Poster Round
海報目錄

時　間：113 年 12 月 15 日(星期日)10：15-10：45

地　點：新竹喜來登大飯店 3F 海報區

主持人：呂聆音醫師

編號	題目	作者
TCR 25	Investigation of renal tubular cell senescence as a future treatment target of lupus nephritis	沈玠妤,呂政勳,鄭喬峯,郭佑民,李克仁,劉津秀,謝松洲,余家利
TCR 26	Crucial Role of MERTK-Mediated Efferocytosis in Hydroxychloroquine's Anti-Inflammatory Effects in Pristane-Induced Lupus Mice MERTK 訊息在 SLE 動物模式調控 Efferocytosis 是 Hydroxychloroquine 引起抗發炎反應之關鍵角色	劉欣怡,葉詠蕙,吳雅雯,吳孟蓁,李偉菁,薛婷尹,謝飛弘, 彭心儀,陳惠珍,蔡嘉哲
TCR 27	全身性紅斑狼瘡患者血漿 IL-18 與蛋白尿、實驗室數據及疾病活動指標之相關性 The correlation of plasma IL-18 with proteinuria, laboratory data, and disease activity measures in patients with systemic lupus erythematosus	蔡秉翰;方耀凡;陳彥輔;陳志杰; 江文瑀;張哲慈;劉烈邦
TCR 28	SARS-CoV-2 spike protein triggers systemic lupus erythematosus disease activity by binding human ACE2 and TLR2 to enhance intra-pulmonary apoptosis and autophagy formation SARS-冠狀病毒 2 之棘蛋白經由結合人類血管收縮素轉化酶 2 及類鐸受體 2 促進肺部內細胞凋亡及自體吞噬的形成來引發全身性紅斑狼瘡疾病活性	王崇任、陳怡成、謝雨彤、蔡弘文、凌斌、蔡青宴、周祐吉
TCR 29	Prognosis Assessment of Lupus Nephritis in Systemic Lupus Erythematosus Using Deep Learning 使用深度學習評估系統性紅斑狼瘡腎炎的預後	盧德宇, 鄭文隆, 劉峰誠
TCR 30	Utilizing Machine Learning to Predict Major Adverse Cardiovascular Events in Patients with Systemic Lupus Erythematosus 利用機器學習預測紅斑性狼瘡病人主要心血管事件	曹彥博, 鄭浩民
TCR 31	Discovery of Genetic Mutations Linked to Lupus Nephritis in a Taiwanese Cohort via Extensive Genetic Screening	李承翰, 洪國勝, 呂家慧, 陳相成, 郭三元, 朱士傑, 盧俊吉, 黎亞綺, 葉富強, 劉峰誠
TCR 32	影像競圖獎	
	Clinical Images: Early Detection of Brain Ischemia by Perfusion MRI in Neuropsychiatric Systemic Lupus Erythematosus	吳佩盈,黃立恒,李克仁
TCR 33	Clinical Images: Lupus Retinopathy with Cotton-wool Spots and Retinal Hemorrhages	林政緯
TCR 34	Clinical Image: Lupus associated jejunum vasculitis	廖顯宗
TCR 35	Clinical Images: Optic Perineuritis (OPN) in a Patient with Systemic Lupus Erythematosus	廖修誼, 陳明翰, 賴建志
TCR 36	Clinical Images: Cerebral sinus thrombosis in a patient with systemic lupus erythematosus	張婷惠, 陳仕淇
TCR 37	Clinical features and outcomes of neuromyelitis optica spectrum disorders in patient with autoimmune diseases	Hung-Cheng Tsai, Ying-Ying Yang, Wei-Sheng Chen, Ming-Han Chen, Chang-Youh Tsai , Hsien-Tzung Liao
TCR 38	個案報告獎	
	Chronic Fibrosing Organizing Pneumonia as an Early Manifestation of Aquaporin-4 Antibody-Positive Neuromyelitis Optica Spectrum Disorder: A Unique Case Presentation	李苡萍, 蘇勤方

海報摘要 TCR25

Investigation of renal tubular cell senescence as a future treatment target of lupus nephritis

Chieh-Yu Shen [1] , Cheng-Hsun Lu[1] , Chiao-feng Cheng[1], Ko-Jen Li[1]., Yu-Min Kuo [1], Chin-Hsiu Liu[1] , Song-Chou Hsieh [1], Chia-Li Yu [1]
沈玠妤, 呂政勳, 鄭喬峯, 郭佑民, 李克仁, 劉津秀, 謝松洲, 余家利
1. Department of Internal Medicine, National Taiwan University Hospital, #7 Chung-Shan South Road, Taipei 10002, Taiwan
國立台灣大學醫學院附設醫院風濕免疫科

Abstract

Introduction: Nephritis is a significant concern in systemic lupus erythematosus (SLE) patients, with about 25% progressing to end-stage renal failure within 10 years. Lupus nephritis (LN) involves not only glomeruli but also renal tubules, which present in about 70% of LN patients and may be associated with advanced renal sclerosis. However, tubulointerstitial nephritis in LN remained to be underexplored. Drawing parallels with diabetic nephropathy, which involves low-grade inflammation and elevated advanced glycation end products (AGEs), can provide insights. AGEs contribute to diabetic nephropathy by inducing proteinuria, degenerative changes, and stimulating pro-fibrotic factors, leading to cellular senescence and fibrosis.

Method: We designed this as AGE modified HSA stimulation on primary renal tubular epithelial cells (HRCEp). The concentration of AGE-HSA is 4 mg/ml. The control group includes medium only, 4mg/ml HSA and PBS, which is the solvent of AGE and HSA. After incubate AGE, HSA, medium or PBS for 24 hours, we collected the culture supernatant and cell extract. We detected IL-6 production to evaluate inflammation and uromodulin formation for epithelial cell function evaluation, in culture supernatant. We also detect senescence associated β-galactosidase for cellular senescence evaluation.

Results: Our data revealed AGE-HSA stimulation, comparing with control group, increase senescence-associated β-galactosidase (SA-β galactosidase) expression and IL-6 production in HRCEp cell. Also, AGE modified HSA decreased uromodulin production. The results are shown in Figure 1.

Conclusion: AGE-HA stimulation may induce renal epithelial cell low grade inflammation and cellular senescence, which may be with consequent epithelial cell dysfunction.

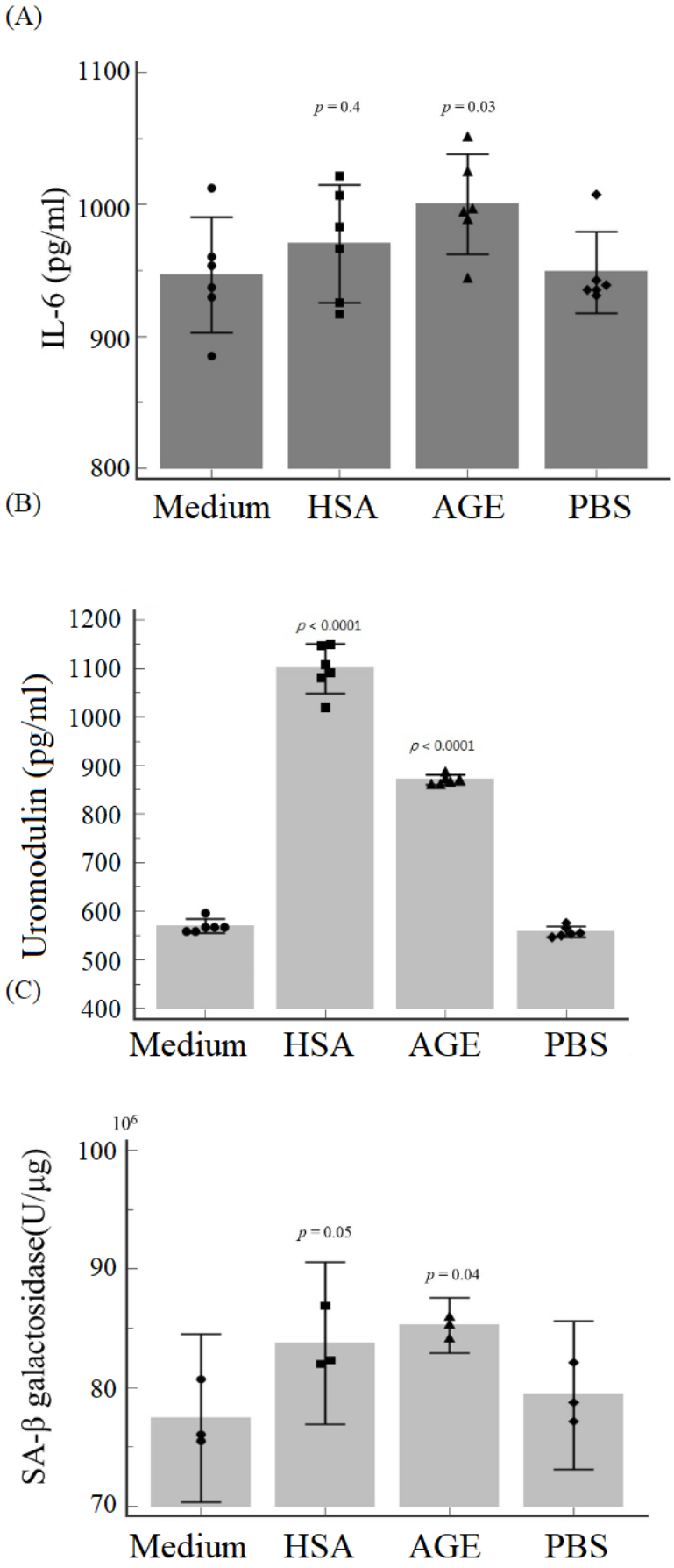


Figure 1. (A) IL-6 production increased after AGE stimulation. (B) Uromodulin production decreased after AGE stimulation. (C) Senescence associated β galactosidase (SA-β galactosidase) increased after AGE stimulation. The *p* value indicated comparison with medium control.

海報摘要 TCR26

Crucial Role of MERTK-Mediated Efferocytosis in Hydroxychloroquine's Anti-Inflammatory Effects in Pristane-Induced Lupus Mice

MERTK 訊息在 SLE 動物模式調控 Efferocytosis 是 Hydroxychloroquine 引起抗發炎反應之關鍵角色

Hsin-Yi Liu[1], Yung-Ju Yeh[2,3], Ya-Wun Wu[3], Meng-Zhen Wu[2,3], Wei-Jing Li[3], Ting-Yin Xue[3], Fei-Hung Hsieh[3], Hsin-Yi Peng[3], Hui-Chen Chen[4], Gregory J Tsay[2,3,5,6]

劉欣怡[1], 葉詠薷[2,3], 吳雅雯[3], 吳孟蓁[2,3], 李偉菁[3], 薛婷尹[3], 謝飛弘[3], 彭心儀[3], 陳惠珍[4], 蔡嘉哲[2,3,5,6]

1. Department of Biomedical Imaging and Radiological Science, China Medical University, Taichung, Taiwan
中國醫藥大學生物醫學影像暨放射科學學系

2. Autoimmune disease laboratory, China Medical University Hospital, Taichung, Taiwan
中國醫藥大學附設醫院自體免疫實驗室

3. Research and Development Center for Immunology, China Medical University, Taichung, Taiwan
中國醫藥大學免疫醫學研發中心

4. College of Medicine, China Medical University, Taichung, Taiwan
中國醫藥大學醫學院微免科

5. Division of Immunology and Rheumatology, Department of Internal Medicine, China Medical University Hospital, Taichung, Taiwan
中國醫藥大學附屬醫院內科免疫與風濕病科

6. College of Medicine, China Medical University, Taichung, Taiwan
中國醫學大學醫學系

Abstract

Background

Hydroxychloroquine (HCQ), an antimalarial agent, is extensively utilized for the long-term management of systemic lupus erythematosus (SLE) due to its immunomodulatory properties and low risk of complications. Efferocytosis, the process of clearing apoptotic cells, is crucial for maintaining tissue homeostasis and defective efferocytosis by macrophages is implicated in the pathogenesis of SLE. This study aims to elucidate the mechanism of action of HCQ on macrophage efferocytosis and its anti-inflammation effects using a pristane-induced lupus (PIL) animal model.

Methods

The therapeutic effects of HCQ in PIL mice were evaluated by assessing levels of inflammatory cytokines, autoantibodies, and lupus nephritis. The efferocytosis index of macrophages treated with HCQ was quantified following co-incubation with apoptotic lymphocytes in vitro. Additionally, the expression of TAM receptors, essential for efferocytosis, was examined in HCQ-treated macrophages at both transcriptional and translational levels. The regulation of efferocytosis by HCQ was further confirmed in vivo using peritoneal macrophages exposed to apoptotic thymocytes.

Results

Long-term HCQ treatment in PIL mice resulted in reduced SLE activity and decreased production of pro-inflammatory cytokines. HCQ administration significantly increased efferocytosis in RAW264.7 cells in a dose-dependent manner. HCQ treatment induced the expression of the TAM receptor MERTK in macrophages. Inhibition of MERTK signaling attenuated the HCQ-mediated enhancement of efferocytosis and inflammation resolution. Peritoneal macrophages from HCQ-treated PIL mice also demonstrated positive regulation of efferocytosis via MERTK expression.

Conclusions

Our research provides in vitro and in vivo evidence that HCQ treatment enhances macrophage efferocytosis, promoting anti-inflammatory reprogramming and secretion of the pro-resolving factors. The HCQ-induced enhancement of macrophage efferocytosis is mediated through the activation of MERTK signaling. Understanding the immunomodulatory function of HCQ offers new insights into the etiopathogenesis of SLE and establishes a molecular foundation for the development of innovative therapeutic agents.

Keywords: hydroxychloroquine, efferocytosis, pristine-induced lupus, autoimmune diseases

海報摘要 TCR27

全身性紅斑狼瘡患者血漿 IL-18 與蛋白尿、實驗室數據及疾病活動指標之相關性

The correlation of plasma IL-18 with proteinuria, laboratory data, and disease activity measures in patients with systemic lupus erythematosus

作者：
蔡秉翰[1,2]; 方耀凡[2]; 陳彥輔[2]; 陳志杰[1]; 江文瑀[1]; 張哲慈[2]; 劉烈邦[1,2,3*]
Authors:
Ping-Han Tsai[1,2], Yao-Fan Fang[2], Yen-Fu Chen[2], Chih-Chieh Chen[1], Wen-Yu Chiang[1], Che-Tzu Chang[2], Lieh-bang Liou[1,2,3*]

服務機關
1. 新北市立土城醫院內科部風濕過敏免疫科
2. 林口長庚紀念醫院內科部風濕過敏免疫科
3. 長庚大學醫學院
Author affiliations:
1. Division of Rheumatology, Allergy and Immunology, Department of Internal Medicine, New Taipei Municipal TuCheng Hospital, New Taipei City 236, Taiwan
2. Division of Rheumatology, Allergy, and Immunology, Department of Internal Medicine, Chang Gung Memorial Hospital at Linkou, Taoyuan 333, Taiwan
3. Chang Gung University College of Medicine, Taoyuan 333, Taiwan
*通訊作者：劉烈邦醫師
地址：236 新北市土城區金城路二段6號 新北市立土城醫院內科部風濕過敏免疫科

*Correspondence to Dr. Lieh-bang Liou
Corresponding author at: Division of Rheumatology, Allergy and Immunology, Department of Internal Medicine, New Taipei Municipal TuCheng Hospital, No.6, Sec.2, Jincheng Rd., Tucheng Dist., New Taipei City 236, Taiwan (R.O.C.)

Abstract
Background: Interleukin-18 (IL-18) is a proinflammatory cytokine involved in both innate and adaptive immunity. Dysregulation of IL-18 can cause autoimmune or inflammatory diseases. While previous studies report higher IL-18 levels in systemic lupus erythematosus (SLE) patients, its association with SLE disease activity is unclear.
Objectives: This study investigates the associations between IL-18 levels, disease activity in SLE, and various laboratory data.
Methods: Patients meeting the 1997 ACR criteria for SLE were enrolled after providing consent. SLE disease activity index 2000 (SLEDAI-2K) scores and blood and urine samples were collected at the 0th, 3rd, 6th, 9th, and 12th months. Nonparametric statistics and the Mann-Whitney U test were used to analyze the relationships between IL-18, SLEDAI-2K scores, and laboratory data.
Results: From January 2022 to February 2024, 95 SLE patients (11 males, 84 females; age range 24-75 years) were enrolled. IL-18 levels showed an inverse correlation with platelet counts (Spearman rho = -0.108, p = 0.05), but no correlation with SLEDAI scores or other laboratory data (e.g., white blood cell count, C3, C4, anti-dsDNA Ab level, urine protein/creatinine ratio, and urine albumin/creatinine ratio). IL-18 levels were significantly higher in patients with abnormal anti-dsDNA antibody levels compared to those with normal levels (p = 0.049).
Conclusion: IL-18 shows a negative correlation with platelet counts and higher levels in patients with abnormal anti-dsDNA antibody levels, indicating IL-18 may be a potential biomarker for SLE assessment.

Table 1. Demographic and laboratory data of 95 SLE patients at baseline

	Mean ± S.D.	*Range*
Gender (n)	Male : Female = 11 : 84	
Age (years)	48.6 ± 12.9	24-75
WBC (1000/μL)	5.85 ± 2.26	1.8-14.6
Platelets (1000/μL)	234.5 ± 71.7	68-482
C3 (mg/dL)	93.42 ± 21.59	41.1-154.8
C4 (mg/dL)	18.39 ± 9.37	4.5-53.6
Anti-dsDNA Ab (WHO units)	127.18 ± 130.62	6.3-601.2
SLEDAI-2K score	3.76 ± 4.05	0-20

WBC: white blood cell; C3: complement 3; C4: complement 4; Anti-ds DNA Ab: Anti-double stranded DNA antibody; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000.

Table 2. The correlation between plasma IL-18 levels and SLEDAI scores or and various laboratory data in lupus patients.

	Spearman rho.	*P value*
SLEDAI-2K score	−0.037	0.507
C3	−0.046	0.410
C4	−0.001	0.987
Anti-dsDNA Ab	0.082	0.140
WBC	0.008	0.891
Platelets	−0.108	0.050*
UPCR	0.263	0.168
UACR	−0.024	0.717

SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000; C3: complement 3; C4: complement 4; Anti-ds DNA Ab: Anti-double stranded DNA antibody; WBC: white blood cell; UPCR: Urine Protein and Creatinine Ratio; UACR: Urine Albumin and Creatinine Ratio.

Table 3. Comparison of IL-18 levels between individuals with normal and abnormal laboratory data among lupus patients.

Laboratory data (Normal/Abnormal)	*n/n (visits/visits)*	*Mean±SD*	*Range*	*P-value (Mann-Whitney U test)*
C3 (90-180mg/dL/Under)	128/198	1335.2 ± 1149.8/ 1315.7 ±1121.7	311.4-6512.0/ 271.7-6594.3	0.807
C4 (10-40mg/dL/Under or Over)	266/60	1307.2 ± 1094.0/ 1395.3 ± 1290.2	271.7-6512.0/ 433.1-6594.3	0.875
Anti-dsDNA Ab (<92.7 /≧ 92.7)	180/151	1307.9 ± 1198.5/ 1363.9 ± 1117.8	271.7-6512.0/ 394.5-6594.3	0.049*
WBC (≧3 /<3 x10^3/μL)	312/21	1362.4 ± 1185.9/ 924.9 ± 429.4	271.7-6594.3/ 378.6-2022.0	0.072
Platelets (≧ 100 /<100 x10^3/μL)	330/3	1339.2 ± 1161.3/ 844.8 ± 477.9	271.7-6549.3/ 500.4-1390.4	0.286
UPCR (<150 /≧150 mg/g)	7/22	1051.3 ± 667.7/ 1384.3 ± 1604.9	431.3-2044.5/ 394.5-6479.8	0.784
UACR (≧30 /<30 mg/g)	165/75	1371.8 ± 1232.3/ 1257.8 ±993.1	271.7-6594.3/ 375.5-5941.6	0.667

C3: complement 3; C4: complement 4; Anti-ds DNA Ab: Anti-double stranded DNA antibody; WBC: white blood cell; UPCR: Urine Protein and Creatinine Ratio; UPCR: Urine Albumin and Creatinine Ratio.

海報摘要 TCR28

SARS-CoV-2 spike protein triggers systemic lupus erythematosus disease activity by binding human ACE2 and TLR2 to enhance intra-pulmonary apoptosis and autophagy formation

Chrong-Reen Wang[1,2,3], Yi-Cheng Chen[1], Yu-Tung Hsieh[2], Hung-Wen Tsai[4], Ping Lin[3], Ching-Yen Tsai[5], Yu-Chi Chou[6]

[1]Department of Internal Medicine, National Cheng Kung University Hospital. [2]Institute of Basic Medical Sciences, [3]Department of Microbiology and Immunology, [4]Department of Pathology, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, [5]Institute of Molecular Biology, Academia Sinica, [6]Biomedical Translation Research Center, Academia Sinica

SARS-冠狀病毒2之棘蛋白經由結合人類血管收縮素轉化酶2及類鐸受體2促進肺部內細胞凋亡及自體吞噬的形成來引發全身性紅斑狼瘡疾病活性

王崇任[1,2,3]、陳怡成[1]、謝雨彤[2]、蔡弘文[4]、凌斌[3]、蔡青宴[5]、周祐吉[6]

[1]成大醫學院附設醫院內科部、[2]成大醫學院基醫所、[3]成大醫學院微免所、[4]成大醫學院附設醫院病理部、[5]中研院分子生物研究所、[6]中研院生醫轉譯研究中心

Background: SLE pathogenesis involves accelerated cell death to release autoantigens, forming circulating immune complexes with visceral deposition to develop lupus nephritis (LN) and alveolar hemorrhage (AH). ROS (reactive oxygen species) and TLR2-mediated MyD88/TRAF6/NF-κB signaling can cause cell death. Although SARS-CoV-2 infection induces SLE activity, spike protein's roles in enhancing intra-pulmonary cell death to trigger disease flare remain unexplored.

Methods: Blood and urine samples were from SLE patients before and after confirming SARS-CoV-2 infection. CRISPR-Cas6/Csm-SNHG16, lentivirus (LV)-miR-146a, LV-sh-TLR2, LV-sh-TRAF6, LV-sh-miR-146a and SARS-CoV-2-spike/LV-pseudovirus were generated. RAW264.7 macrophages were stimulated with spike protein. A549 pulmonary cells were infected with LV-2019-nCoV-S. Created human-ACE2 transgenic mice received LV-2019-nCoV-S or combined LV-2019-nCoV-S/LV-sh-TLR2 intra-pulmonary delivery before pristane induction to evaluate impact to AH. Pristane-induced LN in human-ACE2 transgenic mice obtained LV-2019-nCoV-S intra-tracheal infusion to investigate influence on glomerulonephritis.

Results: There were lower miR-146a and higher TRAF6 (miR-146a-target molecule), SNHG16 (miR-146a-endogenous RNA), p53, LC3, iNOS, IL-6 and IFN-γ levels after SARS-CoV-2 infection. LV-2019-nCoV-S-infected cells had increased ROS expression and apoptosis/autophagy formation, and lower miR-146a and higher TRAF6, SNHG16, p53, LC3, NF-κB-pp65, iNOS, IL-6 and IFN-γ levels. Increased ROS, NF-κB-pp65, p53, LC3, iNOS, IL-6 and IFN-γ levels in spike protein-stimulated cells were reduced by LV-sh-TLR2 transfection. CRISPR-Cas6/Csm-SNHG16-, LV-miR-146a-, or LV-sh-TRAF6-transfected cells had increased viability. LV-2019-nCoV-S and LV-2019-nCoV-S/LV-sh-TLR2 delivery enhanced and suppressed AH through increasing and decreasing apoptosis/autophagy formation, respectively. LV-2019-nCoV-S infusion aggravated glomerulonephritis with increased proteinuria, autoantibody levels and glomerular proliferation/IgG deposition.

Conclusions: SARS-CoV-2 spike protein triggers SLE disease activity by binding human-ACE2 and TLR2 to enhance intra-pulmonary apoptosis/autophagy formation.

海報摘要 TCR29

Prognosis Assessment of Lupus Nephritis in Systemic Lupus Erythematosus Using Deep Learning

使用深度學習評估系統性紅斑狼瘡腎炎的預後

Lu Deyu[1] Wun-Long Jheng[2], **Feng-Cheng Liu**[3]
盧德宇[1], 鄭文隆[2], **劉峰誠**[3]

[1] School of Medicine, National Defense Medical Center, Taipei 114, Taiwan, R.O.C.
[2] Cancer Center, Buddhist Hualien Tzu-Chi Hospital, Buddhist Tzu-Chi Medical Foundation
[3] Rheumatology/Immunology/Allergy, Tri-Service General Hospital, National Defense Medical Center, Taipei 114, Taiwan, R.O.C.
國防醫學院三軍總醫院風濕免疫過敏科

Abstract:

Background: Lupus nephritis (LN) is a severe complication of systemic lupus erythematosus (SLE), affecting up to 60% of patients. Early diagnosis and intervention are crucial for improving outcomes, but current diagnostic methods rely heavily on invasive procedures. This study aims to develop a non-invasive deep learning model using peripheral blood mononuclear cell (PBMC) phenotypes to predict LN development in SLE patients.

Methods: We prospectively collected PBMC data from 61 SLE patients (X with LN, Y without LN) using multi-color flow cytometry. A deep neural network model was constructed using Keras, with PBMC subtype quantities (including T cells, B cells, and Treg cells) as input features and LN development as the target outcome. The model was optimized using k-fold cross-validation, L2 regularization, and dropout layers. Model performance was evaluated using accuracy, area under the receiver operating characteristic curve (AUC), F1-score, and recall.

Results: The optimized model achieved an accuracy of X%, AUC of Y, F1-score of Z, and recall of W in predicting LN development. Key PBMC subtypes associated with LN development were identified, including [insert specific cell types]. The model demonstrated a sensitivity of X% and specificity of Y% in predicting LN, outperforming traditional clinical markers such as anti-dsDNA antibodies and complement levels.

Conclusions: Our deep learning model shows promise as a non-invasive tool for early LN prediction in SLE patients. This approach could aid in timely intervention and personalized treatment strategies, potentially improving long-term outcomes for SLE patients.

海報摘要 TCR30

Utilizing Machine Learning to Predict Major Adverse Cardiovascular Events in Patients with Systemic Lupus Erythematosus

利用機器學習預測紅斑性狼瘡病人主要心血管事件

Yen-Po Tsao[1], Hao-Min Cheng [2]
曹彥博 [1], 鄭浩民 [2]

[1]Division of Allergy, Immunology and Rheumatology, Department of Medicine, Taipei Veterans General Hospital, Taiwan.
[2]Department of Medical Education, Taipei Veterans General Hospital, Taipei, Taiwan.
[1] 臺北榮民總醫院內科部過敏免疫風濕科
[2] 臺北榮民總醫院教學部

Background
Systemic lupus erythematosus (SLE) is an autoimmune disease involved with disorders in multiple organs. Its pathophysiology has been researched for decades and there is still space for comprehensive investigation. Major comorbidities, such as lupus nephritis, myocardial infarction, or other end organ damage remain important issue in SLE patients. Here we present a new model for disease prediction in patient with SLE, and the occurrence of major adverse cardiovascular event (MACE) is specified.

Method
The clinical data were collected from Taipei Veterans General Hospital during 2009-2020 and were integrated by year and person for machine learning classification model. Clinical data of each year by mean value is set as positive if there is an event of MACE in next 5 years. In total, there are 1873 patients with 4845 samples of row records for SLE subjects with MACE. Missing values of features are calculated and those with high missing values were excluded for feature selection with acceptable sample size. Finally, we included 805 samples from 552 patients with 33 clinical features. Bootstrap was applied to split dataset into 0.8 ratio train set for feature selection as well as model training, and 0.2 ratio test set for model validation. For comparison, 3 models for feature selection were used, with 5 classification models.

Results
Eventually, 31 features for SLE subjects with MACE remained and the top 6 features with highest feature importance were anti-dsDNA, time length of SLE, C-reactive protein (CRP), mean corpuscular hemoglobin concentration (MCHC), Aspartate Transaminase (AST) and estimated glomerular filtration rate measured (eGFRm). Among them, anti-dsDNA and SLE time length manifested particularly high correlation with MACE occurrence, as SLE time length with a negative correlation. After bootstrap with 10 times, we obtained the best mean area under curve (AUC) of 0.783 by 5-fold cross validation under Random Forest for feature selection, with XGBoost as classification model.

Conclusion
The results showed high AUC for prediction of MACE, manifesting definite correlation between clinical data and SLE progression. Clinical record with laboratory data, especially the anti-dsDNA and SLE time length, plays an important role in the assessment for organ failure of SLE subjects. It is worth mentioning that SLE time length is negatively correlated with MACE risk, and this may be an unprecedented finding. These findings could provide clinical importance in caring the lupus patients.

海報摘要 TCR31

Discovery of Genetic Mutations Linked to Lupus Nephritis in a Taiwanese Cohort via Extensive Genetic Screening

John Cheng-Han Lee[1], Kuo-sheng Hung[2], Jia-Huei Lyu[2], Hsiang-Cheng Chen[1], San-Yuan Kuo[1], Shi-Jye Chu[1], Chun-Chi Lu[1], Ya-Chi Li[1], Fu-Chiang Yeh[1], Feng-Cheng Liu[1]

李承翰[1], 洪國勝[2], 呂家慧[2], 陳相成[1], 郭三元[1], 朱士傑[1], 盧俊吉[1], 黎亞綺[1], 葉富強[1], 劉峰誠[1]

[1]*Division of Rheumatology/Immunology/Allergies, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan*

三軍總醫院風濕免疫過敏科

[2]*Center for Precision Medicine and Genomic, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan*

三軍總醫院精準醫學暨基因體中心

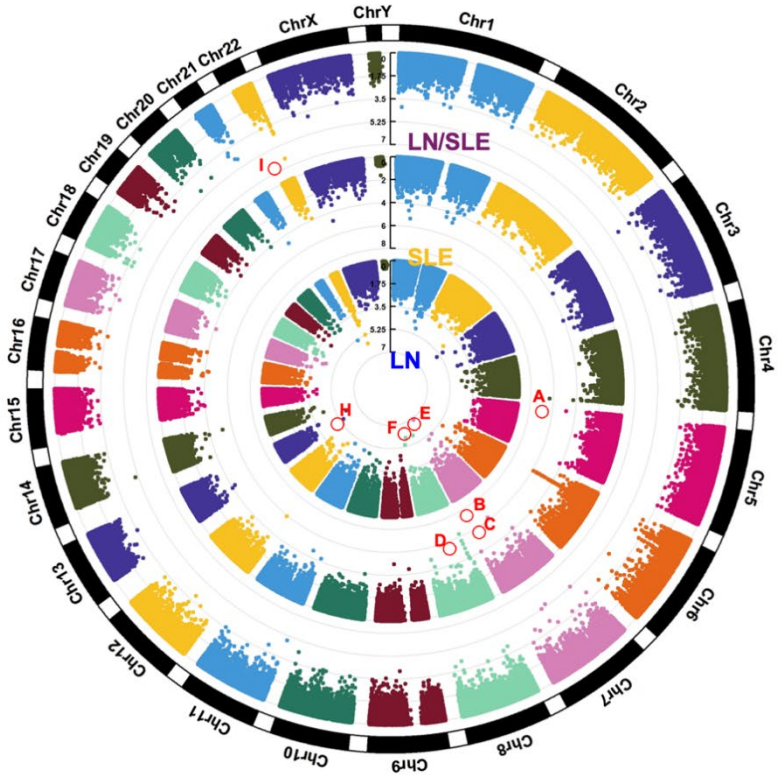
Abstract

Background: Lupus nephritis (LN) is a common manifestation of systemic lupus erythematosus (SLE), affecting about half of the patients. This research uses genotype-phenotype associations to identify genetic markers, enhancing our understanding of LN pathogenesis.

Methods: This study used genotype-phenotype association to explore genetic variants linked to LN in a Taiwanese cohort from the Taiwan Precision Medicine Initiative (TPMI). Genotyping was performed on 244 SLE and 63 LN patients using the TPM array. Genomic DNA underwent quality control via the Axiom Analysis Suite. Chi-squared tests identified significant variants, which were annotated and assessed for functional impacts using the 1000 Genomes Project, gnomAD, and GTEx, enabling comprehensive genetic and expression analysis.

Results: This study on a Taiwanese cohort (LN, SLE, LN/SLE) identified four significant genetic variants (p-values < 10^{-6}) associated with LN: rs1025129 in HGF, rs80282109 in BACH2, rs516119 in SOX1, and rs134545 in TTC28. These variants showed strong effects across various LN classes, particularly class IV (diffuse proliferative), class V (membranous), class VI (advanced sclerosing), class III (focal proliferative)+ IV, and class III + V. Notably, all class III patients had rs80282109 and rs134545, while rs134545 was found in patients across all LN classes. These variants may affect LN pathogenesis through splicing junction changes and gene expression regulation, highlighting their potential as biomarkers.

Conclusions: Our research identified four novel variants (rs134545, rs516119, rs1025129, rs80282109) in LN patients through a genotype-phenotype study on a Taiwanese population, suggesting their roles in LN pathogenesis and supporting their potential as new disease biomarkers.



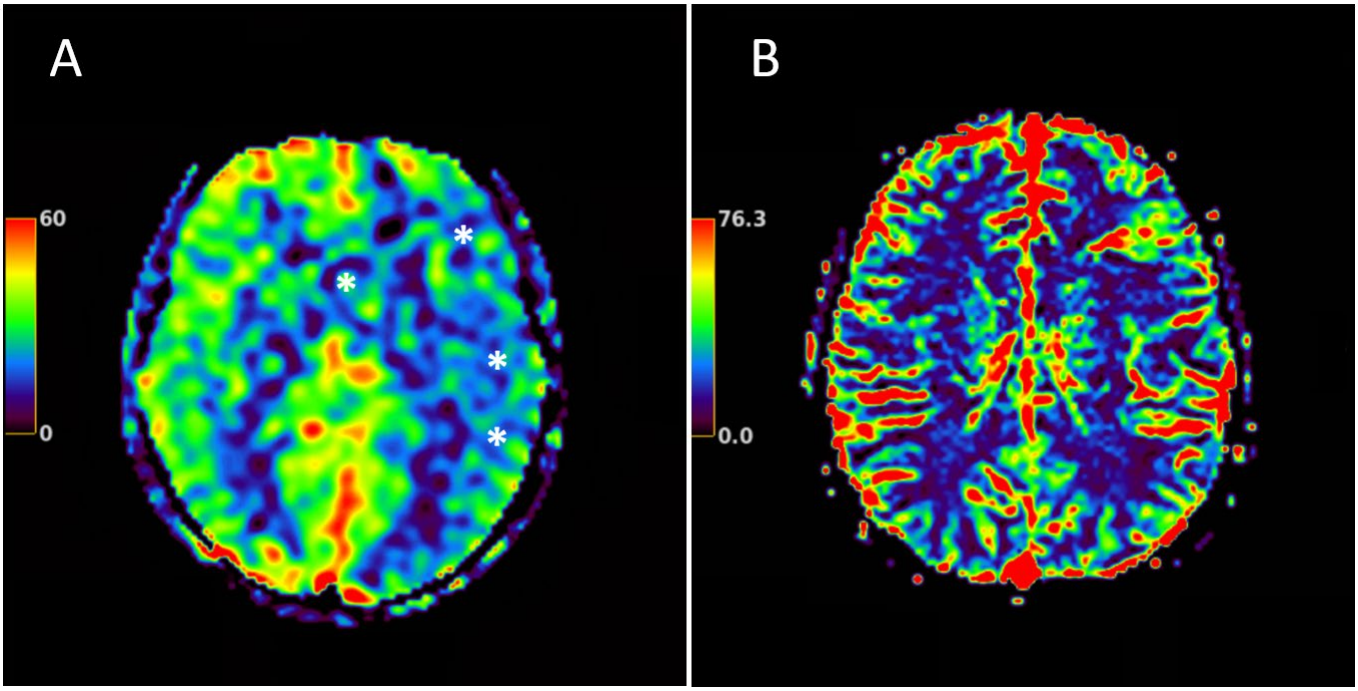
Variant	SNP_ID	Trait
A	rs12508616*	SLE
B	rs117026326*	SLE
C	rs73366469*	SLE
D	rs76267797	SLE
E	rs80282109	LN
F	rs1025129	LN
H	rs516119	LN
I	rs134545	LN/SLE

Figure 1 Manhattan plot of genotype-phenotype association results in four traits.

There were 239,080 variants detected in TSGH TPMI participants through a chi-squared test. Eight highly significant variants were selected according to the *p*-value < 10^{-6} (Bold points A-I on the plot) : rs12508616, rs2027856, rs117026326, rs73366469, rs76267797, rs80282109, rs516119, and rs134545. Variants with star symbol indicate records of associations with SLE in genotype-phenotype association catalog database. Circle from the inside to outside: LN, SLE, and LN/SLE

海報摘要 TCR32

Clinical Images: Early Detection of Brain Ischemia by Perfusion MRI in Neuropsychiatric Systemic Lupus Erythematosus



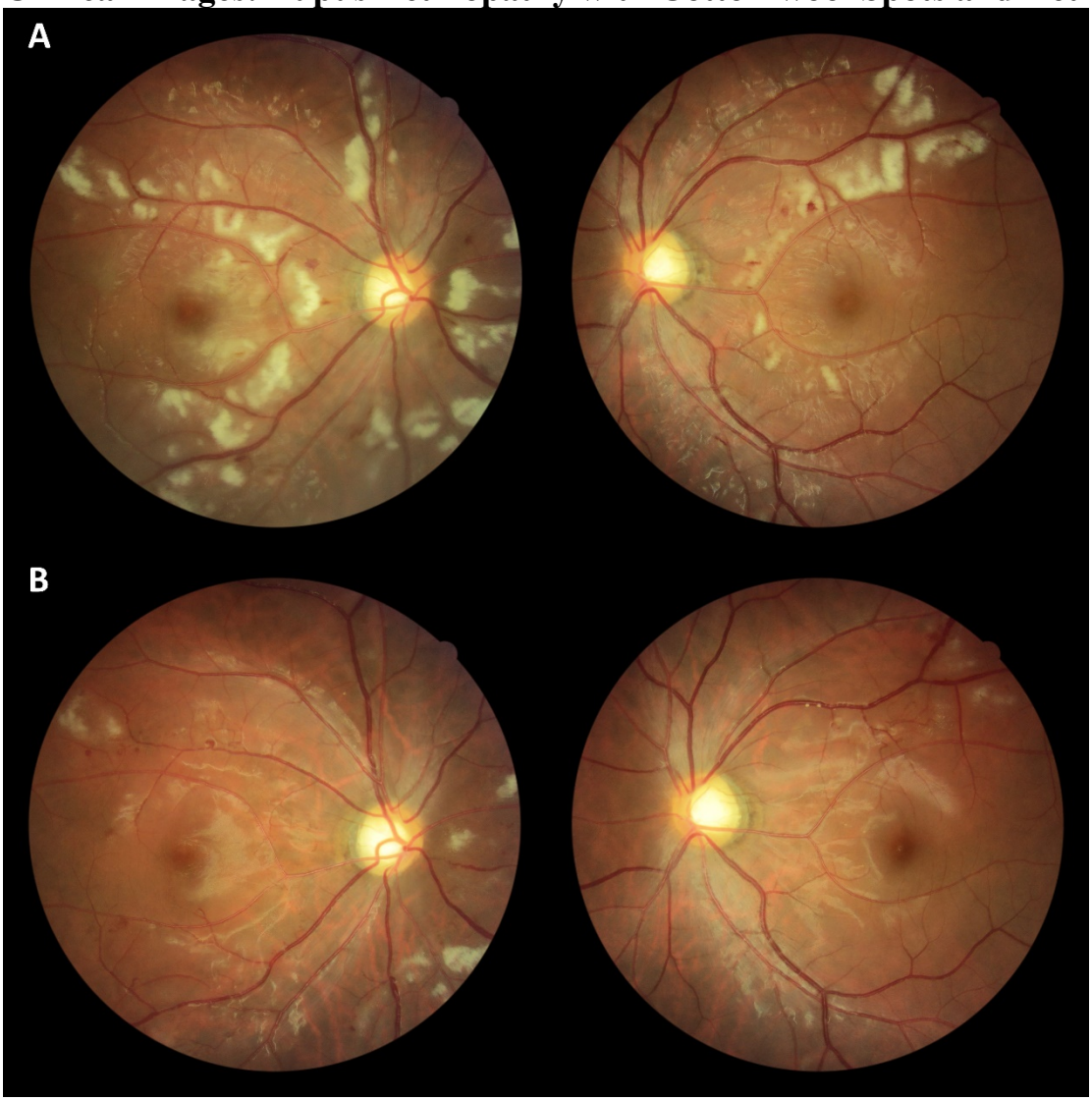
Here we report a case whose perfusion MRI/cerebral-blood-flow mapping facilitates the diagnosis and management. This teenage girl with a history of juvenile myoclonic epilepsy was admitted to neurology service for intermittent headache and visual impairment for six months. Neurologic exams, ophthalmic exams, electroencephalography and cerebrospinal fluid studies were negative. Conventional T1/T2 images, diffusion-weighted images of brain MRI and MR angiography were unremarkable. However, cerebral-blood-flow mapping (Fig. A) revealed ischemic changes (areas in blue color, asterisk) over left frontal, parietal, and paramedian regions.

Subsequent evaluation shows isolated prolongation of activated-prothrombin time (45s (<32.6)) and false-positivity of VDRL. Autoimmune testing shows elevated serum immunoglobulin with polyclonal gammopathy, positive antinuclear antibody (1:160 AC-1, 1:1280 AC-4), anti-Ro/La, Lupus anticoagulant (1.86) and anticardiolipin antibodies (IgG 39U/mL, IgM 20.7U/mL) and malar rashes at her cheeks. SLE with antiphospholipid syndrome was impressed. Hydroxychloroquine, glucocorticoid and Aspirin were prescribed, followed by Rituximab/Belimumab. At one year, she was symptom-free. Symmetry of perfusion was restored, and global perfusion increased on sequential cerebral-blood-flow mapping (Fig. B, yellow and orange area).

Pei-Ying, Wu, Li-Heng Huang, Ko-Jen Li
吳佩盈,黃立恒,李克仁
Division of allergy, immunology and rheumatology, department of internal medicine,
National Taiwan University Hospital, Taipei, Taiwan
國立臺灣大學醫學院附設醫院 風濕免疫過敏科

海報摘要 TCR33

Clinical Images: Lupus Retinopathy with Cotton-wool Spots and Retinal Hemorrhages



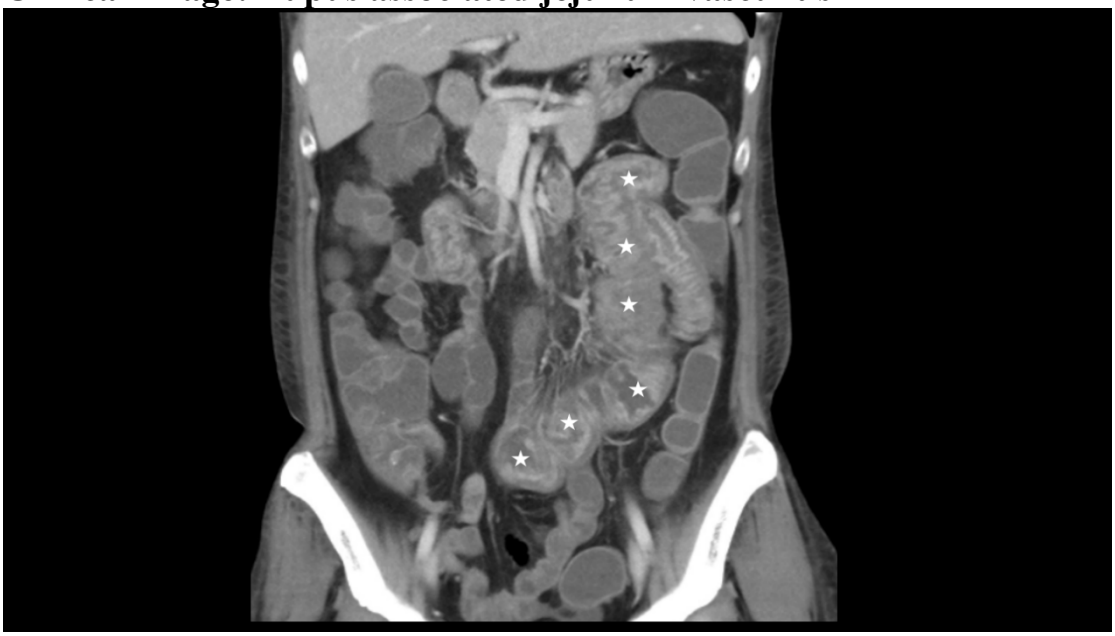
A 24-year-old man with newly diagnosed systemic lupus erythematosus presented primarily with cutaneous involvement and proximal muscle weakness. He also reported blurred vision in both eyes for the past 2 months, with the right eye affected more severely than the left. Color fundus photography revealed multiple cotton-wool spots and retinal hemorrhages located at the nasal macula, as well as along the superior and inferior arcades in the right eye (A). Similar findings of cotton-wool spots and retinal hemorrhages were observed along the superior arcade in the left eye (A). The diagnosis of lupus retinopathy was made.

The patient underwent monthly cyclophosphamide pulse therapies followed by a gradual tapering of prednisolone. Over the subsequent 3 months, follow-up color fundus photography showed significant improvement in retinal findings, with regression of cotton-wool spots and resolution of retinal hemorrhages in both eyes (B).

Jheng-Wei Lin, MD
林政緯
National Taiwan University Hospital, Taipei, Taiwan
國立臺灣大學醫學院附設醫院

海報摘要 TCR34

Clinical Image: Lupus associated jejunum vasculitis

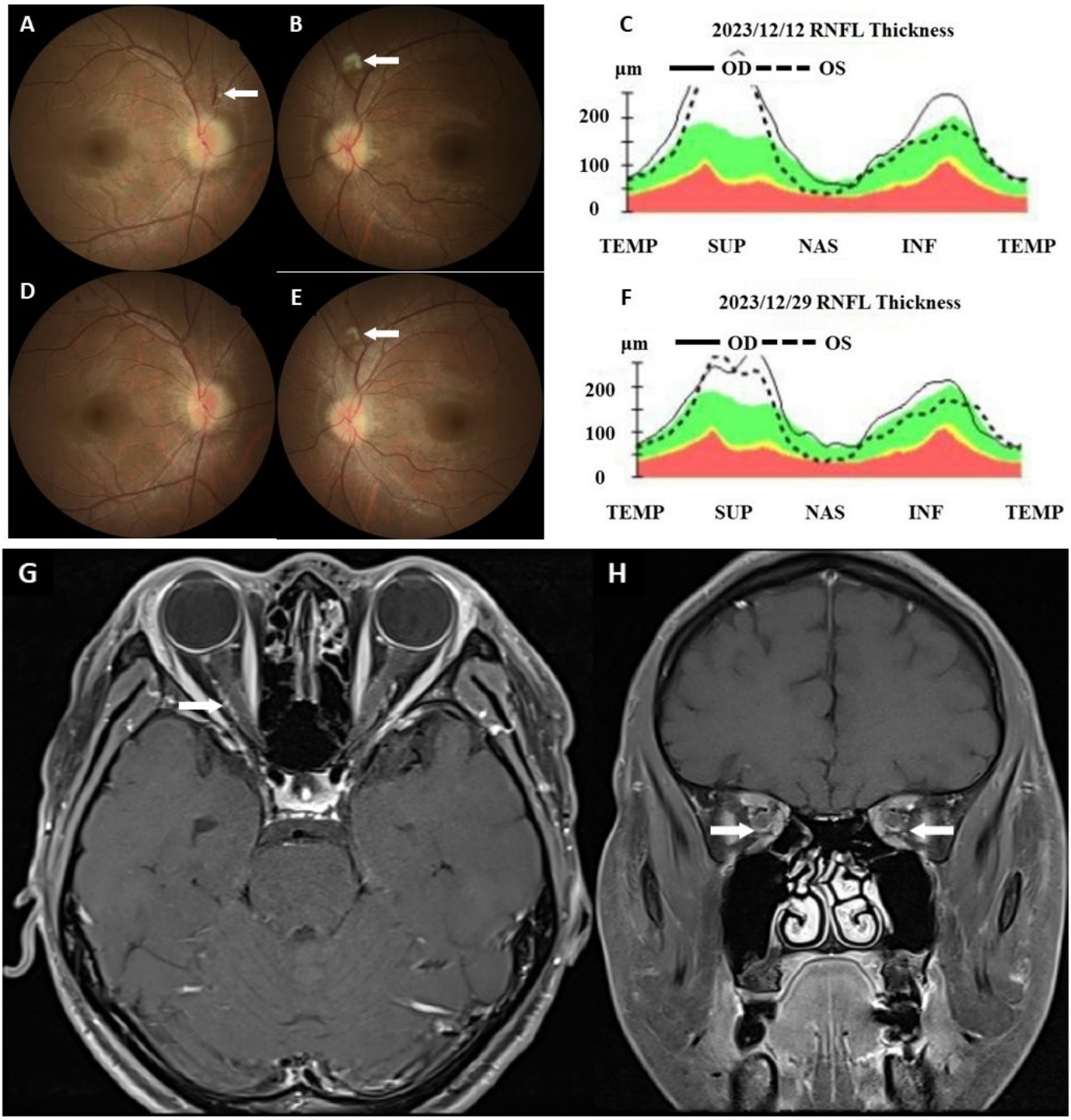


The patient, a 35-year-old female patient with 5-year history of systemic lupus erythematosus, was admitted for progressive left-middle abdominal pain with watery and blood-tinged stool since 3 days ago. Computed tomography of the abdomen revealed severe long-segmental concentric wall thickening of jejunum with submucosal edema, showing the “Rigler sign” (**asterisks**), but neither bowel ischemia nor perforation was found. Lupus related acute jejunum vasculitis was diagnosed.

Hsien-Tzung Liao, MD, PhD
廖顯宗
Taipei Veterans General Hospital, Taipei, Taiwan
臺北榮民總醫院 過敏免疫風濕科

海報摘要 TCR35

Clinical Images: Optic Perineuritis (OPN) in a Patient with Systemic Lupus Erythematosus

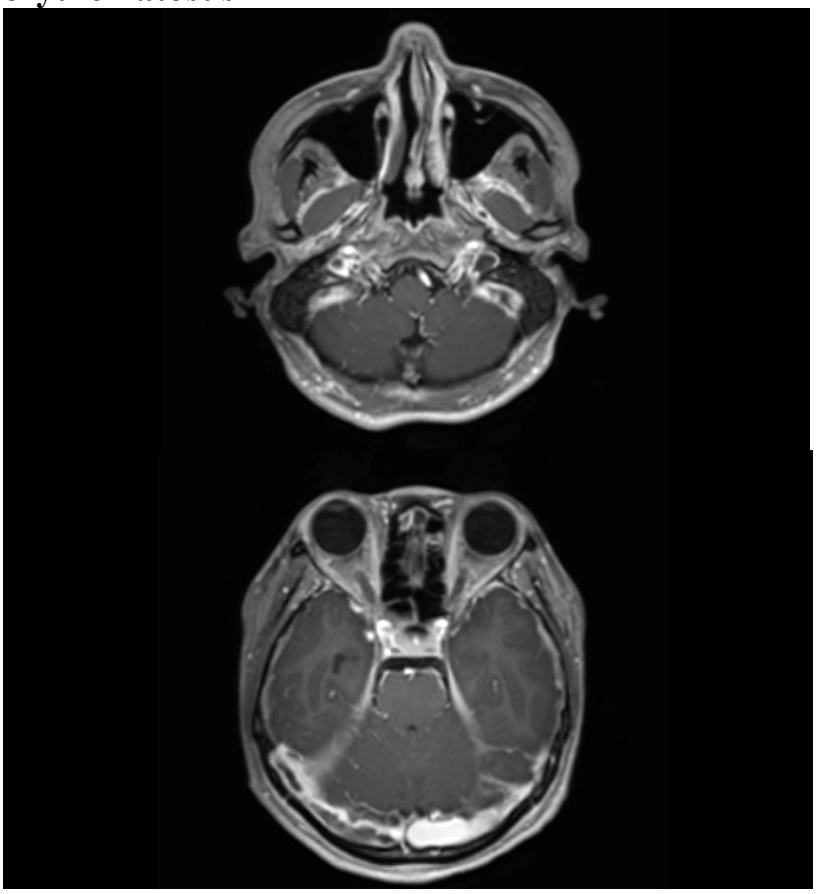


A 27-year-old lady has a history of systemic lupus erythematosus with chronic inflammatory demyelinating polyradiculoneuropathy, hypertension, hyperlipidemia, and gouty arthritis. She presented with redness, fullness, tearing and photophobia at her eyes and facial swelling for 3 days. Physical exam showed increased congestion, episcleral vessel, and mild chemosis at her eyes. Grade 3 disc edema was found at right eye with retinal hemorrhage (white arrow on Figure A) and grade 2 disc edema was found at left eye with cotton wool spot (white arrow on Figure B). An optical coherence tomography (OCT) showed increased thickness of retinal nerve fiber layer (Figure C). Neither intracranial lesion nor dilated ventricle was found by a computed tomography (CT) of brain. A magnetic resonance imaging (MRI) of orbits, with administration of intravenous gadolinium, showed contrast enhancement of the optic nerve sheath on T1 image (white arrow on Figure G & H), which was compatible with optic perineuritis (OPN). She received 31.25 minigames of intravenous methylprednisolone twice a day for a week and her symptoms improved. An ophthalmoscope exam showed no retinal hemorrhage at her right eye (Figure D) and less cotton wool spot at her left eye (white arrow on Figure E). An OCT for follow-up showed improving thickness of retinal nerve fiber layer (Figure F).

Shio-Yi Liao, MD, Ming-Han Chen,MD, Chien-Chih Lai, MD
廖修誼, 陳明翰, 賴建志
Taipei Veterans General Hospital, Taipei, Taiwan
臺北榮民總醫院

海報摘要 TCR36

Clinical Images: Cerebral sinus thrombosis in a patient with systemic lupus erythematosus



This 33-year-old woman visited the emergency room due to a severe headache for three days. A fever of up to 38.3 ℃ was also noted at the triage. Laboratory studies showed anemia, thrombocytopenia, elevated ESR, prolonged aPTT, and elevated creatinine levels with heavy proteinuria. Chest X-ray revealed left lingual lobe consolidation and brain computed tomography (CT) showed subdural effusion. Admission was arranged for further evaluation. Autoimmune workup showed normal complement levels, borderline ANA, negative anti-dsDNA, anti-Sm/RNP, and anti-ribosomal-P IgG. pANCA, anti-β2-GP1 IgG, anti-cardiolipin IgG, and lupus anticoagulant were positive. Pulse glucocorticoid therapy of 500mg was given for 3 days, followed by 500mg of rituximab. Bruising of the right eyelid was noted on the fifth day after admission and binocular diplopia was complained of two days later. Magnetic resonance imaging (MRI) of the brain revealed diffused thrombosis over the right transverse sinus, bilateral sigmoid sinuses, and bilateral internal jugular veins. Increased intracranial pressure (IICP) and cerebral vein thrombosis were suspected to be the cause of the acute visual symptoms.

Ting-Hui, Chang, MD
張婷惠
Shih-Chi, Chen, MD
陳仕淇
Far Eastern Memorial Hospital,
New Taipei City, Taiwan
亞東紀念醫院

海報摘要 TCR37

Clinical features and outcomes of neuromyelitis optica spectrum disorders in patient with autoimmune diseases

Hung-Cheng Tsai[1,2], Ying-Ying Yang[3,5], Wei-Sheng Chen[1,2], Ming-Han Chen[1,2], Chang-Youh Tsai [2,5], Hsien-Tzung Liao[1,2,6]

[1]Division of Allergy, Immunology & Rheumatology, Department of Medicine, Taipei Veterans General Hospital, Taipei (台北榮民總醫院內科部過敏免疫風濕科)

[2]Faculty of Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei (國立陽明交通大學醫學院)

[3]Institute of Clinical Medicine, National Yang-Ming Chiao Tung University Taipei Campus, Taipei （國立陽明交通大學臨床醫學研究所)

[4]Division of Immunology & Rheumatology, Fu Jen Catholic University Hospital, School of Medicine, Fu Jen Catholic University, New Taipei City, Taiwan (天主教輔仁大學過敏免疫風濕科)

[5]Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan (台北榮總內科部肝膽腸胃科)

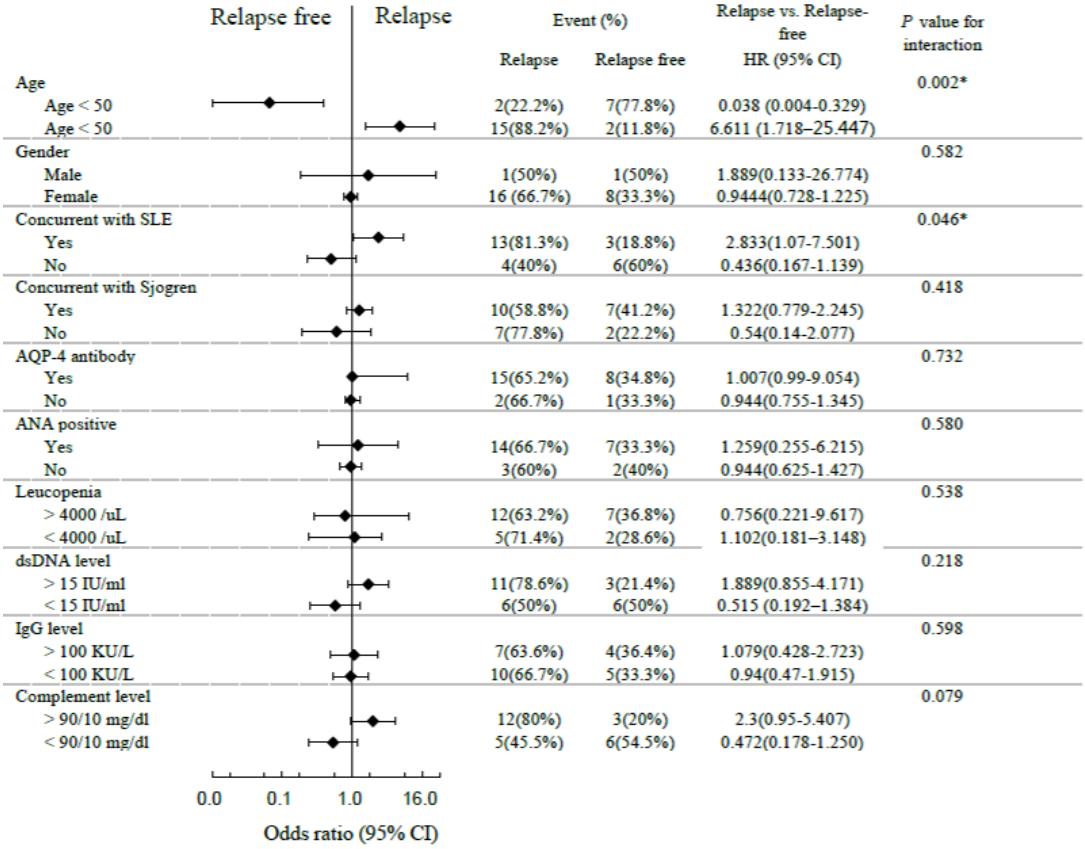
[6]Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan.
(台北醫學大學過敏免疫風濕科)

Objective:
Neuromyelitis optica spectrum disorder (NMOSD) is a rare immune-mediated disorder affecting the spinal cord and optic nerves. While individual NMOSD cases have been extensively studied, less is known about the subset associated with autoimmune diseases (AD-NMOSD), particularly in Asian patients. Furthermore, specific studies on relapse and prognostic factors in AD-NMOSD are lacking.

Method:
From January 2008 to December 2023, a total of 71 cases of NMOSD were confirmed through a review of the electronic medical records database at Taipei Veterans General Hospital. Their clinical features, laboratory findings, concurrent autoimmune diseases, imaging findings, and treatments were comprehensively analyzed. Patients were stratified based on their relapse status and the presence of severe sequelae.

Result:
Among 71 NMOSD patients, 26 had concurrent autoimmune diseases. 16 (62%) had systemic lupus erythematosus (SLE), 8 (30%) had primary Sjogren syndrome (SjS), and 1 (4%) had ankylosing spondylitis (AS) overlapping with SjS, and one (4%) was rheumatoid arthritis (RA). Onset age <50 years old (OR=6.61, p=0.02*), concurrent SLE (OR=2.833, p=0.046*), and SLE precedes NMOSD and lasts longer (p=0.04*) are risk factors for NMOSD relapses. Low complement 3 (C3) level was more common in severe sequelae. The recurrence frequency remained strongest risk factor for severe complications in both univariate and multivariate analysis (OR=3.16, p=0.04*) and multivariate analysis (OR=5.49, p=0.046*).

Conclusion:
In Asian AD-NMOSD, SLE preceding NMOSD and younger onset age (<50 years) coupled with concurrent SLE increase relapse risk. Recurrence frequency is a key determinant of poor prognosis.



	Event (%)		Relapse vs. Relapse-free	*P* value for interaction
	Relapse	Relapse free	HR (95% CI)	
Age				0.002*
Age < 50	2(22.2%)	7(77.8%)	0.038 (0.004-0.329)	
Age < 50	15(88.2%)	2(11.8%)	6.611 (1.718–25.447)	
Gender				0.582
Male	1(50%)	1(50%)	1.889(0.133-26.774)	
Female	16 (66.7%)	8(33.3%)	0.9444(0.728-1.225)	
Concurrent with SLE				0.046*
Yes	13(81.3%)	3(18.8%)	2.833(1.07-7.501)	
No	4(40%)	6(60%)	0.436(0.167-1.139)	
Concurrent with Sjogren				0.418
Yes	10(58.8%)	7(41.2%)	1.322(0.779-2.245)	
No	7(77.8%)	2(22.2%)	0.54(0.14-2.077)	
AQP-4 antibody				0.732
Yes	15(65.2%)	8(34.8%)	1.007(0.99-9.054)	
No	2(66.7%)	1(33.3%)	0.944(0.755-1.345)	
ANA positive				0.580
Yes	14(66.7%)	7(33.3%)	1.259(0.255-6.215)	
No	3(60%)	2(40%)	0.944(0.625-1.427)	
Leucopenia				0.538
> 4000 /uL	12(63.2%)	7(36.8%)	0.756(0.221-9.617)	
< 4000 /uL	5(71.4%)	2(28.6%)	1.102(0.181–3.148)	
dsDNA level				0.218
> 15 IU/ml	11(78.6%)	3(21.4%)	1.889(0.855-4.171)	
< 15 IU/ml	6(50%)	6(50%)	0.515 (0.192–1.384)	
IgG level				0.598
> 100 KU/L	7(63.6%)	4(36.4%)	1.079(0.428-2.723)	
< 100 KU/L	10(66.7%)	5(33.3%)	0.94(0.47-1.915)	
Complement level				0.079
> 90/10 mg/dl	12(80%)	3(20%)	2.3(0.95-5.407)	
< 90/10 mg/dl	5(45.5%)	6(54.5%)	0.472(0.178-1.250)	

Figure 1: Forest plot showing odds ratios for relapse or relapse-free outcomes.

海報摘要 TCR38

Chronic Fibrosing Organizing Pneumonia as an Early Manifestation of Aquaporin-4 Antibody-Positive Neuromyelitis Optica Spectrum Disorder: A Unique Case Presentation

I-Ping Lee[1], Chin-Fang Su[1]
李苡萍, 蘇勤方
1. Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, Shuang Ho Hospital, Taipei Medical University
衛生福利部雙和醫院

Background

Organizing pneumonia (OP) is an infrequent extra-neurological manifestation associated with Aquaporin-4 antibody (AQP4)-positive neuromyelitis optica spectrum disorder (NMOSD). It may precede or occur concurrently with NMOSD diagnosis. We present a case involving progressive fibrosing OP preceding the onset of NMOSD.

Case presentation

A 68-year-old non-smoking female was admitted with a 2-week history of progressive respiratory distress, non-productive cough, and weight loss. Chest CT revealed scattered patchy opacities indicative of OP (Figure A). Bronchoalveolar lavage was negative for microbiology and cytology. Despite partial improvement with empirical antibiotics, outpatient follow-up revealed progression of consolidation resistant to oral prednisolone. Three months later, the patient developed paresthesia, lower limbs weakness, and urinary retention. Neurological examination disclosed sensory deficits at T2 and muscle weakness (grade 1/5) in the lower limbs. Lumbar puncture disclosed elevated protein, without pleocytosis, oligoclonal bands, or evidence of infection. Brain MRI showed no abnormalities, but spine MRI indicated longitudinally extensive transverse myelitis (Figure C). AQP4 antibody was positive, with negative results for antibodies to MOG, SSA, SSB, ds-DNA, Sm, RF, CCP, ANCA, and myositis specific antibodies. A diagnosis of AQP4-antibody-positive NMOSD was made. Concurrently, progressive fibrosing OP was observed (Figure B). Treatment with pulse corticosteroids, plasma exchange, and rituximab led to partial neurological recovery and improvement of pulmonary involvement. Maintenance therapy with azathioprine ensured sustained improvement.

Conclusion

Rheumatologists play a pivotal role in multidisciplinary approach to interstitial lung disease. Consideration of AQP4 antibody testing is crucial in the evaluation of interstitial pneumonia with autoimmune features, particularly cases presenting with OP.

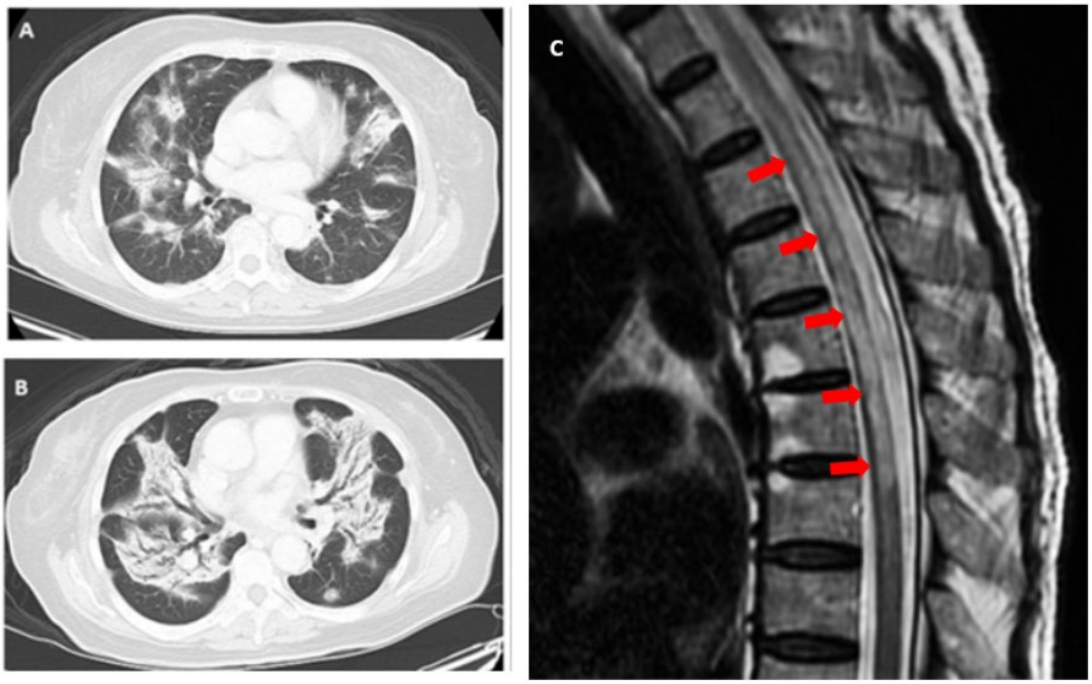


Figure A: Chest CT revealing peri-bronchial patchy consolidation in bilateral lungs, indicative of organizing pneumonia. B: Chest CT illustrating progressive fibrosing organizing pneumonia. C: T2-weighted MRI imaging displaying an intramedullary lesion with high signal intensity, suggestive of acute transverse myelitis