Poster Round 海報目錄

時 間:113年12月14日(星期六)10:45-11:10

地 點:新竹喜來登大飯店 3F 海報區

主持人:余光輝醫師

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HDAC6 suppression is associated with sarcopenia in RA patients by up-regulation of PLIN2 and the P53 pathway

Authors: <u>Tzu-Jung Fang</u>^{1,2}, Min-Hsi Chiu^{3,4}, Ming-Shyan Huang^{5,6}, Yao-Tsung Yeh^{3,4,*}, Jeng-Hsien Yen^{7,8,9}

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Background: The prevalence of sarcopenia in people with RA is twice that in people without RA. The expression of Histone deacetylases 6 (HDAC6) in RA patients was lower than controls and associated with sarcopenia without uncertain mechanism.

Methods: We extracted peripheral blood mononuclear cell DNA and RNA from the 69 RA patients and 57 controls. The quantitative real-time PCR of HDAC6 and PLIN2 was performed. We treated tubacin (HDAC6 inhibitor) on C2C12 myotubes. The western blot were done to check the myogenin, HDAC6, PLIN2, p53 and caspase-3 from the treated myotubes. Then, we performed oil red stain, immunofluorescent stating, and β -Galactosidase staining on the treated myotubes. The Fluorescence Activated Cell Sorting(FACS) analysis was performed to check the cell cycle.

Result: The RA patients with sarcopenia had the lowest HDAC6 and the highest PLIN2 mRNA expression levels. The fluorescence microscopy showed that the PLIN2 increased in those myotubes treated by HDAC6 inhibitor (tubacin). Treatment C2C12 myoblast cell by tubacin significantly increased the expression of p53 and Caspase-3. HDAC6 inhibitor treatment induced cell cycle arrest in the C2C12 myotube, but not via the apoptosis.

Conclusion: We found the decreased HDAC6 and increased PLIN2 mRNA expression in RA patients with sarcopenia. While suppressing the HDAC6 in muscle cells, the PLIN2 raised and induced lipid droplet formation in myotubes. Besides, the myogenesis was suppressed. HDAC6 down-regulation in the muscle cells increased P53 and the caspase-3 in protein level. The myotubes cell cycle arrest and cell senescence may contribute to sarcopenia in RA patients.

Anti-SNRK and anti-HUWE1 antibodies as the potential biomarkers for predicting good response to tofacitinib therapy in rheumatoid arthritis patients Der-Yuan Chen^{1,2}, Yi-Ming Chen^{3,4}, Jeremy JW Chen^{4,5}, Po-Ku Chen^{1,2} ¹Rheumatology and Immunology Center, China Medical University Hospital; Taiwan ²College of Medicine, China Medical University, Taiwan ³Department of Medical Research, Taichung Veterans General Hospital, Taiwan ⁴College of Medicine, National Chung Hsing University, Taiwan; ⁵Institute of Biomedical Sciences, National Chung Hsing University, Taiwan SNRK 及 HUWE1 胜肽抗體可預測類風濕關節炎患者對於捷抑炎療效良好的可行生物標誌 陳得源,陳一銘,陳健尉,陳柏谷 中國醫大附醫風濕免疫中心、中國醫大醫學院、中榮醫研部、中興大學醫學院、中興大學生醫所

Background: To achieve a treat-to-target goal and maximize cost-effectiveness of tofacitinib, one of Janus kinase inhibitors (JAKi), there is an unmet need to identify predictors of therapeutic response to tofacitinib. Utilizing phage immunoprecipitation sequencing (PhIP-Seq), we aim to identify the predictors of good response tofacitinib therapy in rheumatoid arthritis (RA) patients.

Materials and Methods: A total of 107 RA patients who had received 24-week tofacitinib therapy were enrolled. Disease activity was assessed using the 28-joint disease activity score-erythrocyte sedimentation rate (DAS28-ESR), and therapeutic response at week 24 was evaluated using EULAR response criteria. The PhIP-Seq results were validated with enzyme-linked immunosorbent assay (ELISA) and replicated in another independent cohort. Plasma levels of caspase-1, IL-6, IL-10, and IL-18 were determined by ELISA.

Results: PhIP-Seq analysis identified antibodies to sucrose non-fermenting-related kinase (SNRK) and HUWE1 (the ubiquitin E3 ligase) as significant biomarkers for discriminating good therapeutic response from poor response. With ELISA for validation, an optimal cut-off value of SNRK for predicting good response was 0.381, with AUC of 0.823, specificity of 80.6%, and sensitivity of 78.1% (p=3.01E-07), and HUWE1 at cut-off of 0.362, with AUC of 0.740, specificity of 74.2%, and sensitivity of 62.5% (p<0.001). Plasma levels of anti-HUWE1 antibody were positively correlated with plasma levels of caspase-1 and IL-18 (both p<0.05). **Conclusion**: We firstly identify two novel peptide antibodies, anti-SNRK and anti-HUWE1 antibodies, as the predictors of good therapeutic response to tofacitinib in RA patients. Significant correlation between anti-HUWE-1 antibody levels and caspase-1 or IL-18 levels support an involvement of HUWE1 in inflammasome activation.

[The summary is illustrated in a figure in the next page]



Figure. Study design/workflow and clinical application of plasma anti-SNRK and anti-HUWE1 antibodies in predicting good EULAR response to tofactinib therapy in patients with rheumatoid arthritis. Patients who have >1.2 decreases of DAS28 from baseline (Δ DAS28) and DAS28 \leq 3.2 at evaluation time were considered the good responders. PhIP-Seq: phage immunoprecipitation sequencing; ELISA: enzyme-linked immunosorbent assay; SNRK: SNF-related serine/threonine-protein kinase; HUWE1: E3 ubiquitin-protein ligase-1.

Real-World Effectiveness of Upadacitinib for Achieving and Maintenance of Remission in Patients With Moderate-to-Severe Rheumatoid Arthritis: Data from the Taiwan Cohort of the UPHOLD Study

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ABSTRACT

Background:

Despite the efficacy and safety of Upadacitinib (UPA) being evaluated in clinical trials in patients with moderate-to-severe rheumatoid arthritis (RA), ¹⁻³ the real-world (RW) data are limited.

Methods:

This interim analysis of the Taiwan cohort from UPHOLD (NCT04497597) included data from October 16, 2020, to August 10, 2023. Co-primary endpoints were the proportion of patients achieving DAS28(CRP) remission (<2.6) at 6-months and maintaining remission at 12-months (or had a \leq 0.6-point increase in DAS28[CRP]). DAS28(CRP) remission and low-disease-activity (LDA) were analyzed by modified non-responder imputation ([mNRI]: discontinuations for any reason before the pre-specified timepoints were treated as non-responders in modified full analysis set [mFAS]1* and mFAS2, and as observed (AO) in patients with non-missing data). Safety of UPA data was assessed in all patients receiving \geq 1 UPA dose. **Results:**

From the full analysis set (N=76), 17 did not complete the full 6-month treatment or had missing data at 6-months (mFAS1=59). 50.8% (mNRI) and 55.6% (AO) achieved DAS28(CRP) remission at 6-months, and of those, 77.3% (both mNRI and AO) maintained remission at 12-months (Figure 1). Improvements in patient-reported outcomes were observed at 6 and 12 months. There were 99 treatment-emergent adverse event (TEAE) of interest (97.69 E/100PY), with exposure-adjusted-event-rates (EAER) for herpes zoster and serious infection of 8.88 and 2.96 E/100PY (Figure 2).

Conclusion:

The Taiwan cohort of the UPHOLD study supports the effectiveness of UPA 15 mg QD for the treatment of moderate-to-severe RA in RW practice with consistent benefit-risk profile as phase 3 clinical trial data.

*Modified full analysis set-1 (mFAS1) includes all patients within the mFAS who completed 6 months of upadacitinib treatment and had DAS28-CRP data available, and who discontinued the study before 6 months for any reason; modified full analysis-2 (mFAS2) includes all patients within mFAS1 who achieved remission at month 6 and have completed 12-month treatment with upadacitinib in the study, and have DAS28-CRP data available at month 12.

References

- 1. Conaghan PG, et al. Drug Saf 2021;44:515–30
- 2. Cohen, Stanley B., et al. Ann Rheum Dis 2021; 80:304-311.
- 3. van Vollenhoven, R, et al. Arthritis Rheum 2020; 72:1607-1620.

Figure 1. Achievement and Maintenance of DAS28(CRP) Remission (< 2.6) and LDA (≤3.2) in Patients with Moderate-to-Severe RA Treated With UPA 15 mg (mNRI and AO)



^aThe proportion of patients with the mFAS1 as the denominator. ^bThe proportion of patients maintaining remission at 12 months with the mFAS2 as the denominator. ^cThe proportion of patients maintaining LDA at 12 months is calculated using the number of patients within mFAS1 who achieved LDA at month 6 and have completed 12-month treatment with UPA in the study, and have DAS28(CRP) data available at month 12 visit or who discontinued the study prematurely between month 6 and month 12 with non-missing data as the denominator. AQ, as observed; DAS28(CRP), disease activity score 28-joint count C reactive protein; LDA, low disease activity; mFAS, modified full analysis set; mNRI, modified non-responder imputation; UPA, upadacitinib.

Figure 2. Safety of Upadacitinib 15 mg in RA Patients*



*Safety was assessed based on all TEAEs occurring in the FAS by the cutoff date of August 10, 2023. **Excluding tuberculosis and herpes zoster E, events; EAER, exposure-adjusted event rates; CI, confidence interval; MACE, major cardiovascular event; PY, patient-years; RA, rheumatoid arthritis; TEAE, treatment-emergent adverse events; UPA, upadacitinib

Deep Learning Analysis of PBMC Immunophenotype for Early Diagnosis of Rheumatoid Arthritis 周邊血單核球免疫表型的深度學習分析用於類風濕性關節炎的早期診斷 Pete Hsu¹ Wun-Long Jheng², <u>Feng-Cheng Liu³</u> 許丕澤¹, 鄭文隆², <u>劉峰誠³</u>

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Abstract:

Background: Early diagnosis of rheumatoid arthritis (RA) remains challenging due to limitations in current diagnostic criteria and the heterogeneous nature of the disease. This study aims to develop a deep learning model using peripheral blood mononuclear cell (PBMC) immunophenotype data for early RA diagnosis, potentially facilitating timely intervention and improved patient outcomes.

Methods: PBMC samples from 230 individuals (RA patients and healthy controls) were analyzed using multicolor flow cytometry. A deep learning model was constructed using TensorFlow and Keras to analyze 106 immunophenotype features. Model performance was rigorously evaluated using accuracy, F1 score, AUC, sensitivity, and specificity. Cross-validation was employed to ensure model robustness.

Results: The deep learning model achieved [insert performance metrics] in the test set. Key immunophenotype markers associated with RA were identified using Boruta and ANN importance analysis, providing insights into disease pathogenesis and potential therapeutic targets.

Conclusion: Our deep learning approach offers a promising tool for early RA diagnosis, potentially improving patient outcomes through earlier intervention. Future studies should focus on prospective validation in diverse patient cohorts and integration with clinical and serological data for enhanced diagnostic accuracy.

Discovering the genetic basis of rheumatoid arthritis in Taiwan: a detailed analysis of variants and their functional impacts

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Background: Rheumatoid arthritis (RA) is a multifactorial autoimmune disease with largely unknown genetic factors and significant regional variations. This study explored the genetic determinants of RA through an indepth genome-wide association study (GWAS) on a cohort from Tri-Service General Hospital in Taiwan.

Methods: We collected genotyping data from the Taiwan precision medicine initiative (TPMI), with genome typing conducted using the TPM array. The initial analysis involved stringent quality control measures and variant identification, paving the way for subsequent fine-mapping, structural modeling, and functional impact prediction analyses.

Results: We analyzed a dataset comprising 29,094 control individuals and 699 RA patients, identifying 472,245 genetic variants. Notably, the examination of chromosome 6 revealed 188 variants significantly associated with RA, each with *p*-values $< 10^{-7}$. Among these, 16 variants were found within the exonic regions of the *HLA-DQB1*, *HLA-DQA1*, *BTNL2*, and *NOTCH4* genes. Focused analysis revealed that four variants (rs2071282, rs41441651, rs707952, and rs9272785) demonstrated exceptionally high posterior inclusion probabilities (PIPs). Specifically, these variants included nonsynonymous mutations rs2071282 (p.P204L), rs41441651 (p.D336N), rs707952 (p.T130I), and rs9272785 (p.A210T), located in the EGF-CA domain of *NOTCH4* and the Ig domains of *HLA-DQA1* and *HLA-DQB1*. Structural and functional assessments provided detailed insights into the specific effects of these genetic variants within the Taiwanese population.

Conclusion: Our study elucidated RA genetics in Taiwanese individuals by identifying 16 exonic variants in *HLA-DQB1*, *HLA-DQA1*, *BTNL2*, and *NOTCH4*, including 5 novel variants. Notably, four variants with high PIP scores exhibited nonsynonymous mutations, providing significant insights into the genetic basis of RA.

Anti-NMDA Receptor Encephalitis in a Patient with Rheumatoid Arthritis Receiving Biologics Treatment

接受生物製劑治療的類風濕性關節炎患者出現抗 NMDA 受體腦炎

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Abstract

A 44-year-old woman with a history of hypertension, type 2 diabetes mellitus, and rheumatoid arthritis under treatment with etanercept presented with progressive altered behavior and acute convulsions. Initial workup revealed leukocytosis and hyponatremia. Different diagnoses include septic encephalitis, lupus encephalitis, or other immune encephalitis. Despite initial treatment, she exhibited signs of autoimmune encephalitis confirmed by positive NMDAR antibodies in CSF. Comprehensive management, including IVIG, plasma exchange, and steroids, led to significant improvement in psychiatric symptoms. This case underscores the importance of considering autoimmune encephalitis in patients with new-onset psychiatric and neurological symptoms, particularly in those with underlying autoimmune conditions.

Introduction

Autoimmune encephalitis is a severe inflammatory condition of the brain often characterized by psychiatric and neurological symptoms. Early recognition and treatment are crucial for improving outcomes. This report describes the case of a 44-year-old woman with multiple chronic conditions, including rheumatoid arthritis (received DMARDs and etanercept), who developed limbic encephalitis, highlighting the diagnostic and therapeutic challenges in managing such complex cases.

Case Presentation

Patient History: A 44-year-old woman with a history of hypertension, type 2 diabetes mellitus, and rheumatoid arthritis was regularly followed up in our outpatient department. Her rheumatoid arthritis was diagnosed more then 5 years, and under bioagent Etanercept 50mg once a week for more then 3 years. Her family found that her behavior more different then before about 2 month, including restlessness, irritable, and want to drink water more and more, and also want to go wandering. Psychiatrist was visit but the patient condition did not improve, even fainting and seizure attack with eye hanging with e when she was at work. Hyponatremia was noted at first with the Sodium fluid correct at first, but the patient consciousness became more drowsy, so, she was refer to Taipei Hospital (ministry of health and welfare).

Current Symptoms: The patient experienced dyspnea and palpitations for several days without chest pain, abdominal pain, or dysuria. At our emergency department, her vital signs were TPR: 36.5/129/18, BP: 132/75 mmHg, and SpO2: 97% on room air. The chest X-ray was unremarkable, but laboratory tests showed leukocytosis (WBC: 17200) and elevated blood glucose. The patient with tremor and sit one the wheel chair without any reasonable verbal response. GCS evaluation E2V3M3.

Initial Impression and Admission: The patient was admitted with an initial diagnosis of consciousness disturbance.

Physical Examination:

- General Appearance: Alert (-), Weakness (+), Acutely Ill-Looking (+), Unstable (-), Critical Condition (-)
- Vital Signs: BP: 111/72 mmHg, PR: 108/min, BT: 36.8°C, RR: 16/min, SpO2: 93%
- **Consciousness:** Clear (+), Confusion (-), Drowsy (-), Stupor (-), Coma (-), Glasgow Coma Scale: E4 M6 V5 = 15
- **HEENT:** Normal, Pupil Size 2.5/2.5mm, Light Reflex +/+, Conjunctiva Pale (-), Sclera Icteric (-), Throat Injected (-)

- Neck: Supple (+), Carotid Bruit (-), Lymphadenopathy (-), Jugular Vein Engorgement (-), Thyroid Enlargement (-)
- Chest/Lung: Clear Breath Sounds (+), No Wheezing, Rales, Rhonchi, or Crackles
- **Heart:** Regular Heartbeat (+), No Murmurs, PMI at 5th Intercostal Space, No Heave or Thrill, S3(-), S4(-)
- Abdomen: Soft and Flat, Normoactive Bowel Sounds, No Hepatosplenomegaly, Tympanic Percussion (+), No Tenderness or Rebound Tenderness, Negative Murphy's Sign, No Flank Knocking Pain, Shifting Dullness (-), Caput Medusae (-)
- **Extremities:** No Pitting Edema, Fair Skin Turgor, Freely Movable Joints, No Asterixis, No Ecchymosis or Cyanosis, Fair Peripheral Pulse, No Erythema, Blanching, Local Heat, or Hypothermia. Rheuamtoid arthirits joint swelling over bilateral PIPs.

Past Medical History:

- Systemic Disease: Hypertension, Type 2 Diabetes Mellitus, Rheumatoid Arthritis, Bipolar Disorder
- Admission History: None
- **Operation History:** None
- Drug Allergy: None
- Food Allergy: None
- Important Medications:
 - Insulin Glargine
 - Indapamide
 - Atorvastatin
 - Glimepiride; Metformin
 - Valsartan; Amlodipine
 - Ertugliflozin; Sitagliptin
 - Perisdone
 - o Eurodin
 - o Ligilin
 - Alpraline
 - Methotrexate
 - o Folina
 - o Enbrel
- Personal History: Denied smoking, alcohol, and betel nut use.
- TOCC: No relevant travel, occupational, contact, or cluster history.
- Family History: Non-contributory.

Hospital Course:

- **Destructive Behavior:** Noted after admission, including emotional instability and restlessness. and rapid progression to coma status with NG and foley catheter to support the life status
- Consultations:
 - **Neurologist and Psychiatrist:** Evaluated for acute psychosis and seizures, with lumbar puncture revealing elevated protein levels in CSF.
 - **Infection Specialist:** Ceftriaxone for suspect bacterial infection. Acyclovir was initiated for suspected viral meningitis.
 - **GYN:** Evaluated for limbic encephalitis, no ovarian tumors found.
 - **Rehabilitation:** Arranged for physical therapy post-recovery.
- Key Investigations:
 - **EEG:** Diffuse cortical dysfunction.
 - Brain MRI with MRA and DWI: Slightly dilated ventricles, old insult at right corona radiata.
 - **CSF Studies:** Positive NMDAR antibodies [1:10], elevated protein.
 - Autoimmune antibody: lupus special antibody all negative.
 - NMDAR (blood) : positive ; NMDAR (CSF) : positive
- Treatment:
 - Levetiracetam: For suspected seizures.
 - **IVIG:** Administered for 5 days.
 - Steroid Pulse Therapy: Followed by oral Compession.
 - Plasma Exchange: Conducted for NMDAR encephalitis.
 - Antibiotics and Antifungals: Treated suspected urinary tract infection and C. difficile infection.

• **Outcome:** Significant improvement in cognition and behavior, regained ability to walk and communicate. After that, the patient was clear and could walk by herself to clinic, with clear speak and normal behavior, but the patient did not remember the whole chaos disease coarse.

Discussion

This case highlights the complexity of diagnosing and managing autoimmune encephalitis in patients with multiple chronic conditions. The presence of rheumatoid arthritis and positive NMDAR antibodies directed the diagnosis towards autoimmune limbic encephalitis. Early and aggressive immunotherapy, including IVIG, steroids, and plasma exchange, proved effective in managing her condition.

Conclusion

Autoimmune encephalitis should be considered in patients with new-onset psychiatric and neurological symptoms, especially those with underlying autoimmune disorders. Early diagnosis and multidisciplinary management are crucial for improving patient outcomes.

Accelerated Nodulosis or Rheumatoid Nodules in a Patient with Rheumatoid Arthritis

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類風濕關節炎患者出現藥物結節之案例分享

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Abstract:

Rheumatoid nodules is frequently extra-articular manifestation of RA, and are often associated with more aggressive and erosive course of RA. Drug-induced accelerated nodulosis reportedly occurs in patients with rheumatoid arthritis receiving MTX, anti-TNF and occasionally with leflunomide, tocilizumab and azathioprine treatment. It is often confused with rheumatoid nodules. Compared to classic rheumatoid nodules, accelerated nodules have more rapid onset and growth, are smaller and follow a different distribution (hand, foot, Palm). Accelerated nodules generally develop while there is low disease activity. A 58-year-old female patient, with a diagnosis of seropositive RA for 6 years, was on MTX treatment 5years and add tocilizumab s.c. qw for one year with low disease activity status. She presented with newly developed nodules on the fingers and palms. A diagnosis of accelerated nodulosis was suspected, MTX was switched to sulfasalazine and tocilizumab tapering to q2w and colchicine was started with improvement in her symptoms. After follow-up of half year, there were no newly formed nodules and there was improvement in the previously formed nodules. We present a case of accelerated nodulosis in a patient with RA use of MTX and tocilizumab.

Serial Anti-MDA5 Antibody Levels correlates with disease activity and outcome in Dermatomyositis-Associated Interstitial Lung Disease 抗 MDA5 抗體效價與皮肌炎相關間質性肺病之疾病活動度和預後分析

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Background:

Anti-melanoma differentiation-associated gene 5 antibody (anti-MDA5-Ab) is linked to rapidly progressive interstitial lung disease (RP-ILD) with high mortality in dermatomyositis (DM) patients. This study aimed to investigate the impact of anti-MDA5-Ab on outcomes in DM-ILD patients.

Methods:

Serum samples were collected from 46 anti-MDA5-Ab-positive DM patients (by Euroimmune immunoblot assay) and further analyzed for anti-MDA5 titers using ELISA kit. Associations between clinical parameters, image findings, pulmonary function tests, and survival outcomes were assessed.

Results:

Among 46 patients (33 females, 13 males; mean age 53 years [25-78 years]), all had ILD, with 18 (39%) developing RP-ILD. Fourteen (30%) patients died acutely within 3 months of diagnosis, and another one within 6 months. Of the 29 survivors, 16 showed improved ILD, 8 had stable disease, and 4 exhibited progressive pulmonary fibrosis during a median 3-year follow-up (maximum 8 years). Pre-treatment anti-MDA5-Ab titers did not predict RP-ILD, progressive fibrosis, or acute death. Responders (stable/improved disease) had significantly lower post-treatment anti-MDA5-Ab titers than non-responders (141.6 vs. 44.5 U/mL, P=0.0002). Serial anti-MDA5-Ab levels correlated inversely with pulmonary function test results and positively with ferritin levels.

Conclusions:

Serial monitoring of anti-MDA5 antibody levels is crucial for assessing ILD outcomes and disease activity in DM patients.

A case of MDA5 dermatomyositis associated with primary biliary cholangitisautoimmune hepatitis overlap syndrome

MDA5 皮肌炎合併原發性膽汁性膽管炎-自體免疫性肝炎重疊症候群之罕見案例報告

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Introduction

Anti-MDA5 amyopathic dermatomyositis is a subtype of idiopathic inflammatory myopathies characterized by the absence of muscle involvement. The occurrence of overlap syndrome involving dermatomyositis, autoimmune hepatitis (AIH), and primary biliary cholangitis (PBC) is exceedingly rare, with only a limited number of case reports documented in the literature.

Case

We present the case of a 60-year-old woman with a medical history of anti-MDA5 amyopathic dermatomyositis, diagnosed three years prior. Her initial presentation included Gottron's sign, reverse Gottron's sign, skin ulcers, arthritis of the fingers, severe digital vasculitis leading to gangrene and auto-amputation of the right-hand fingers, as well as interstitial lung disease. Following treatment with glucocorticoids and mycophenolate mofetil, both her skin lesions and lung condition exhibited significant improvement.

In the past year, she experienced septic arthritis of the right first finger, left third finger, and left ankle joint, attributed to a non-tuberculous mycobacterial infection. Throughout the course of antibiotic treatment, elevated liver function tests indicating cholestatic hepatic dysfunction were observed, persisting even after the cessation of antibiotic therapy. A liver biopsy confirmed a diagnosis of PBC-AIH overlapping. In response, ursodeoxycholic acid was prescribed, in conjunction with a careful titration of prednisolone and mycophenolate mofetil dosages. The patient's liver function tests gradually improved following these interventions.

Discussion

This is the first case report of the association between PBC-AIH and idiopathic inflammatory myopathies in Taiwan. It is crucial to differentiate between drug-induced hepatitis, myositis-related hepatitis, and infection-related liver dysfunction to ensure timely and accurate treatment.



The under detected anti-OJ antibody positive antisynthetase syndrome: a case report and case-based review in Taiwanese

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Background:

Anti-OJ antibodies are rare and challenging to detect using standard multiplex assays, such as line/blot immunoassays and ELISAs, due to the complex nature of the autoantigen, which is part of a multi-enzyme synthetase complex. This complexity often leads to the underdetection of anti-OJ antibodies. Most patients with anti-OJ antibodies respond to glucocorticoid therapy, making their detection crucial for appropriate treatment.

Methods & Results:

Case Report: A 44-year-old male presented with 12 months of cough and exertional dyspnea. He denied a history of rash, myalgia, muscle weakness, RP. Evaluation revealed normal ESR, CRP, and CPK. HRCT scan of the chest showed NSIP pattern. Antinuclear antibody test showed ICAP AC-19. Euroimmun Line immunoassay for myositis-specific showed no myositis specific antibodies. RNA IP showed positive bands in t-RNA region (Figure 1). The protein IP showed typical characteristic multiple bands (Figure 2). The protein IP-IB revealed positive for Anti-KARS. So a diagnosis of antisynthetase syndrome with sole manifestation of ILD was made.

Case based review: Data from those patients with anti-OJ antibody positive antisynthetase syndrome from CMUH were summarized in (Table 1). Isolated ILD was the most common form of presentation (43%) followed by myositis with ILD (25%), isolated arthritis (6.3%), and isolated myositis (0%).

Conclusion: Detection of anti-OJ antibodies is challenging but essential for proper diagnosis and treatment. Clinicians should be aware of the possibility of under detection of anti-OJ antibodies is not rare and should be familiar with various method to enhance the detection of this antibody.

Figure 1 20240710 RNAIP

Figure 2





Table 1: Clinical and laboratory Feature of anti-OJ antibody positive Taiwanese patient (CMUH).

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Case No.	11	12	14	15	1	2	7	17	3	6	5	13	8	10	4	16
收案编號	L0555	1389	L0137	2797	1003	1042	2237	2861	1168	1922	1615	L0095	L0758	1966	1271	L2495
收案年齡	74	49	52	60	75	57	48	72	67	69	76	57	54	67	51	67
Sex 1man 2woman	2	2	2	2	2	1	2	2	2	2	1	2	2	2	2	1
Mechanic hand	N	Х	Х	N	V	V	v	V	Х	Ν	V	V	V	V	V	V
Gottron	N	Х	N	N	V	Х	Х	Х	Х	Х	V	V	Х	Х	V	V
Heliotrope	N	N	N	N	Х	Х	Х	Х	Х	Х	V	Ν	Х	Х	Х	N
ILD 1yes	1	1	1	2	1	1	1	1	1	1	1	1	1	1	1	1
arthritis/arthralgia	Х	V	N	V	Х	Х	Х	Х	V	Х	N	Х	V	V	V	V
СК	199	49	148	23	64	141	71	258	93	2553	1160	3270	50	54	2992	1598
ANA	AC-19	AC-19	AC-19	AC-19	AC- 19	AC-19	AC-19	AC-19	AC-19	AC-19	AC-19	AC-19	AC-19	AC-19	AC-19	AC-19
Euroimmun myositis Pannels	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
COMMENT	ILD	ILD	ILD	Arthritis	ILD MH	ILD MH	ILD MH	ILD MH	ILD Arthritis	ILD CK	ILD MH CK	ILD MH CK	ILD Arthritis MH	ILD Arthritis MH	ILD Arthritis MH CK	ILD Arthritis MH CK

Anti-Ro52/SSA antibody and disease duration as predictive markers for the development of pulmonary arterial hypertension in connective tissue disease patients with interstitial lung disease

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抗 Ro52/SSA 抗體與疾病期間可作為結締組織疾病併發間質肺病變患者發生肺動脈 高壓之預測標誌

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Background: Despite pulmonary arterial hypertension (PAH) and interstitial lung disease (ILD) being common manifestations in connective tissue disease (CTD) patients, there are scarce data on the occurrence of PAH in patients with CTD-ILD. Moreover, no data have been reported regarding the predictors of PAH development in patients with CD-ILD.

Materials and Methods: We consecutively enrolled a total of 221 CTD patients who had ILD validated by a multidisciplinary discussion (MDD) process based on clinical characteristics, pulmonary function test results, and HRCT images. Patients with CTD include idiopathic inflammatory myopathies (IIM, n=86), progressive systemic sclerosis (SSc, n=56), rheumatoid arthritis (RA, n=55), and primary Sjögren's syndrome (pSS, n=24). The diagnosis of PAH was made if right ventricular systolic pressure >40 mmHg or a tricuspid regurgitant jet velocity>3.4 m/s shown by echocardiography. The IIM- and SSc-related antibodies were determined by Euroimmune-immunoblot.

Results: Among the enrolled patients, 25 (11.3%) had concomitant PAH in patients with CTD-ILD: SSc (19.6%), IIM (11.6%), RA (5.5%), and pSS (4.2%). Patients with PAH had significantly lower body mass index, longer CTD duration, and higher positive rate of anti-Ro52/SSA antibody compared to patients without PAH (all p-values <0.05). The multivariate regression analysis revealed that anti-Ro52/SSA antibody and disease duration were significant predictors of developing PAH in patients with CTD-ILD (Odds ratio, 2.55, 95%CI 1.06-6.11; 1.13, 95%CI 1.00-1.28; respectively, both p-values <0.05). Besides, four patients (16.0%) died after a mean period of 4.8 years after the diagnosis of PAH.

Conclusion: These findings suggest that anti-Ro52/SSA antibody positivity and CTD duration are potential predictors of PAH development in patients with CTD-ILD.

Clinical Presentations in Patients with Anti-RP155 and Coexisting Anti-Ro52 Antibodies, with a Focus on Pulmonary Arterial Hypertension

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Background:

Anti-RP155 autoantibody, an Anti-RNA polymerase III, is a significant biomarker in systemic sclerosis (SSc) with distinct clinical implications. While existing research suggests an augmentative role for Anti-Ro52, the combined impact of Anti-RP155 and Anti-Ro52 antibodies remains unexplored. This study investigates their relationship, particularly with pulmonary and cardiovascular involvement in SSc patients.

Methods:

We conducted a retrospective analysis of patients positive for Anti-RP155 antibodies from January 2019 to December 2021, with follow-up on disease diagnosis and complications until December 2023. We focused on patients diagnosed with Interstitial Lung Disease through CT or HRCT. Pulmonary Arterial Hypertension (PAH) was diagnosed per the 2022 ESC/ERS Guidelines, confirmed via right heart catheterization or 2D echocardiogram. Cancer diagnoses were based on pathological biopsy, and all patients met the 2013 SSc criteria. Other system diseases, including cardiovascular, gastrointestinal, renal, endocrine, infections, and psychological aspects, were also examined.

Results:

Among 752 patients tested, 34 were positive for Anti-RP155, with 16 showing strong positivity. Strong positivity for Anti-RP155 was significantly associated with SSc (P = 0.0343). Concurrent Anti-RP155 and Anti-Ro52 positivity significantly increased PAH risk (P = 0.014). No significant differences were found in cardiovascular, gastrointestinal, renal, endocrine, infective, and psychological manifestations except for PAH.

Conclusion:

Anti-RP155 strongly correlates with increased SSc risk, especially diffuse cutaneous SSc. Concurrent Anti-RP155 and Anti-Ro52 positivity suggests an increased risk of PAH. This information enhances our understanding of Anti-RP155 and highlights the additive effects of different specific antibodies. Further large-scale studies and long-term follow-up are needed to confirm these findings.