

# World Journal of *Clinical Cases*

*World J Clin Cases* 2022 September 26; 10(27): 9550-9969



## Contents

Thrice Monthly Volume 10 Number 27 September 26, 2022

## OPINION REVIEW

- 9550 Psychiatric disorders and pain: The recurrence of a comorbidity  
*Vyshka G*

## REVIEW

- 9556 Cardiovascular disease and COVID-19, a deadly combination: A review about direct and indirect impact of a pandemic  
*Vidal-Perez R, Brandão M, Pazdernik M, Kresoja KP, Carpenito M, Maeda S, Casado-Arroyo R, Muscoli S, Pöss J, Fontes-Carvalho R, Vazquez-Rodriguez JM*
- 9573 Molecular factors, diagnosis and management of gastrointestinal tract neuroendocrine tumors: An update  
*Pavlidis ET, Pavlidis TE*

## MINIREVIEWS

- 9588 Human-induced pluripotent stem cell-atrial-specific cardiomyocytes and atrial fibrillation  
*Leowattana W, Leowattana T, Leowattana P*
- 9602 COVID-19 and the cardiovascular system-current knowledge and future perspectives  
*Chatzis DG, Magounaki K, Pantazopoulos I, Bhaskar SMM*

## ORIGINAL ARTICLE

## Case Control Study

- 9611 PDCA nursing in improving quality management efficacy in endoscopic submucosal dissection  
*He YH, Wang F*

## Retrospective Study

- 9619 Impact of COVID-19 pandemic on the ocular surface  
*Marta A, Marques JH, Almeida D, José D, Sousa P, Barbosa I*
- 9628 Anatomy and clinical application of suprascapular nerve to accessory nerve transfer  
*Wang JW, Zhang WB, Li F, Fang X, Yi ZQ, Xu XL, Peng X, Zhang WG*
- 9641 Therapeutic effect of two methods on avulsion fracture of tibial insertion of anterior cruciate ligament  
*Niu HM, Wang QC, Sun RZ*
- 9650 Efficacy of transcatheter arterial chemoembolization using pirarubicin-loaded microspheres combined with lobaplatin for primary liver cancer  
*Zhang C, Dai YH, Lian SF, Liu L, Zhao T, Wen JY*

- 9657** Prognostic significance of sex determining region Y-box 2, E-cadherin, and vimentin in esophageal squamous cell carcinoma

*Li C, Ma YQ*

- 9670** Clinical characteristics and prognosis of orbital solitary fibrous tumor in patients from a Chinese tertiary eye hospital

*Ren MY, Li J, Wu YX, Li RM, Zhang C, Liu LM, Wang JJ, Gao Y*

### Observational Study

- 9680** Altered heart rate variability and pulse-wave velocity after spinal cord injury

*Tsou HK, Shih KC, Lin YC, Li YM, Chen HY*

- 9693** Intra and extra pelvic multidisciplinary surgical approach of retroperitoneal sarcoma: Case series report

*Song H, Ahn JH, Jung Y, Woo JY, Cha J, Chung YG, Lee KH*

### META-ANALYSIS

- 9703** Meta-analysis of gemcitabine plus nab-paclitaxel combined with targeted agents in the treatment of metastatic pancreatic cancer

*Li ZH, Ma YJ, Jia ZH, Weng YY, Zhang P, Zhu SJ, Wang F*

- 9714** Clinical efficacy analysis of mesenchymal stem cell therapy in patients with COVID-19: A systematic review

*Cao JX, You J, Wu LH, Luo K, Wang ZX*

### CASE REPORT

- 9727** Treatment of gastric cancer with dermatomyositis as the initial symptom: Two case reports and review of literature

*Sun XF, Gao XD, Shen KT*

- 9734** Gallbladder hemorrhage—An uncommon surgical emergency: A case report

*Valenti MR, Cavallaro A, Di Vita M, Zanghi A, Longo Trischitta G, Cappellani A*

- 9743** Successful treatment of stage IIIB intrahepatic cholangiocarcinoma using neoadjuvant therapy with the PD-1 inhibitor camrelizumab: A case report

*Zhu SG, Li HB, Dai TX, Li H, Wang GY*

- 9750** Myocarditis as an extraintestinal manifestation of ulcerative colitis: A case report and review of the literature

*Wang YY, Shi W, Wang J, Li Y, Tian Z, Jiao Y*

- 9760** Endovascular treatment of traumatic renal artery pseudoaneurysm with a Stanford type A intramural haematoma: A case report

*Kim Y, Lee JY, Lee JS, Ye JB, Kim SH, Sul YH, Yoon SY, Choi JH, Choi H*

- 9768** Histiocytoid giant cellulitis-like Sweet syndrome at the site of sternal aspiration: A case report and review of literature

*Zhao DW, Ni J, Sun XL*

- 9776** Rare giant corneal keloid presenting 26 years after trauma: A case report  
*Li S, Lei J, Wang YH, Xu XL, Yang K, Jie Y*
- 9783** Efficacy evaluation of True Lift®, a nonsurgical facial ligament retightening injection technique: Two case reports  
*Huang P, Li CW, Yan YQ*
- 9790** Synchronous primary duodenal papillary adenocarcinoma and gallbladder carcinoma: A case report and review of literature  
*Chen J, Zhu MY, Huang YH, Zhou ZC, Shen YY, Zhou Q, Fei MJ, Kong FC*
- 9798** Solitary fibrous tumor of the renal pelvis: A case report  
*Liu M, Zheng C, Wang J, Wang JX, He L*
- 9805** Gastric metastasis presenting as submucosa tumors from renal cell carcinoma: A case report  
*Chen WG, Shan GD, Zhu HT, Chen LH, Xu GQ*
- 9814** Laparoscopic correction of hydronephrosis caused by left paraduodenal hernia in a child with cryptorchism: A case report  
*Wang X, Wu Y, Guan Y*
- 9821** Diagnosed corrected transposition of great arteries after cesarean section: A case report  
*Ichii N, Kakinuma T, Fujikawa A, Takeda M, Ohta T, Kagimoto M, Kaneko A, Izumi R, Kakinuma K, Saito K, Maeyama A, Yanagida K, Takeshima N, Ohwada M*
- 9828** Misdiagnosis of an elevated lesion in the esophagus: A case report  
*Ma XB, Ma HY, Jia XF, Wen FF, Liu CX*
- 9834** Diagnostic features and therapeutic strategies for malignant paraganglioma in a patient: A case report  
*Gan L, Shen XD, Ren Y, Cui HX, Zhuang ZX*
- 9845** Infant with reverse-transcription polymerase chain reaction confirmed COVID-19 and normal chest computed tomography: A case report  
*Ji GH, Li B, Wu ZC, Wang W, Xiong H*
- 9851** Pulmonary hypertension secondary to seronegative rheumatoid arthritis overlapping antisynthetase syndrome: A case report  
*Huang CY, Lu MJ, Tian JH, Liu DS, Wu CY*
- 9859** Monitored anesthesia care for craniotomy in a patient with Eisenmenger syndrome: A case report  
*Ri HS, Jeon Y*
- 9865** Emergency treatment and anesthesia management of internal carotid artery injury during neurosurgery: Four case reports  
*Wang J, Peng YM*

- 9873** Resolution of herpes zoster-induced small bowel pseudo-obstruction by epidural nerve block: A case report  
*Lin YC, Cui XG, Wu LZ, Zhou DQ, Zhou Q*
- 9879** Accidental venous port placement *via* the persistent left superior vena cava: Two case reports  
*Zhou RN, Ma XB, Wang L, Kang HF*
- 9886** Application of digital positioning guide plates for the surgical extraction of multiple impacted supernumerary teeth: A case report and review of literature  
*Wang Z, Zhao SY, He WS, Yu F, Shi SJ, Xia XL, Luo XX, Xiao YH*
- 9897** Iatrogenic aortic dissection during right transradial intervention in a patient with aberrant right subclavian artery: A case report  
*Ha K, Jang AY, Shin YH, Lee J, Seo J, Lee SI, Kang WC, Suh SY*
- 9904** Pneumomediastinum and subcutaneous emphysema secondary to dental extraction: Two case reports  
*Ye LY, Wang LF, Gao JX*
- 9911** Hemorrhagic shock due to submucosal esophageal hematoma along with mallory-weiss syndrome: A case report  
*Oba J, Usuda D, Tsuge S, Sakurai R, Kawai K, Matsubara S, Tanaka R, Suzuki M, Takano H, Shimoizawa S, Hotchi Y, Usami K, Tokunaga S, Osugi I, Katou R, Ito S, Mishima K, Kondo A, Mizuno K, Takami H, Komatsu T, Nomura T, Sugita M*
- 9921** Concurrent severe hepatotoxicity and agranulocytosis induced by *Polygonum multiflorum*: A case report  
*Shao YL, Ma CM, Wu JM, Guo FC, Zhang SC*
- 9929** Transient ischemic attack after mRNA-based COVID-19 vaccination during pregnancy: A case report  
*Chang CH, Kao SP, Ding DC*
- 9936** Drug-induced lung injury caused by acetaminophen in a Japanese woman: A case report  
*Fujii M, Kenzaka T*
- 9945** Familial mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episode syndrome: Three case reports  
*Yang X, Fu LJ*
- 9954** Renal pseudoaneurysm after rigid ureteroscopic lithotripsy: A case report  
*Li YH, Lin YS, Hsu CY, Ou YC, Tung MC*

**LETTER TO THE EDITOR**

- 9961** Role of traditional Chinese medicine in the initiative practice for health  
*Li Y, Li SY, Zhong Y*
- 9964** Impact of the COVID-19 pandemic on healthcare workers' families  
*Helou M, El Osta N, Husni R*

- 9967 Transition beyond the acute phase of the COVID-19 pandemic: Need to address the long-term health impacts of COVID-19

*Tsioutis C, Tofarides A, Spernovasilis N*

**ABOUT COVER**

Editorial Board Member of *World Journal of Clinical Cases*, Yusuf Tutar, PhD, Chairman, Director, Full Professor, Department of Basic Pharmaceutical Sciences, Division of Biochemistry, University of Health Sciences, Istanbul 34668, Turkey. ytutar@outlook.com

**AIMS AND SCOPE**

The primary aim of *World Journal of Clinical Cases* (WJCC, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

**INDEXING/ABSTRACTING**

The WJCC is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Current Contents®/Clinical Medicine, PubMed, PubMed Central, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 Edition of Journal Citation Reports® cites the 2021 impact factor (IF) for WJCC as 1.534; IF without journal self cites: 1.491; 5-year IF: 1.599; Journal Citation Indicator: 0.28; Ranking: 135 among 172 journals in medicine, general and internal; and Quartile category: Q4. The WJCC's CiteScore for 2021 is 1.2 and Scopus CiteScore rank 2021: General Medicine is 443/826.

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: *Ying-Yi Yuan*; Production Department Director: *Xiang Li*; Editorial Office Director: *Jin-Lei Wang*.

**NAME OF JOURNAL**

*World Journal of Clinical Cases*

**ISSN**

ISSN 2307-8960 (online)

**LAUNCH DATE**

April 16, 2013

**FREQUENCY**

Thrice Monthly

**EDITORS-IN-CHIEF**

Bao-Gan Peng, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati, Ja Hyeon Ku

**EDITORIAL BOARD MEMBERS**

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

**PUBLICATION DATE**

September 26, 2022

**COPYRIGHT**

© 2022 Baishideng Publishing Group Inc

**INSTRUCTIONS TO AUTHORS**

<https://www.wjgnet.com/bpg/gerinfo/204>

**GUIDELINES FOR ETHICS DOCUMENTS**

<https://www.wjgnet.com/bpg/GerInfo/287>

**GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH**

<https://www.wjgnet.com/bpg/gerinfo/240>

**PUBLICATION ETHICS**

<https://www.wjgnet.com/bpg/GerInfo/288>

**PUBLICATION MISCONDUCT**

<https://www.wjgnet.com/bpg/gerinfo/208>

**ARTICLE PROCESSING CHARGE**

<https://www.wjgnet.com/bpg/gerinfo/242>

**STEPS FOR SUBMITTING MANUSCRIPTS**

<https://www.wjgnet.com/bpg/GerInfo/239>

**ONLINE SUBMISSION**

<https://www.f6publishing.com>



## Pulmonary hypertension secondary to seronegative rheumatoid arthritis overlapping antisynthetase syndrome: A case report

Cheng-Yan Huang, Ming-Jie Lu, Jia-Hua Tian, Dai-Shun Liu, Chun-Yan Wu

**Specialty type:** Rheumatology

**Provenance and peer review:**

Unsolicited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review report's scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): B

Grade C (Good): C, C

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** Faraji N, Iran; Pradhan A, India; Tangsuwanaruk T, Thailand

**Received:** May 2, 2022

**Peer-review started:** May 2, 2022

**First decision:** May 30, 2022

**Revised:** June 11, 2022

**Accepted:** August 15, 2022

**Article in press:** August 15, 2022

**Published online:** September 26, 2022



**Cheng-Yan Huang, Ming-Jie Lu, Jia-Hua Tian, Chun-Yan Wu,** Department of Respiratory Medicine, The Third Affiliated Hospital of Zunyi Medical University (The First People's Hospital of Zunyi), Zunyi 563000, Guizhou Province, China

**Dai-Shun Liu,** Clinical School, Zunyi Medical University, Zunyi 563000, Guizhou Province, China

**Corresponding author:** Dai-Shun Liu, MD, Chief Physician, Postdoc, Clinical School, Zunyi Medical University, No. 6 Xuefu West Road, Xipu New District, Zunyi 563000, Guizhou Province, China. [ldslwtg@126.com](mailto:ldslwtg@126.com)

### Abstract

#### BACKGROUND

Polyarthritides is the most frequent clinical manifestation in antisynthetase syndrome (ASS) forms of idiopathic inflammatory myositis and may be misdiagnosed as rheumatoid arthritis (RA), particularly in patients with seronegative RA (SNRA). It is unclear whether there is an overlap between ASS and RA, or if ASS sometimes mimics RA. Pulmonary hypertension (PAH) is common in connective tissue diseases (CTDs). However, published reports on CTD-PAH do not include overlapping CTDs, and its incidence and impact on patient prognosis are unclear.

#### CASE SUMMARY

We report the case of a 63-year-old woman who presented with a 3-mo history of symptom aggravation of recurrent symmetrical joint swelling and pain that had persisted for over 10 years. The patient was diagnosed with RA and interstitial lung disease. The patient repeatedly presented to the hospital's respiratory and rheumatology departments with arthralgia, plus shortness of breath after activity. Relevant tests indicated that anti-CCP and RF remained negative, while anti-Jo-1 and anti-Ro-52 were strongly positive. It was not until recently that we recognized that this could be an unusual case of SNRA with concurrent ASS. Joint pain was relieved after regular anti-rheumatic treatment. Chest computed tomography scans showed that pulmonary interstitial changes did not progress significantly over several years; however, they showed gradual widening of the pulmonary artery, and cardiac ultrasound indicated elevated pulmonary artery systolic pressure. The prescribed treatment of PAH was not effective in improving shortness of breath.

#### CONCLUSION

Overlap of RA and ASS may be missed. Further research is necessary to facilitate

early diagnosis, effective evaluation, and prognosis.

**Key Words:** Rheumatoid arthritis; Arthritis; Antisynthetase syndrome; Pulmonary hypertension; Pulmonary arterial hypertension; Case report

©The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core Tip:** The joint manifestations of antisynthetase syndrome are usually difficult to distinguish from rheumatoid arthritis (RA), particularly seronegative RA (SNRA); consequently, rheumatologists and respiratory pathologists should be aware of this rare and underrecognized special clinical phenotype. Whether this phenotype is more prone to pulmonary hypertension than a single connective tissue disease remains unknown. However, further research into anti-Jo1 antibodies, anti-RO-52, and other extractable nuclear antigen autoantibodies is necessary to facilitate the early diagnosis, evaluation, and prognosis of this overlapping clinical syndrome.

**Citation:** Huang CY, Lu MJ, Tian JH, Liu DS, Wu CY. Pulmonary hypertension secondary to seronegative rheumatoid arthritis overlapping antisynthetase syndrome: A case report. *World J Clin Cases* 2022; 10(27): 9851-9858

**URL:** <https://www.wjgnet.com/2307-8960/full/v10/i27/9851.htm>

**DOI:** <https://dx.doi.org/10.12998/wjcc.v10.i27.9851>

## INTRODUCTION

Rheumatoid arthritis (RA) is a multifactorial, chronic, autoimmune disease characterized by significant heterogeneity in clinical presentations and outcomes among individuals with the same formal diagnosis [1]. The 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria for RA include autoantibodies [rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibodies (ACPA)] as biomarkers of the disease [2]. However, a sizeable subgroup of RA patients is negative for both ACPA and rheumatoid factor (seronegative RA, SNRA) [3]. Furthermore, the clinical presentation of SNRA is more heterogeneous than that of seropositive RA [1].

Antisynthetase syndrome (ASS) was first designated in 1990 as the first clinical serological syndrome described in patients with polymyositis and dermatomyositis [4]. This syndrome is characterized by the binding of an autoantibody to an aminoacyl-transfer RNA synthase, most commonly the Jo-1 antibody [4]. Clinical manifestations of ASS are diverse, including idiopathic inflammatory myositis (IIM), arthralgia and arthritis, interstitial pneumonia, Raynaud's phenomenon, and skin lesions characterized by "mechanic's hands" [5]. The pathogenesis of ASS is unclear, but it is thought to be associated with chronic immune system activation [6]. It is also unclear whether there is an overlap between ASS and RA, or if ASS in some cases mimics RA [4]. In this report, we describe the case of a rare association of SNRA with ASS. Overlap between RA and ASS has only been reported previously in a few case reports [7].

Pulmonary hypertension (PAH) is a life-threatening complication associated with connective tissue diseases (CTD) such as RA [8]. While most patients with CTD have relatively stable interstitial changes in their lungs during follow-up, a disproportionate number of patients with PAH have gradually emerged [9]. Although PAH is relatively common in most forms of CTD, there are currently no reports of PAH secondary to RA overlapping with ASS [10]. In this report, we describe the case of a rare overlap of SNRA with ASS in a patient with PAH.

## CASE PRESENTATION

### Chief complaints

A 63-year-old woman presented with a 3-mo history of aggravation of recurrent symmetrical joint swelling and pain, which she had experienced episodically over 10 years. She first presented to our hospital in April 2018 for these symptoms.

### History of present illness

The patient had a history of painful metacarpophalangeal joints in both hands with no obvious cause, with symmetrical and persistent attacks, starting from the interphalangeal and metacarpophalangeal joints of both hands and gradually involving both wrist joints, elbow joints, shoulder joints, and knee

joints. Her symptoms were accompanied by morning stiffness lasting more than 1 h, which could be relieved by routine daily activities.

### **History of past illness**

The patient was diagnosed with depression more than four years prior and was treated with antidepressant medication (medication type, dose, and duration were unknown). She denied any other disease history, including heart or lung diseases.

### **Personal and family history**

Aside from the depression noted above, the patient's medical history was uneventful. There was no history of a similar illness in the family.

### **Physical examination**

On initial evaluation, the patient's vital signs were as follows: Body temperature, 36.0 °C; pulse, 93 beats/min; respiration, 20 times/min; and blood pressure, 108/72 mmHg. The patient also exhibited anxiety, slightly coarse breath sounds in both lungs, inspiratory dry rales in both lower lung fields, swan neck-like deformity in both hands, localized swelling, elevated skin temperature, abduction deformity of both thumbs, and slightly restricted movement of both knees. No significant abnormalities were observed during cardiac and abdominal examinations. No edema in the lower extremities was observed, and no pathological signs were found.

### **Laboratory examinations**

Initial laboratory examinations were as follows: Erythrocyte sedimentation rate, 74 mm/h; hypersensitivity C-reactive protein, 17.7 mg/L; creatine kinase, 1002.1 U/L; antinuclear antibody cytoplasmic granular positive (1:100); J0-1 +++; and Ro-52 +++. She was negative for anti-CCP and RF. Arterial blood gas analysis under oxygen absorption (nasal cannula 2 L/min) revealed a partial pressure of carbon dioxide (PCO<sub>2</sub>) of 29.7 mmHg and a partial oxygen pressure (PaO<sub>2</sub>) of 70.6 mmHg. Liver and kidney function, coagulation and D-dimer levels, and white blood cell and neutrophil ratios were normal.

### **Imaging examinations**

Plain radiographs of both hands (**Figure 1**) suggested degeneration, marked osteoporosis of the wrists, partial interphalangeal joint dislocation, and subluxation consistent with RA. Ultrasound of both knees suggested a luminal effusion and synovitis. Chest computed tomography (CT) revealed emphysema and interstitial degeneration in both lungs and interstitial pneumonia in both lower lung fields (**Figure 2A-C**). Pulmonary function tests suggested moderate restrictive ventilation dysfunction (forced vital capacity < 80%) and moderate diffuse function (diffusion capacity for carbon monoxide < 80%).

---

## **FINAL DIAGNOSIS**

Considering the patient's previous medical history and the results of our recent examinations, the patient was diagnosed with RA and interstitial lung disease (ILD).

---

## **TREATMENT**

The patient refused hormone and anti-rheumatic drug therapy. After providing analgesic and oxygen therapy, the patient's symptoms were relieved, and she was discharged uneventfully.

---

## **OUTCOME AND FOLLOW-UP**

After 3 mo, the patient was readmitted to the hospital due to a pulmonary infection. Her inflammatory and rheumatic immune indices had not changed significantly compared with the first hospitalization. However, cardiac ultrasound indicated PAH, and she was started on an anti-infective and anti-rheumatic treatment plan of leflunomide 20 mg QD, sulfasalazine enteric-coated tablets 0.5 g TID, and triptolide tablets 10 mg TID. She was instructed to have the treatment plan adjusted at regular follow-up visits with the rheumatology department.

Over the next 2 years, the patient repeatedly presented to the hospital's respiratory and rheumatology departments with arthralgia, shortness of breath after activity, and dyspnea. Relevant tests (**Table 1**) indicated that anti-CCP and RF remained negative while anti-nuclear antibody titers gradually increased, and anti-J0-1 and anti-Ro-52 were strongly positive. After two years of treatment and testing, we recognized that this could be an unusual case of SNRA with concurrent ASS. Joint pain was relieved

**Table 1 Primary laboratory test results**

Lab	Apr-18	Apr-19	Sep-20	Apr-21	Reference values
ESR	74.0	88.0	56.3	82.1	0-20 mm/h
CRP	17.7	55.8	28.7	36.8	< 10 mg/L
Rheumatoid factor	< 20	20.3	< 20	< 20	< 20 U/mL
Anti-cyclic citrullinated peptide antibody	0.9	0.9	< 0.5	< 0.5	< 5.0 U/mL
Antinuclear antibody titer	1/100	1/100	1/100	1/1000	Negative
C3	0.82	0.9	1.01	1.08	0.79-1.52 g/L
C4	0.13	0.18	0.20	0.19	0.16-0.38 g/L
RO-52 antibody	Positive	Positive	Strong positive	Strong positive	Negative
JO-1 antibody	Positive	Positive	Strong positive	Strong positive	Negative
p-ANCA	Negative	Negative	Negative	Negative	Negative
c-ANCA	Negative	Negative	Negative	Negative	Negative
Creatine kinase	700.8	159.5	-	358.0	26-140 U/L
PaCO <sub>2</sub>	70.6	68.4	-	62.8	83-108 mmHg
PaO <sub>2</sub>	29.4	29.4	-	29.0	35-45 mmHg
Pulmonary artery systolic pressure	47	55	-	72	15-30 mmHg

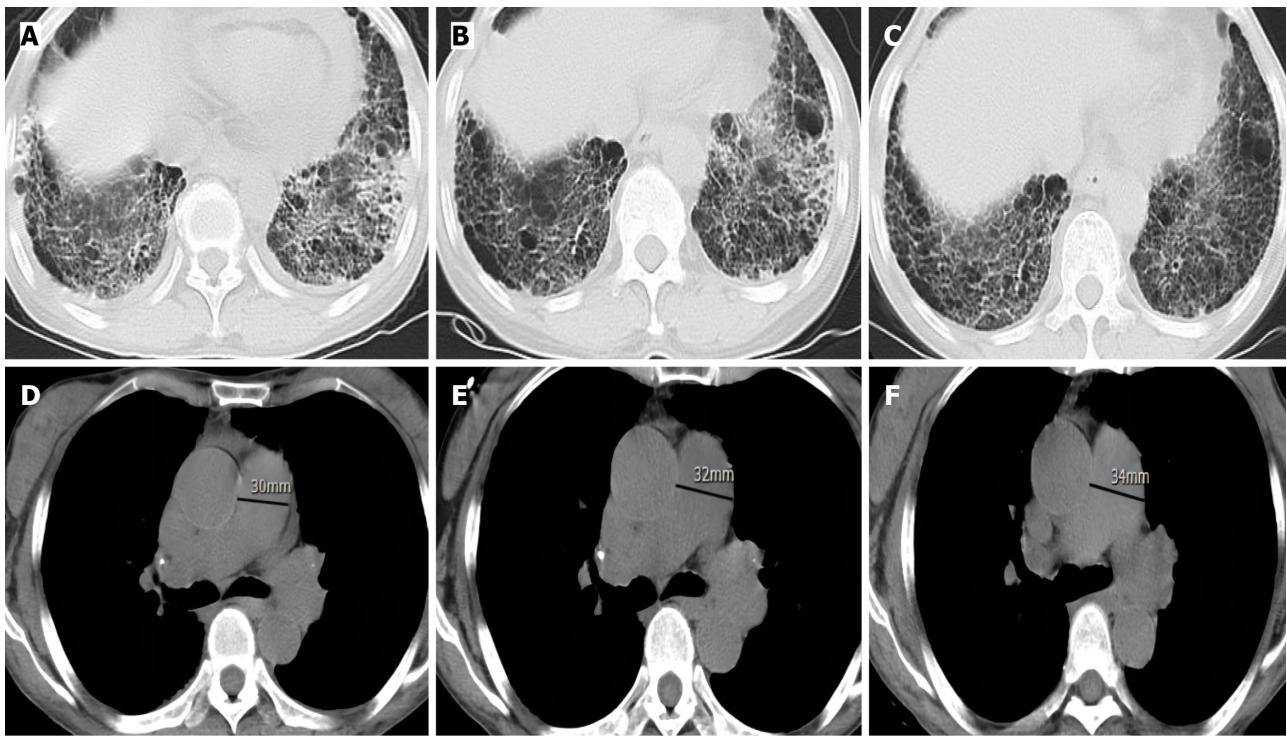
ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; ANCA: Anti-neutrophil cytoplasmic antibodies; PaO<sub>2</sub>: Partial oxygen pressure; PaCO<sub>2</sub>: Partial carbon dioxide pressure.



DOI: 10.12998/wjcc.v10.i27.9851 Copyright ©The Author(s) 2022.

**Figure 1 Plain radiograph of both hands and wrists.** Most of the interphalangeal joints, metacarpal joints, and wrist joints in both hands are narrowed and exhibit bone hyperplasia. Decreased bone density, multiple joint deformities, multiple areas of testicular and insect erosion bone absorption, and soft tissue spindle swelling are also visible.

after regular anti-rheumatic treatment (prednisone acetate tablets 30 mg QD and leflunomide 20 mg QN) and anti-pulmonary fibrosis treatment (pirfenidone 100 mg TID and acetylcysteine vescent tablets 0.6 g BID). Chest CT scans (Figure 2A-C) showed that the pulmonary interstitial changes did not progress significantly over several years; however, they did show gradual widening of the pulmonary artery (Figure 2D-F), and cardiac ultrasound indicated elevated pulmonary artery systolic pressure. The prescribed treatment for PAH (ambrisentan tablets 5 mg BID) was not effective in improving the



DOI: 10.12998/wjcc.v10.i27.9851 Copyright ©The Author(s) 2022.

**Figure 2** Computed tomography scans over 3 years. A-C: Chest computed tomography (CT) shows the thickening of both lungs, a subpleural and lower lung mesh texture, and multiple patchy, blurred shadows in the lower lobe of both lungs; the left to right contrast showed no significant progression over 3 years; D-F: Chest CT mediastinal window, with contrast from left to right, showing gradual widening of the pulmonary artery over 3 year.

patient's shortness of breath.

## DISCUSSION

RA is a heterogeneous systemic inflammatory disease characterized by painful polyarthritis, which has a significant impact on a patient's quality of life, morbidity, and mortality[11]. Serological typing divides this condition into seropositive and seronegative RA based on the presence or absence of RF and anti-CCP antibodies, and both RA subtypes may have similar clinical manifestations despite different etiologies[12].

This report describes the case of a patient with SNRA who was previously treated for depression. Her diagnosis of ASS was delayed for 2 years because the joint manifestations of this condition were indistinguishable from RA, despite the presence of positive antibodies related to ASS. A review of cardiac ultrasound and chest CT images also revealed that the patient had progressively developed disproportionate PAH, based on stable interstitial lung changes. The following sections discuss these puzzling clinical presentations.

### SNRA and ASS

It has been reported that 18%-55% of patients with IIM have arthritis. As with RA, the most typical manifestation of joint disease in patients with IIM is symmetric non-erosive polyarthritis, primarily affecting the small joints of the hand[13]. Arthritis is particularly common in the ASS-associated form of IIM (20%-70%), with the highest prevalence associated with anti-Jo-1 positivity[13]. Radiological erosions are occasionally found in ASS, particularly in patients with overlapping RA[13]. RF and ACPA are relatively common in ASS patients with arthritis, as seen in 27.0%-31.5% and 11.0%-13.5% of patients with active arthritis, respectively[14]. The absence of arthritis is associated with a much lower prevalence of these antibodies, with only 8.0% and 1.5% of cases being positive for RF and ACPA, respectively[14,15]. Notably, our patient had arthritis but was negative for RF and ACPA, thereby complicating the distinction between RA and ASS. A study by Kumar *et al*[16] reported six patients with ASS and RA; while RA was diagnosed after the development of symmetrical facet polyarthritis, ASS was only detected many years after the development of IIM and ILD. We also considered RA first in our patient, and only 2 years later were we able to diagnose ASS owing to the increased severity of ILD and PAH. It is unclear whether there is true overlap between ASS and RA, or whether ASS in some cases only mimics RA[4]. Polyarthritis is the most frequent clinical manifestation among patients with IIM

and may be misdiagnosed as RA[13]. ASS should be specifically considered as a differential diagnosis in patients with SNRA and ILD or Raynaud's phenomenon.

### **SNRA-ASS-associated ILD progressed steadily, but with disproportionately increased PAH**

PAH is a life-threatening complication associated with CTD, particularly in systemic sclerosis and systemic lupus erythematosus. RA is the most common CTD, but the prevalence of PAH in patients with RA is lower than that in patients with CTDs such as scleroderma, mixed collagen tissue disease, and dermatomyositis/polymyositis[17]. Fayed *et al*[18] provided an overview of CTD-associated PAH types and reported that post-capillary PAH is most common in patients with RA, while lung disease-associated PAH is commonly seen in patients with IIM and sarcoidosis. The case of RA-associated PAH presented by Szturmowicz *et al*[17] illustrates the complexity of PAH in a single individual, with ILD-PAH dominating the early stage and CTD-PAH developing later.

Among patients with ASS, ILD is the main clinical feature and prognostic factor with an incidence of up to 80%, while PAH secondary to ILD is also frequently reported[9]. Approximately 7.9% of patients with ASS develop PAH[19]. It has been shown that PAH is usually severe and is believed to be related to Raynaud's phenomenon, which is commonly associated with ASS[19]. A case report and literature review by García-Fernández *et al*[9] explored the relationship between ASS and PAH, and revealed that while their patients had stable and mild ILD, PAH at follow-up was disproportionate and unrelated to ILD severity. This study suggested that direct vascular involvement may lead to PAH in patients with ASS; both anti-Jo-1 positive and anti-PL-12 positive cases were found to have intimal proliferation on histological analysis of pulmonary arterial muscles, further supporting this pathophysiological theory [9].

PAH is common in most forms of CTD, but there are no reports of PAH secondary to RA overlapping ASS[10]. Current reports on CTD-PAH do not include overlapping CTDs, and its incidence and impact on patient prognosis are unclear[10]. There are currently no specific recommendations or guidelines for screening or treating patients with CTD, particularly those with PAH and ASS; however, routine echocardiography, electrocardiograms, pulmonary function tests, and timely initiation of specific treatments may improve prognosis[10].

There is no standardized protocol for the treatment of RA-ASS. While our patient's case primarily manifested as joint and pulmonary conditions, for such an unusual clinical phenotype of SNRA overlapping with ASS, more clinical studies are required to specify and confirm an appropriate treatment protocol. One strength of our case study is that it is the first report of this particular phenotype, but a limitation is that although cardiac ultrasound can screen for PAH, our patient did not undergo the "gold standard" test.

## **CONCLUSION**

The joint manifestation of ASS is usually difficult to distinguish from RA, particularly in patients with SNRA; as a result, rheumatologists and respiratory pathologists should be aware of this rare and underrecognized clinical phenotype. Whether patients with this phenotype are more prone to PAH compared with those with a single CTD remains unknown. However, further research into anti-Jo1 antibodies, anti-RO-52 antibodies, and other extractable nuclear-antigen autoantibodies is necessary to facilitate the early diagnosis, effective evaluation, and prognosis of this overlapping clinical syndrome.

## **ACKNOWLEDGEMENTS**

We thank The First People's Hospital of Zunyi (The Third Affiliated Hospital of Zunyi Medical University) for providing clinical information and patient assistance.

## **FOOTNOTES**

**Author contributions:** Huang CY was responsible for obtaining the patient's informed consent, collecting patient data, and writing the manuscript; Lu MJ and Tian JH reviewed the literature and contributed to manuscript drafting; Wu CY and Liu DS revised the manuscript; all authors issued final approval for the version to be submitted.

**Supported by** the Natural Science Foundation of China, No. 82060010.

**Informed consent statement:** Informed written consent was obtained from the patients for the publication of this report and any accompanying images.

**Conflict-of-interest statement:** The authors declare that they have no conflict of interest.

**CARE Checklist (2016) statement:** The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non-Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

**Country/Territory of origin:** China

**ORCID number:** Cheng-Yan Huang 0000-0003-0417-0405; Ming-Jie Lu 0000-0003-3670-6163; Jia-Hua Tian 0000-0003-0569-4921; Dai-Shun Liu 0000-0002-8889-2909; Chun-Yan Wu 0000-0002-7390-7151.

**S-Editor:** Chen YL

**L-Editor:** A

**P-Editor:** Chen YL

## REFERENCES

- 1 **De Stefano L**, D'Onofrio B, Manzo A, Montecucco C, Bugatti S. The Genetic, Environmental, and Immunopathological Complexity of Autoantibody-Negative Rheumatoid Arthritis. *Int J Mol Sci* 2021; **22** [PMID: 34830268 DOI: 10.3390/ijms222212386]
- 2 **Aletaha D**, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO 3rd, Birnbaum NS, Burmester GR, Bykerk VP, Cohen MD, Combe B, Costenbader KH, Dougados M, Emery P, Ferraccioli G, Hazes JM, Hobbs K, Huizinga TW, Kavanaugh A, Kay J, Kvien TK, Laing T, Mease P, Ménard HA, Moreland LW, Naden RL, Pincus T, Smolen JS, Stanislawski-Biernat E, Symmons D, Tak PP, Upchurch KS, Vencovsky J, Wolfe F, Hawker G. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum* 2010; **62**: 2569-2581 [PMID: 20872595 DOI: 10.1002/art.27584]
- 3 **Erre GL**, Mundula N, Colombo E, Mangoni AA, Sechi LA, Oggiano M, Irde R, Zinellu A, Passiu G, Carru C. Diagnostic Accuracy of Anticarbamylated Protein Antibodies in Established Rheumatoid Arthritis: A Monocentric Cross-Sectional Study. *ACR Open Rheumatol* 2019; **1**: 433-439 [PMID: 31777823 DOI: 10.1002/acr2.11063]
- 4 **Marco JL**, Collins BF. Clinical manifestations and treatment of antisynthetase syndrome. *Best Pract Res Clin Rheumatol* 2020; **34**: 101503 [PMID: 32284267 DOI: 10.1016/j.berh.2020.101503]
- 5 **Alfajri N**, Mazahir U, Chaudhri M, Miskoff J. Anti-synthetase syndrome: a rare and challenging diagnosis for bilateral ground-glass opacities-a case report with literature review. *BMC Pulm Med* 2021; **21**: 11 [PMID: 33407281 DOI: 10.1186/s12890-020-01388-0]
- 6 **Gallay L**, Gayed C, Hervier B. Antisynthetase syndrome pathogenesis: knowledge and uncertainties. *Curr Opin Rheumatol* 2018; **30**: 664-673 [PMID: 30239350 DOI: 10.1097/BOR.0000000000000555]
- 7 **Emad Y**, Ragab Y, Abd-Elsalam M, Rasker JJ. Antisynthetase syndrome complicating the course of established case with rheumatoid arthritis: A rare and under-recognized overlapping disease. *Reumatol Clin (Engl Ed)* 2020; **16**: 419-422 [PMID: 30120021 DOI: 10.1016/j.reuma.2018.06.002]
- 8 **Hernandez-Gonzalez I**, Tenorio-Castano J, Ochoa-Parra N, Gallego N, Pérez-Olivares C, Lago-Docampo M, Palomino Doza J, Valverde D, Lapunzina P, Escribano-Subias P. Novel Genetic and Molecular Pathways in Pulmonary Arterial Hypertension Associated with Connective Tissue Disease. *Cells* 2021; **10** [PMID: 34199176 DOI: 10.3390/cells10061488]
- 9 **García-Fernández A**, Quezada-Loaiza CA, de la Puente-Bujidos C. Antisynthetase syndrome and pulmonary hypertension: report of two cases and review of the literature. *Mod Rheumatol Case Rep* 2021; **5**: 152-155 [PMID: 32697139 DOI: 10.1080/24725625.2020.1794521]
- 10 **Xiao YS**, Zhu FY, Luo L, Xing XY, Li YH, Zhang XW, Shen DH. [Clinical and immunological characteristics of 88 cases of overlap myositis]. *Beijing Da Xue Xue Bao Yi Xue Ban* 2021; **53**: 1088-1093 [PMID: 34916687 DOI: 10.19723/j.issn.1671-167X.2021.06.014]
- 11 **Yoshida K**, Lin TC, Wei MY, Malspeis S, Chu SH, Camargo CA Jr, Raby BA, Choi HK, Tedeschi SK, Barbhuiya M, Lu B, Costenbader KH, Karlson EW, Sparks JA. Roles of Postdiagnosis Accumulation of Morbidities and Lifestyle Changes in Excess Total and Cause-Specific Mortality Risk in Rheumatoid Arthritis. *Arthritis Care Res (Hoboken)* 2021; **73**: 188-198 [PMID: 31811708 DOI: 10.1002/acr.24120]
- 12 **Paalanen K**, Puolakka K, Nikiphorou E, Hannonen P, Sokka T. Is seronegative rheumatoid arthritis true rheumatoid arthritis? *Rheumatology (Oxford)* 2021; **60**: 2391-2395 [PMID: 33175968 DOI: 10.1093/rheumatology/keaa623]
- 13 **Klein M**, Mann H, Vencovsky J. Arthritis in Idiopathic Inflammatory Myopathies. *Curr Rheumatol Rep* 2019; **21**: 70 [PMID: 31813070 DOI: 10.1007/s11926-019-0878-x]
- 14 **González-Gay MA**, Montecucco C, Selve-O'Callaghan A, Trallero-Araguas E, Molberg O, Andersson H, Rojas-Serrano J, Perez-Roman DI, Bauhammer J, Fiehn C, Neri R, Barsotti S, Lorenz HM, Doria A, Ghirardello A, Iannone F, Giannini M, Franceschini F, Cavazzana I, Triantafyllidis K, Benucci M, Infantino M, Manfredi M, Conti F, Schwarting A, Sebastiani G, Iuliano A, Emmi G, Silvestri E, Govoni M, Scirè CA, Furini F, Lopez-Longo FJ, Martínez-Barrio J, Sebastiani M, Manfredi A, Bachiller-Corral J, Sifuentes Giraldo WA, Cimmino MA, Cosso C, Belotti Masserini A, Cagnotto G, Codullo V, Romano M, Paolazzi G, Pellerito R, Saketkoo LA, Ortego-Centeno N, Quartuccio L, Batticciotto A, Bartoloni Bocci E,

- Gerli R, Specker C, Bravi E, Selmi C, Parisi S, Salaffi F, Meloni F, Marchioni E, Pesci A, Dei G, Confalonieri M, Tomietto P, Nuno L, Bonella F, Pipitone N, Mera-Valera A, Perez-Gomez N, Gerzeli S, Lopez-Mejias R, Matos-Costa CJ, Pereira da Silva JA, Cifrian J, Alpini C, Olivieri I, Blázquez Cañamero MÁ, Rodríguez Cambrón AB, Castañeda S, Cavagna L; AENEAS (American and European Network of Antisynthetase Syndrome) collaborative group. Timing of onset affects arthritis presentation pattern in antisynthetase syndrome. *Clin Exp Rheumatol* 2018; **36**: 44-49 [PMID: [28770709](#)]
- 15 **Noguchi E**, Uruha A, Suzuki S, Hamanaka K, Ohnuki Y, Tsugawa J, Watanabe Y, Nakahara J, Shiina T, Suzuki N, Nishino I. Skeletal Muscle Involvement in Antisynthetase Syndrome. *JAMA Neurol* 2017; **74**: 992-999 [PMID: [28586844](#) DOI: [10.1001/jamaneurol.2017.0934](#)]
- 16 **Kumar RR**, Jha S, Dhooria A, Naidu GSRSNK, Minz RW, Kumar S, Sharma SK, Sharma A, Jain S, Dhir V. Anti-Jo-1 Syndrome Often Misdiagnosed as Rheumatoid Arthritis (for Many Years): A Single-Center Experience. *J Clin Rheumatol* 2021; **27**: 150-155 [PMID: [31895110](#) DOI: [10.1097/RHU.0000000000001234](#)]
- 17 **Szturmowicz M**, Franczuk M, Jędrych ME, Wyrostkiewicz D, Oniszh K, Darocha S, Kasperowicz K, Kurzyna M. Dominating Cause of Pulmonary Hypertension May Change Over Time-Diagnostic and Therapeutic Considerations in a Patient with Pulmonary Hypertension Due to Rheumatoid Arthritis with Lung Involvement. *Diagnostics (Basel)* 2021; **11** [PMID: [34679629](#) DOI: [10.3390/diagnostics11101931](#)]
- 18 **Fayed H**, Coghlan JG. Pulmonary Hypertension Associated with Connective Tissue Disease. *Semin Respir Crit Care Med* 2019; **40**: 173-183 [PMID: [31137058](#) DOI: [10.1055/s-0039-1685214](#)]
- 19 **Kay D**, Kadri F, Fitzpatrick G, Alnuaimat H, Reddy R, Ataya A. Anti-synthetase syndrome-associated pulmonary veno-occlusive disease. *Pulm Circ* 2020; **10**: 2045894020935289 [PMID: [32655855](#) DOI: [10.1177/2045894020935289](#)]



Published by **Baishideng Publishing Group Inc**  
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

**Telephone:** +1-925-3991568

**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

**Help Desk:** <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

