# World Journal of *Clinical Cases*

World J Clin Cases 2020 September 6; 8(17): 3621-3919





Published by Baishideng Publishing Group Inc

W J C C World Journal of Clinical Cases

#### Contents

#### Semimonthly Volume 8 Number 17 September 6, 2020

#### **REVIEW**

3621 Autoimmunity as the comet tail of COVID-19 pandemic

Talotta R, Robertson E

3645 Gender medicine: Lessons from COVID-19 and other medical conditions for designing health policy Machluf Y, Chaiter Y, Tal O

#### **MINIREVIEWS**

3669 Complexities of diagnosis and management of COVID-19 in autoimmune diseases: Potential benefits and detriments of immunosuppression

Georgiev T, Angelov AK

#### **ORIGINAL ARTICLE**

#### **Retrospective Study**

- 3679 Incidental anal <sup>18</sup>fluorodeoxyglucose uptake: Should we further examine the patient? Moussaddaq AS, Brochard C, Palard-Novello X, Garin E, Wallenhorst T, Le Balc'h E, Merlini L'heritier A, Grainville T, Siproudhis L, Lièvre A
- 3691 Emergency surgery in COVID-19 outbreak: Has anything changed? Single center experience D'Urbano F, Fabbri N, Koleva Radica M, Rossin E, Carcoforo P
- 3697 Somatostatin receptor scintigraphy in the follow up of neuroendocrine neoplasms of appendix Saponjski J, Macut D, Sobic-Saranovic D, Ognjanovic S, Bozic Antic I, Pavlovic D, Artiko V
- 3708 Efficacy of stool multiplex polymerase chain reaction assay in adult patients with acute infectious diarrhea Ahn JS, Seo SI, Kim J, Kim T, Kang JG, Kim HS, Shin WG, Jang MK, Kim HY
- 3718 Comparison of gemcitabine plus nab-paclitaxel and FOLFIRINOX in metastatic pancreatic cancer Han SY, Kim DU, Seol YM, Kim S, Lee NK, Hong SB, Seo HI
- 3730 Shear wave elastography may be sensitive and more precise than transient elastography in predicting significant fibrosis

Yao TT, Pan J, Qian JD, Cheng H, Wang Y, Wang GQ

- 3743 Radioactive <sup>125</sup>I seed implantation for locally advanced pancreatic cancer: A retrospective analysis of 50 cases Li CG, Zhou ZP, Jia YZ, Tan XL, Song YY
- 3751 Active surveillance in metastatic pancreatic neuroendocrine tumors: A 20-year single-institutional experience

Gao HL, Wang WQ, Xu HX, Wu CT, Li H, Ni QX, Yu XJ, Liu L



Cartan	World Journal of Clinical Cases Semimonthly Volume 8 Number 17 September 6, 2020	
Conten		
3763	Clinical efficacy of tocilizumab treatment in severe and critical COVID-19 patients	
	Zeng J, Xie MH, Yang J, Chao SW, Xu EL	
3774	Phosphatidylinositol-3,4,5-trisphosphate dependent Rac exchange factor 1 is a diagnostic and prognostic biomarker for hepatocellular carcinoma	
	Cai Y, Zheng Q, Yao DJ	
	Observational Study	
3786	Awareness and attitude of fecal microbiota transplantation through transendoscopic enteral tubing among inflammatory bowel disease patients	
	Zhong M, Sun Y, Wang HG, Marcella C, Cui BT, Miao YL, Zhang FM	
	CASE REPORT	
3797	Cauda equina arachnoiditis - a rare manifestation of West Nile virus neuroinvasive disease: A case report	
	Santini M, Zupetic I, Viskovic K, Krznaric J, Kutlesa M, Krajinovic V, Polak VL, Savic V, Tabain I, Barbic L, Bogdanic M, Stevanovic V, Mrzljak A, Vilibic-Cavlek T	
3804	Portal gas in neonates; is it always surgical? A case report	
	Altokhais TI	
3808	Large lingual heterotopic gastrointestinal cyst in a newborn: A case report	
	Lee AD, Harada K, Tanaka S, Yokota Y, Mima T, Enomoto A, Kogo M	
3814	Osteochondral lesion of talus with gout tophi deposition: A case report	
	Kim T, Choi YR	
3821	Traumatic neuroma of remnant cystic duct mimicking duodenal subepithelial tumor: A case report	
	Kim DH, Park JH, Cho JK, Yang JW, Kim TH, Jeong SH, Kim YH, Lee YJ, Hong SC, Jung EJ, Ju YT, Jeong CY, Kim JY	
3828	Autoimmune hepatitis in a patient with immunoglobulin A nephropathy: A case report	
	Jeon YH, Kim DW, Lee SJ, Park YJ, Kim HJ, Han M, Kim IY, Lee DW, Song SH, Lee SB, Seong EY	
3835	Diagnosis of an actively bleeding brachial artery hematoma by contrast-enhanced ultrasound: A case report	
	Ma JJ, Zhang B	
3841	Lung adenocarcinoma harboring rare epidermal growth factor receptor L858R and V834L mutations treated with icotinib: A case report	
	Zhai SS, Yu H, Gu TT, Li YX, Lei Y, Zhang HY, Zhen TH, Gao YG	
3847	Gastroduodenitis associated with ulcerative colitis: A case report	
	Yang Y, Li CQ, Chen WJ, Ma ZH, Liu G	
3853	Majocchi's granuloma caused by <i>Trichophyton rubrum</i> after facial injection with hyaluronic acid: A case report	
	Liu J, Xin WQ, Liu LT, Chen CF, Wu L, Hu XP	



Combon	World Journal of Clinical Cases			
Conten	Semimonthly Volume 8 Number 17 September 6, 2020			
3859	Novel deletion mutation in Bruton's tyrosine kinase results in X-linked agammaglobulinemia: A case report			
	Hu XM, Yuan K, Chen H, Chen C, Fang YL, Zhu JF, Liang L, Wang CL			
3867	Multidisciplinary treatment of life-threatening hemoptysis and paraplegia of choriocarcinoma with pulmonary, hepatic and spinal metastases: A case report			
	Lin YY, Sun Y, Jiang Y, Song BZ, Ke LJ			
3875	Diagnostic value of ultrasound in the spontaneous rupture of renal angiomyolipoma during pregnancy: A case report			
	Zhang T, Xue S, Wang ZM, Duan XM, Wang DX			
3881	Gallbladder sarcomatoid carcinoma: Seven case reports			
	Qin Q, Liu M, Wang X			
3890	Surgical strategy used in multilevel cervical disc replacement and cervical hybrid surgery: Four case reports			
	Wang XF, Meng Y, Liu H, Hong Y, Wang BY			
3903	Diagnosis and treatment of an elderly patient with 2019-nCoV pneumonia and acute exacerbation of chronic obstructive pulmonary disease in Gansu Province: A case report			
	He TP, Wang DL, Zhao J, Jiang XY, He J, Feng JK, Yuan Y			
3911	Diagnosis and treatment of mixed infection of hepatic cystic and alveolar echinococcosis: Four case reports			
	A JD, Chai JP, Wang H, Gao W, Peng Z, Zhao SY, A XR			



#### Contents

#### Semimonthly Volume 8 Number 17 September 6, 2020

#### **ABOUT COVER**

Editorial board member of World Journal of Clinical Cases, Dr. Elia de Maria is Adjunct Professor of Arrhythmology Lab in the Cardiology Unit, Ramazzini Hospital in Carpi, Italy. He graduated in Medicine and Surgery from the University of Napoli in 1999, continuing on to obtain specialization in Cardiology in 2003. He also holds the distinction of High Degree Master in Electrophysiology and Cardiac Stimulation. Since 2005, he has practiced as a Permanent Consultant Cardiologist in the Italian Public Hospitals, and since 2015 as an External Contract Professor in the Faculty of Medicine and Surgery of University of Verona. His clinical and research interests encompass pharmacological therapy in acute and chronic cardiac conditions, temporary and definitive pacing, thoracentesis and pericardiocentesis, and hemodynamic monitoring. (L-Editor: Filipodia)

#### **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 indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, PubMed, and PubMed Central. The 2020 Edition of Journal Citation Reports® cites the 2019 impact factor (IF) for WJCC as 1.013; IF without journal self cites: 0.991; Ranking: 120 among 165 journals in medicine, general and internal; and Quartile category: Q3.

#### **RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: Yan-Xia Xing; Production Department Director: Yun-Xiaojian Wu; Editorial Office Director: Jin-Lei Wang.

NAME OF JOURNAL	INSTRUCTIONS TO AUTHORS
World Journal of Clinical Cases	https://www.wjgnet.com/bpg/gerinfo/204
ISSN	GUIDELINES FOR ETHICS DOCUMENTS
ISSN 2307-8960 (online)	https://www.wjgnet.com/bpg/GerInfo/287
LAUNCH DATE	GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
April 16, 2013	https://www.wjgnet.com/bpg/gerinfo/240
FREQUENCY	PUBLICATION ETHICS
Semimonthly	https://www.wjgnet.com/bpg/GerInfo/288
EDITORS-IN-CHIEF	PUBLICATION MISCONDUCT
Dennis A Bloomfield, Sandro Vento, Bao-Gan Peng	https://www.wjgnet.com/bpg/gerinfo/208
EDITORIAL BOARD MEMBERS	ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/2307-8960/editorialboard.htm	https://www.wjgnet.com/bpg/gerinfo/242
PUBLICATION DATE	STEPS FOR SUBMITTING MANUSCRIPTS
September 6, 2020	https://www.wjgnet.com/bpg/GerInfo/239
COPYRIGHT	ONLINE SUBMISSION
© 2020 Baishideng Publishing Group Inc	https://www.f6publishing.com

© 2020 Baishideng Publishing Group Inc. All rights reserved. 7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA E-mail: bpgoffice@wjgnet.com https://www.wjgnet.com



W J C C World Journal of Clinical Cases

Submit a Manuscript: https://www.f6publishing.com

World J Clin Cases 2020 September 6; 8(17): 3828-3834

DOI: 10.12998/wjcc.v8.i17.3828

ISSN 2307-8960 (online)

CASE REPORT

# Autoimmune hepatitis in a patient with immunoglobulin A nephropathy: A case report

You Hyun Jeon, Da Woon Kim, So Jeong Lee, Young Joo Park, Hyo Jin Kim, Miyeun Han, Il Young Kim, Dong Won Lee, Sang Heon Song, Soo Bong Lee, Eun Young Seong

ORCID number: You Hyun Jeon 0000-0001-7318-5753; Da Woon Kim 0000-0002-9471-5976: So Jeong Lee 0000-0002-6465-9811; Young Joo Park 0000-0001-8416-0615; Hyo Jin Kim 0000-0001-9289-9073; Miyeun Han 0000-0001-7304-2496; Il Young Kim 0000-0002-1731-6357; Dong Won Lee 0000-0003-0282-484X; Sang Heon Song 0000-0002-8218-6974; Soo Bong Lee 0000-0002-3388-7993; Eun Young Seong 0000-0002-6006-0051.

Author contributions: Jeon YH collected clinical data and contributed manuscript drafting; Kim DW collected clinical data and drafted table and figures; Lee SJ performed the histological analyses and interpretation; Park YJ was physician who provided treatment and intellectual content; Kim HJ, Han M, Kim IY and Lee DW reviewed the manuscript and provided intellectual content; Song SH, Lee SB and Seong EY reviewed the literature and revised the manuscript; all authors approved the final version of the manuscript.

Supported by Pusan National University Hospital Education and Research Team, No 219.

Informed consent statement:

Informed written consent was obtained from the patient for publication of this report and any

You Hyun Jeon, Da Woon Kim, Department of Internal Medicine, Pusan National University School of Medicine, Busan 49241, South Korea

So Jeong Lee, Department of Pathology, Pusan National University Hospital, Busan 49241, South Korea

Young Joo Park, Division of Gastroenterology, Department of Internal Medicine, Biomedical Research Institute, Pusan National University Hospital, Busan 49241, South Korea

Hyo Jin Kim, Miyeun Han, Sang Heon Song, Eun Young Seong, Division of Nephrology, Department of Internal Medicine, Biomedical Research Institute, Pusan National University Hospital, Busan 49241, South Korea

Il Young Kim, Dong Won Lee, Soo Bong Lee, Division of Nephrology, Department of Internal Medicine, Pusan National University Yangsan Hospital, Yangsan 626-770, South Korea

Corresponding author: Eun Young Seong, MD, PhD, Associate Professor, Division of Nephrology, Department of Internal Medicine, Biomedical Research Institute, Pusan National University Hospital, 179 Gudeok-ro, Seo-gu, Busan 49241, South Korea. sey-0220@hanmail.net

## Abstract

#### BACKGROUND

Immunoglobulin A nephropathy (IgAN) is the most commonly encountered glomerular disease in Asian countries. It has a broad clinical presentation, and it is frequently associated with other conditions. Chronic liver disease is well recognized as the leading cause of secondary IgAN. However, cases of IgAN associated with autoimmune hepatitis (AIH) have seldom been reported.

#### CASE SUMMARY

A 63-year-old Korean woman was admitted to Pusan National University Hospital for an evaluation of abdominal pain and elevated liver enzymes. Two weeks prior, she had presented to our hospital with proteinuria of approximately 1350 mg/d and hematuria and was diagnosed with IgAN. Autoimmune profiles were highly positive for antinuclear antibodies, and symptoms related to portal hypertension including ascites and peripheral edema were present. A diagnosis of AIH was made according to the simplified scoring system of the International Autoimmune Hepatitis Group. Despite immunosuppression with prednisolone



WJCC | https://www.wjgnet.com

accompanying images.

Conflict-of-interest statement: The authors declare that they have no conflicts 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 NonCommercial (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: htt p://creativecommons.org/licenses /by-nc/4.0/

#### Manuscript source: Unsolicited manuscript

Received: June 29, 2020 Peer-review started: June 29, 2020 First decision: July 24, 2020 Revised: August 5, 2020 Accepted: August 20, 2020 Article in press: August 20, 2020 Published online: September 6, 2020

P-Reviewer: Ferreira GSA, Tanabe Κ S-Editor: Yan IP L-Editor: A P-Editor: Xing YX



and azathioprine, rapid deterioration of liver function led to end-stage liver disease. After a living-donor liver transplantation, liver function gradually improved, and she had maintained stable liver and kidney function at the six months follow-up.

#### CONCLUSION

Cases of secondary IgAN with chronic liver disease have been frequently reported in the literature but are rarely associated with AIH. We encountered an IgAN patient with concurrent progressive liver failure due to AIH.

Key words: Immunoglobulin A nephropathy; Secondary immunoglobulin A nephropathy; Autoimmune hepatitis; Liver transplantation; Case report

©The Author(s) 2020. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Immunoglobulin A nephropathy (IgAN) is an autoimmune disease and may be related to other autoimmune conditions. To the best of our knowledge, only two cases of IgAN with autoimmune hepatitis have been reported, and the pathophysiological associations of both diseases have not been established.

Citation: Jeon YH, Kim DW, Lee SJ, Park YJ, Kim HJ, Han M, Kim IY, Lee DW, Song SH, Lee SB, Seong EY. Autoimmune hepatitis in a patient with immunoglobulin A nephropathy: A case report. World J Clin Cases 2020; 8(17): 3828-3834 URL: https://www.wjgnet.com/2307-8960/full/v8/i17/3828.htm DOI: https://dx.doi.org/10.12998/wjcc.v8.i17.3828

### INTRODUCTION

Immunoglobulin A nephropathy (IgAN) is the most prevalent glomerular disease worldwide and is an important cause of end-stage kidney disease. IgAN is an autoimmune disorder characterized by diffuse mesangial deposition of immunoglobulin A (IgA)<sup>[1]</sup>. The accumulation of mesangial IgA associated with chronic liver disease, such as alcoholic liver cirrhosis and chronic viral hepatitis, is the most common form of secondary IgAN<sup>[2]</sup>. Secondary IgAN is usually clinically silent, and the most common symptom is microscopic hematuria. IgAN has also been reported to be associated with other autoimmune conditions, including ankylosing spondylitis, psoriasis, inflammatory bowel disease and Hashimoto's thyroiditis<sup>[2,3]</sup>. However, few cases have been reported in the literature of IgAN associated with autoimmune hepatitis (AIH).

#### CASE PRESENTATION

#### Chief complaints

A 63-year-old woman presented with right upper quadrant abdominal discomfort.

#### History of present illness

The patient's symptoms developed insidiously over 3 d. She did not show any symptoms related to portal hypertension.

#### History of past illness

Two weeks ago, she presented to our hospital with proteinuria of approximately 1350 mg/d and hematuria and was diagnosed with IgAN. Light microscopic findings of kidney biopsy showed a moderate increase in mesangial matrix and mesangial cellularity (Figure 1A) with focal severe tubular atrophy and interstitial infiltration of mononuclear cells. Out of 37 glomeruli, 2 glomeruli (5%) showed global sclerosis. Immunofluorescence microscopy showed predominant mesangial IgA staining (Figure 1B) and C3 staining (Figure 1C). Electron microscopy revealed mesangial electron-dense deposits and focal effacement of the epithelial cell foot processes



Jeon YH et al. AIH in a patient with IgAN



**Figure 1** Kidney histopathology. A: Light microscopy, mesangial hypercellularity in a glomerulus; B: Immunofluorescence microscopy, the staining of immunoglobulin A (3+); C: Immunofluorescence microscopy; the staining of C3 (1+); D: Electron microscopy, mesangial electron- dense deposits.

(Figure 1D). Laboratory findings were as follows: aspartate aminotransferase (AST), 20 IU/L; alanine aminotransferase (ALT), 8 IU/L; and serum creatinine, 1.21 mg/dL. She was not taking any other medications except an angiotensin II receptor blocker.

#### Physical examination

On admission, she had a height of 155.5 cm, a weight of 53.7 kg, a blood pressure of 120/70 mmHg, a regular heart rate of 64 bpm, and a temperature of 36.1 °C. The patient had mild right upper quadrant pain and tenderness and icteric sclera. She denied taking any new medication or alcohol consumption.

#### Laboratory examinations

Laboratory findings were as follows: white blood cell count, 4090/ $\mu$ L; hemoglobin, 10.6 g/dL; platelet count, 99 × 10<sup>3</sup>/ $\mu$ L; AST, 771 IU/L; ALT, 488 IU/L; alkaline phosphatase, 92 IU/L; total bilirubin, 3.04 mg/dL; direct bilirubin, 1.86 mg/dL; total protein, 6.89 g/dL; albumin, 3.13 g/dL; and prothrombin international normalized ratio, 1.57. Serum creatinine and estimated glomerular filtration rate were 1.26 mg/dL and 45.6 mL/min per 1.73 m<sup>2</sup>, respectively, similar to the values 2 wk prior. She was negative for anti-hepatitis B surface antigen, anti-hepatitis B core antibody, antihepatitis C virus antibody and anti-hepatitis A virus IgM. The results of immunological studies and serum iron and copper studies are shown in Tables 1 and 2.

#### Imaging examinations

A contrast-enhanced computed tomography (CT) scan of the abdomen revealed a distal common bile duct (CBD) stone with mild upstream bile duct dilatation and an intrahepatic portosystemic shunt in the left lobe of the liver. There was not any evidence of chronic liver injury or portal hypertension such as esophageal varix, splenomegaly and ascites. Endoscopic retrograde cholangiopancreatography showed CBD stone without bile duct narrowing.

WJCC | https://www.wjgnet.com

Table 1 The results of immunological studies						
		Reference values				
IgG (mg/dL)	1822.0	700-1600				
IgA (mg/dL)	550.4	70-400				
IgM (mg/dL)	144.3	40-230				
IgE (mg/dL)	40.4	0-100				
C3 (mg/dL)	123.7	90-180				
C4 (mg/dL)	26.8	10-40				
FANA	1:320	Below 1:40				
Anti-smooth muscle Ab	Negative	Negative				
Anti-mitochondrial Ab	Negative	Negative				
Anti-LKM-1 Ab	Negative	Negative				
Anti-ds DNA IgG	Negative	Negative				
Anti-Sm Ab	Negative	Negative				
Anti-cardiolipin Ab IgG	Negative	Negative				
Anti-cardiolipin Ab IgM	Negative	Negative				
Anti-Ro	Negative	Negative				
Anti-La	Negative	Negative				
Anti-centromere Ab	Negative	Negative				
Anti-Scl-70	Negative	Negative				
Anti-RNP Ab	Negative	Negative				

IgG: Immunoglobulin G; IgA: Immunoglobulin A; IgM: Immunoglobulin M; IgE: Immunoglobulin E; FANA: Fluorescent antinuclear antibodies; Anti-LKM-1 Ab: Anti-liver/kidney microsomal antibodies; Anti-RNP Ab: Anti-ribonucleoproteins antibodies.

Table 2 The results of serum iron and copper studies					
		Reference values			
Iron (µg/dL)	88	33-193			
TIBC (µg/dL)	260	264-448			
Transferrin saturation (%)	33.85				
Ferritin (ng/mL)	128.0	6-282			
Copper (µg/dL)		75-145			
Ceruloplasmin (mg/dL)		16-45			
24 h urinary copper excretion ( $\mu g/24$ h)		15-60			

TIBC: Total iron binding capacity.

#### **FINAL DIAGNOSIS**

After endoscopic removal of CBD stones, liver enzyme levels started to decrease. On the fourth day, AST, ALT and total bilirubin gradually increased to 896 IU/L, 579 IU/L, and 5.05 mg/dL, respectively. Symptoms related to portal hypertension, including ascites and peripheral edema, occurred. Based on the abovementioned findings, the diagnosis of AIH was made according to the simplified scoring system of the International Autoimmune Hepatitis Group<sup>[4]</sup>. The score prior to steroid therapy was 6 points: Antinuclear antibodies (2), IgG (2) and absence of viral hepatitis (2).

Raisbideng® WJCC https://www.wjgnet.com

#### TREATMENT

She was treated with prednisolone 0.5 mg/kg in combination with azathioprine for 2 wk. Despite the treatment, liver function rapidly deteriorated, and hepatorenal syndrome requiring renal replacement therapy developed subsequently. The patient was not exposed to the nephrotoxic agents and had no episode of bleeding or septic shock. The model for end-stage liver disease score was 37 points at the time of waiting list registration for liver transplantation. Approximately two months after hospitalization, she underwent living-donor liver transplantation from her son. Hepatectomy specimens showed submassive necrosis. Prominent necrosis involved entire lobules in most of the liver parenchyma (Figure 2A), and the remaining parenchyma showed canalicular type cholestasis (Figure 2B).

#### OUTCOME AND FOLLOW-UP

After having a well-functioning allograft, the general condition and laboratory findings improved. Immunosuppressive drugs, including corticosteroids, tacrolimus and mycophenolate, were used. Three weeks after surgery, hemodialysis was stopped because of improving renal function. Two months later, the serum creatinine level was 1.5 mg/dL, and the spot urine protein/creatinine ratio was 193.3 mg/g.

#### DISCUSSION

IgAN associated with chronic liver disease is the most prevalent pattern of secondary IgAN. Mesangial IgA deposition is frequently found in autopsy specimens in the general population without medical illness<sup>[5]</sup>. IgAN has been found in 25% of kidney biopsy specimens from 60 patients with end-stage liver disease<sup>[6]</sup>. Serum IgA levels are frequently elevated in patients with alcoholic liver cirrhosis. In an ex-vivo study, peripheral blood mononuclear cells of alcoholic liver cirrhosis patients secreted more IgA than those of healthy controls<sup>[7]</sup>. The accumulation of IgA is thought to result from decreased clearance of IgA, which can be explained in two ways. As cirrhosis progresses, the number of hepatocytes and Kupffer cells, which express the asialoglycoprotein receptor and Fc receptors that bind galactose residues of IgA and remove it from circulation, also decreases<sup>[8,9]</sup>. Portal hypertension may play a role in hyperimmunoglobulinemia because of the portal venous flow directly from the portal vein to the systemic circulation. Our patient had no clinical evidence of portal hypertension before fulminant hepatic failure, though she did have a portosystemic shunt on CT scan at the time of diagnosis of IgAN. A portosystemic shunt is a communication between the portal vein and the systemic vein, and it is caused by a congenital malformation, liver cirrhosis or trauma. Portosystemic shunts can be found incidentally in the absence of other signs of portal hypertension<sup>[10,11]</sup>.

Secondary IgAN associated with autoimmune disorders, including Sjogren's disease, ankylosing spondylitis and coeliac disease, has been reported in the literature<sup>[2,12,13]</sup>. However, IgAN with AIH has been reported in only a limited number of patients, and most of them had other autoimmune diseases such as Sjogren's disease which is often reported to be associated with IgAN<sup>[14,15]</sup>. In our case, two different diseases that do not share a common pathogenesis were diagnosed sequentially. AIH is a chronic inflammatory liver disease and that may progress to liver cirrhosis or fulminant hepatitis<sup>[4]</sup>. The pathogenesis of AIH is not fully understood. The destruction of self-tolerance to hepatocyte antigen may play a key role in the pathogenesis of AIH. Autoimmune liver injury is characterized by autoreactive CD4 and CD8 T cells via cellular immune mechanisms. Currently, regulatory T cells that suppress excessive immune reactions are considered important mediator cells in the immunopathology of AIH<sup>[16]</sup>.

Since there are a limited number of cases, the renal outcome of patients with secondary IgAN receiving liver transplantation is not clear. A retrograde observational study suggested that kidney function tends to be relatively favorable after liver transplantation. Among 7 patients who underwent liver transplantation, only one progressed to end-stage kidney disease during the 5 years follow-up period<sup>[17]</sup>. In this report, liver transplantation did not affect the disease progression of IgAN.

There is neither a clear definition of secondary IgAN, which is recognized when IgAN coexists with other conditions, nor a histopathological feature to distinguish primary IgAN from secondary IgAN<sup>[18]</sup>. Moreover, reported cases of IgAN concurrent



WJCC | https://www.wjgnet.com



Figure 2 Liver histopathology. A: Hematoxylin and eosin staining (magnification, 40 ×), submassive necrosis of the liver parenchyma with prominent bile duct proliferation; B: Hematoxylin and eosin staining (magnification, 100 ×), canalicular type cholestasis.

with AIH are sparse, and the pathophysiological relationship between the two diseases has not been well established. In our patient, the clinical activity of IgAN did not correlate with the acute onset of AIH, which indicates that the possibility of the coexistence of primary IgAN with AIH cannot be excluded. Therefore, the analysis of additional cases is required in the future. Additional case reports are necessary to promote studies on the relevance of IgAN and AIH.

#### CONCLUSION

We report a rare case of IgAN associated with AIH presenting as fulminant hepatic failure treated with liver transplantation. Both diseases were diagnosed simultaneously, even though they were thought to have different pathogeneses. Whether the secondary IgAN was related to AIH or the two diseases coincidentally occurred remains uncertain. Further case reports and analyses of IgAN concurrent with other diseases, which is known to be rare, are needed to determine potential pathophysiological relationships.

#### REFERENCES

- Wyatt RJ, Julian BA. IgA nephropathy. N Engl J Med 2013; 368: 2402-2414 [PMID: 23782179 DOI: 10.1056/NEJMra1206793]
- Saha MK, Julian BA, Novak J, Rizk DV. Secondary IgA nephropathy. Kidney Int 2018; 94: 674-681 2 [PMID: 29804660 DOI: 10.1016/j.kint.2018.02.030]
- Ambruzs JM, Walker PD, Larsen CP. The histopathologic spectrum of kidney biopsies in patients with 3 inflammatory bowel disease. Clin J Am Soc Nephrol 2014; 9: 265-270 [PMID: 24262508 DOI: 10.2215/CJN.04660513]
- Manns MP, Lohse AW, Vergani D. Autoimmune hepatitis--Update 2015. J Hepatol 2015; 62: S100-S111 4 [PMID: 25920079 DOI: 10.1016/j.jhep.2015.03.005]
- Sinniah R. Occurrence of mesangial IgA and IgM deposits in a control necropsy population. J Clin Pathol 5 1983; 36: 276-279 [PMID: 6338054 DOI: 10.1136/jcp.36.3.276]
- Calmus Y, Conti F, Cluzel P, Hill G, Antoine C, Scatton O, Soubrane O, Glotz D, Pillebout E, Nochy D. 6 Prospective assessment of renal histopathological lesions in patients with end-stage liver disease: effects on long-term renal function after liver transplantation. J Hepatol 2012; 57: 572-576 [PMID: 22612996 DOI: 10.1016/j.jhep.2012.04.028]
- 7 Massonnet B, Delwail A, Ayrault JM, Chagneau-Derrode C, Lecron JC, Silvain C. Increased immunoglobulin A in alcoholic liver cirrhosis: exploring the response of B cells to Toll-like receptor 9 activation. Clin Exp Immunol 2009; 158: 115-124 [PMID: 19737238 DOI: 10.1111/j.1365-2249.2009.04004.x
- 8 Tomana M, Kulhavy R, Mestecky J. Receptor-mediated binding and uptake of immunoglobulin A by human liver. Gastroenterology 1988; 94: 762-770 [PMID: 3338646 DOI: 10.1016/0016-5085(88)90252-1]
- 9 Rifai A, Mannik M. Clearance of circulating IgA immune complexes is mediated by a specific receptor on Kupffer cells in mice. J Exp Med 1984; 160: 125-137 [PMID: 6736868 DOI: 10.1084/jem.160.1.125]
- Kim M, Lee KY. Understanding the Pathophysiology of Portosystemic Shunt by Simulation Using an 10 Electric Circuit. Biomed Res Int 2016; 2016: 2097363 [PMID: 27868061 DOI: 10.1155/2016/2097363]
- Remer EM, Motta-Ramirez GA, Henderson JM. Imaging findings in incidental intrahepatic portal venous 11 shunts. AJR Am J Roentgenol 2007; 188: W162-W167 [PMID: 17242223 DOI: 10.2214/AJR.05.1115]
- Chen Y, Zhao X, Tang D, Xu C, Sun L, Sun L, Wu J, Mei C. IgA nephropathy in two patients with Sjögren's 12 syndrome: one with concomitant autoimmune hepatitis. Intern Med 2010; 49: 37-43 [PMID: 20045999 DOI:



10.2169/internalmedicine.49.2722]

- 13 Habura I, Fiedorowicz K, WoÅoniak A, Idasiak-Piechocka I, Kosikowski P, Oko A. IgA nephropathy associated with coeliac disease. Cent Eur J Immunol 2019; 44: 106-108 [PMID: 31114445 DOI: 10.5114/ceji.2019.84021
- Grønbaek L, Vilstrup H, Pedersen L, Jepsen P. Extrahepatic autoimmune diseases in patients with 14 autoimmune hepatitis and their relatives: A Danish nationwide cohort study. Liver Int 2019; 39: 205-214 [PMID: 30218621 DOI: 10.1111/liv.13963]
- 15 Singri N, Gleason B, Flamm SL, Kanwar YS, Ghossein C. Secondary IgA nephropathy presenting as nephrotic syndrome with glomerular crescentic changes and acute renal failure in a patient with autoimmune hepatitis. J Nephrol 2004; 17: 125-129 [PMID: 15151269 DOI: 10.1111/j.1442-2042.2004.00727.x]
- Wang M, Zhang H. The pathogenesis of autoimmune hepatitis. Front Lab Med 2018; 2: 36-39 [DOI: 16 10.1016/j.flm.2018.03.002]
- Hommos MS, El-Zoghby ZM. Renal Outcomes in Patients With IgA Nephropathy Undergoing Liver 17 Transplant: A Retrospective Cohort Study. Transplant Direct 2017; 3: e193 [PMID: 28795144 DOI: 10.1097/TXD.000000000000708]
- 18 **Obrișcă B**, Ștefan G, Gherghiceanu M, Mandache E, Ismail G, Stancu S, Boitan B, Ion O, Mircescu G. "Associated" or "Secondary" IgA nephropathy? An outcome analysis. PLoS One 2019; 14: e0221014 [PMID: 31398224 DOI: 10.1371/journal.pone.0221014]





## 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 Help Desk: https://www.f6publishing.com/helpdesk https://www.wjgnet.com

