病毒感染者的 Afatinib 相關重症肺炎：病例報告

邱華彥 * 江起陸 *,** 陳沛谷 * 柯信國 *,** 李毓芹 *,***

Afatinib 為二代 EGFR-TKI，已被證實對有 EGFR 突變的非小細胞肺癌有療效。人類免疫不全病毒感染的患者是肺癌的高風險族群，而此類患者使用的抗病毒藥物雞尾酒療法會產生的藥物交互作用。使用 EGFR-TKI 治療肺癌，有 1% 的機率會產生嚴重的藥物引起的間質性肺炎。過去關於 EGFR-TKI 藥物引起的間質性肺炎病例報告都著眼於 gefitinib 或 erlotinib，尚未有人分享過發生於人類免疫不全病毒感染的患者的間質性肺炎。因此，我們提出第一位同時使用 afatinib 及雞尾酒療法後發生間質性肺炎的人類免疫不全病毒感染的肺癌患者，在經過類固醇脈衝治療後恢復的案例。（*胸腔醫學 2019; 34: 197-204*）

關鍵詞：藥物相關肺炎，人體免疫不全病毒，妥復克（afatinib），EGFR-TKI，TKI，非小細胞肺癌

* 台北榮民總醫院 胸腔部，** 國立陽明大學 醫學系，*** 汐止國泰綜合醫院 呼吸胸腔科
索取抽印本請聯絡：李毓芹醫師，汐止國泰綜合醫院 呼吸胸腔科，221 新北市汐止區建成路 59 巷 2 號

Hemodynamic Instability Caused by Cardiac Metastases of Non-small Cell Lung Cancer – Case Studies

Chia-I Shen*, Chi-Lu Chiang*, **, Bo-Wei Hu*, Yuan-Hung Wu**,
Chao-Hua Chiu*, ***, Yuh-Min Chen*, ***, Yu-Chin Lee*, ****

The incidence of cardiac metastases is 9.1% in oncologic patients, and lung cancer is the leading source. Most patients are asymptomatic, and if symptoms exist, they may mimic cardiovascular diseases. Hemodynamic instability is often life-threatening. Here, we report 2 rare cases of fatal cardiac metastases in patients with non-small cell lung cancer with hemodynamic instability. With the advances in clinical treatment and prolonged survival, the incidence of cardiac metastases is increasing. Physicians should be alert that new cardiac symptoms in patients with known malignancy can be caused by cardiac metastases. Although limited, some data shows early detection and multidisciplinary management in selected patients may improve the outcome. (*Thorac Med 2019; 34: 205-212*)

Key words: non-small cell lung cancer (NSCLC), cardiac metastases (CM)

*Department of Chest Medicine, Taipei Veterans General Hospital; **Department of Oncology, Taipei Veterans General Hospital; ***School of Medicine, National Yang-Ming University, Taipei, Taiwan; ****Department of Respiratory Therapy & Chest Medicine, Sijhih Cathay General Hospital

Address reprint requests to: Dr. Yu-Chin Lee, Department of Respiratory Therapy & Chest Medicine, Sijhih Cathay General Hospital, No. 2, Lane 59, Jiancheng Rd., Sijhih District, New Taipei City, Taiwan

非小細胞肺癌心臟轉移引起之血流動力不穩－案例報告

沈佳儀 * 江起陸 * ,*** 胡柏璋 * 吳元宏 ** 邱昭華 * ,*** 陳育民 * ,*** 李毓芹 * ,****

癌症病人心臟轉移之發生率約為 9.1%，其中肺癌是心臟轉移主因。多數病人沒有症狀，臨床表徵和心血管疾病也不好區分，血流動力學不穩則通常有致命性。隨著治療技術的進步，癌症病人存活率增加，同時心臟轉移的盛行率也增加。本文呈現兩個少見的非小細胞肺癌引起之致命性心臟轉移，試圖提高臨床醫師對於心臟轉移的警覺性。對於已知有癌症診斷的病患，任何新出現的心血管相關症狀，都可能是心臟轉移的徵兆。目前已有的資料顯示，提早偵測到心臟轉移，進而配合多專科團隊的介入，有機會提高特定族群病患的存活率。(胸腔醫學 2019; 34: 205-212)

關鍵詞：非小細胞肺癌，心臟轉移

* 臺北榮民總醫院 胸腔部, ** 臺北榮民總醫院 腫瘤醫學部, *** 國立陽明大學醫學院, **** 汐止國泰醫院 胸腔科
索取抽印本請聯絡：李毓芹醫師，汐止國泰醫院 胸腔科，新北市汐止區建成路 59 巷 2 號

Idiopathic Chronic Eosinophilic Pneumonia Successfully Treated with Corticosteroids: A Case Report

Jia-Jun Wu*, Kuo-Hsuan Hsu*, **, ***

Chronic eosinophilic pneumonia (CEP) is a rare disorder, with an incidence rate of approximately 0.23 cases per 10 million persons per year; CEP primarily affects non-smoking females. The disease is cryptogenic, and is characterized by the accumulation of eosinophils in the alveola and interstitium of the lung. CEP usually manifests as a subacute clinical course, with respiratory symptoms including cough and shortness of breath. Diagnosis depends upon chest images and bronchoalveolar lavage results. The disease responds well to corticosteroid treatment. We present the case of a 55-year-old male who had complained of progressive shortness of breath for 1 month. Chest images showed bilateral consolidation in the upper lung field. The patient had been healthy prior to admission, and denied a history of exposure to drugs or allergens. He was diagnosed with CEP with eosinophilia, as evidenced by his peripheral blood ($8,472/\text{mm}^3$) and bronchoalveolar lavage results (eosinophils, 51%). Systemic corticosteroid was administered during admission, and his symptoms gradually improved. There was no relapse of the disease after steroid treatment was terminated. (*Thorac Med 2019; 34: 213-220*)

Key words: chronic eosinophilic pneumonia, bronchoalveolar lavage, corticosteroid

*Division of Chest Medicine, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan; **Institute of Biomedical Sciences, National Chung Hsing University, Taichung, Taiwan; ***Division of Critical Care and Respiratory Therapy, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan

Address reprint requests to: Dr. Kuo-Hsuan Hsu, Division of Chest Medicine, Department of Internal Medicine, Taichung Veterans General Hospital, No. 1650 Taiwan Boulevard, Sect. 4, Taichung, Taiwan 40705

慢性嗜伊紅性白血球肺炎－病例報告

吳珈潤 * 徐國軒 **,***

慢性嗜伊紅性白血球肺炎(Chronic eosinophilic pneumonia)為一種罕見的肺部疾病。過去的文獻指出，慢性嗜伊紅性白血球肺炎的發生率約為每十萬人年有 0.23 個案例，且好發於女性及沒有吸菸史的病人。此疾病的發生原因不明，病理上可以看到肺泡以及肺間質中有嗜伊紅性白血球浸潤。慢性嗜伊紅性白血球肺炎的病程為亞急性或慢性，通常以咳嗽或喘等呼吸道症狀為表現。慢性嗜伊紅性白血球肺炎需仰賴胸腔影像檢查以及支氣管肺泡灌洗的結果來診斷，使用類固醇治療通常有良好的效果。本文案例為一 55 歲男性，因為一個月來漸進性呼吸困難至急診就醫。就醫過程胸部 X 光及電腦斷層皆有雙側上肺野浸潤，抽血以及支氣管肺泡灌洗檢查皆發現嗜伊紅性白血球升高，因此被診斷為慢性嗜伊紅性白血球肺炎。其病況在接受類固醇治療後逐漸改善，於類固醇停藥後也沒有復發的狀況。(胸腔醫學 2019; 34: 213-220)

關鍵詞：慢性嗜伊紅性白血球肺炎，支氣管肺泡灌洗，類固醇

* 台中榮民總醫院 內科部胸腔內科，** 國立中興大學生物醫學研究所，*** 台中榮民總醫院 內科部呼吸治療科
索取抽印本請聯絡：徐國軒醫師，台中榮民總醫院 胸腔內科，台中市西屯區台灣大道四段 1650 號

A Case of Pleuroparenchymal Fibroelastosis with Coexisting Features of Usual Interstitial Pneumonia

I-Hsien Lee, Min-Shu Hsieh*, Ping-Hung Kuo

Pleuroparenchymal fibroelastosis (PPFE) is a rare idiopathic interstitial pneumonitis. The diagnosis of PPFE can be based on clinical and radiological features, and pathological findings. PPFE can coexist with usual interstitial pneumonia (UIP) on both high-resolution computed tomography (HRCT) and lung biopsy. Therefore, it may cause a diagnostic dilemma in the differentiation of PPFE from idiopathic pulmonary fibrosis (IPF) with upper lung involvement. We report a 71-year-old woman suffering from progressive dyspnea and dry cough for 1 year. HRCT revealed dense pleural thickening and subpleural fibrosis and consolidations in the upper lobes. There was also diffuse subpleural reticulation and traction bronchiectasis/bronchiolectasis. She underwent surgical lung biopsy and the pathology was consistent with PPFE after elastin staining. Histological features of UIP were also found in the upper lobes. Her cough and exertional dyspnea partially improved after off-label treatment with pirfenidone. Our experience with this case suggests that PPFE patients may have HRCT and pathological features of UIP. We also reviewed the differential diagnoses of PPFE and IPF and their clinical outcomes in the literature. (*Thorac Med* 2019; 34: 221-229)

Key words: idiopathic pulmonary fibrosis (IPF), pleuroparenchymal fibroelastosis (PPFE), usual interstitial pneumonia (UIP)

Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan; *Department of Pathology, National Taiwan University Hospital, Taipei, Taiwan

Address reprint requests to: Dr. Ping-Hung Kuo, Department of Internal Medicine, National Taiwan University Hospital, No. 7, Chung-Shan South Road, Taipei 100, Taiwan

肋膜肺實質彈性纖維增生合併尋常性間質性肺炎之影像學 / 病理學變化的個案：案例報告及文獻回顧

李奕嫻 謝明書 * 郭炳宏

肋膜肺實質彈性纖維增生是一種罕見的間質性肺病，其診斷需要參考臨床、影像學、病理的發現。在高解析度電腦斷層以及病理切片中，可與尋常性間質性肺炎同時存在，因此在鑑別肋膜肺實質彈性纖維增生以及在波及上肺野的特發性肺纖維化時可能遭遇困難。本個案為一位 72 歲女性，因漸進性乾咳及活動喘一年來就診，高解析度電腦斷層顯現尋常性間質性肺炎型態以外，也在上肺葉有肋膜增厚以及肋膜下纖維化的影像，經胸腔鏡楔形肺葉切片手術後病理診斷為肋膜肺實質彈性纖維增生但併有特發性肺纖維化的特徵，經多團隊會議討論後認為個案傾向肋膜肺實質彈性纖維增生的疾病，但仍給予 pirfenidone 藥物治療嘗試，病患症狀獲得改善。除呈現本個案診斷過程外，我們亦進行文獻回顧比較特發性肺纖維化及肋膜肺實質彈性纖維增生的差異。(胸腔醫學 2019; 34: 221-229)

關鍵詞：特發性肺纖維化，肋膜肺實質彈性纖維增生，高解析度電腦斷層