A Case of Hepatorenal Syndrome and Abdominal Compartment Syndrome with High Renal Congestion

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

AEF 1 **Hiroteru Kamimura**
B 1 **Takayuki Watanabe**
BC 1 **Tomoyuki Sugano**
B 1 **Nao Nakajima**
D 1 **Junji Yokoyama**
D 1 **Kenya Kamimura**
D 1 **Atsunori Tsuchiya**
D 1 **Masaaki Takamura**
D 1 **Hirokazu Kawai**
BD 2 **Takashi Kato**
B 2 **Gen Watanabe**
DE 1 **Satoshi Yamagiwa**
A 1 **Shuji Terai**

1 Division of Gastroenterology and Hepatology, Niigata University Graduate School of Medical and Dental Sciences, Niigata City, Niigata, Japan
2 Division of Molecular and Diagnostic Pathology, Niigata University Graduate School of Medical and Dental Sciences, Niigata City, Niigata, Japan

Corresponding Author: Hiroteru Kamimura, e-mail: hiroteruk@med.niigata-u.ac.jp
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Patient: **Male, 40**
Final Diagnosis: **Hepatorenal syndrome**
Symptoms: **Abdominal distension**
Medication: **—**
Clinical Procedure: **—**
Specialty: **Nephrology**

Objective: **Rare co-existance of disease or pathology**
Background: Hepatorenal syndrome (HRS) is a reversible renal impairment that occurs in patients with acute liver failure and advanced liver cirrhosis. HRS is due to a renal vasoconstriction that results from extreme vasodilatation. It is therefore a functional disorder, not associated with structural kidney damage. On the other hand, end-stage liver diseases are often complicated by massive ascites. Massive ascites may cause abdominal compartment syndrome (ACS), which includes impairment of renal blood flow, but there are no reports indicating that kidney lesions caused by ACS may pathologically contribute to end-stage liver diseases.
Case Report: A 40-year-old man with acute liver failure was admitted to our hospital. He was diagnosed with type 1 HRS and showed ACS at the same time. He died 30 days after admission. There were signs of congestion in the kidneys upon dissection and advanced erythroid fullness in the renal tubules.
Conclusions: We report an autopsy case with HRS and ACS diagnosed with a clinical and histopathological consideration of liver and kidney. Further clinical studies are needed to improve management of renal failure in patients with acute liver failure and advanced liver cirrhosis.

MeSH Keywords: **Acute Kidney Injury • Hepatorenal Syndrome • Intra-Abdominal Hypertension**

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Background

Hepatorenal syndrome (HRS) was originally described in 1863 by Flint as an association between liver disease and oliguric renal failure in the absence of significant renal histological change [1]. It is characterized by marked reduction in glomerular filtration rate (GFR) and renal plasma flow in patients with liver cirrhosis and hepatic failure in the absence of other causes of renal failure [2]. Renal failure is caused by vasoconstriction resulting from systematic vasodilation, and HRS patients are thought to recover from renal failure after receiving a liver transplant [3]. However, the mechanisms governing HRS pathology are not completely understood. Abdominal ascites occurs typically at the end stage of liver failure. Massive ascites also influences intraabdominal pressure (IAP) pathogenesis [4]. Abdominal compartment syndrome (ACS) results in organ failure, including renal failure. Although elevation of renal parenchymal and renal vein pressure are likely mechanisms of renal impairment in ACS patients, oliguria and acute kidney injury (AKI) are early and frequent consequences of ACS and can be present at relatively low levels of IAP [5]. That issue has not been taken into account in the definition of HRS. Song et al. described the role of urea transporter protein within the state of HRS and ACS by successfully making ACS murine model [6]. Chang et al. suggested that renal pathologic changes occur due to massive abdominal ascites as gleaned from studying a murine model of cirrhosis [7]. However, there are no reports indicating that kidney lesions with massive abdominal ascites due to subacute liver failure may pathologically contribute to HRS. This autopsy case report serves to highlight kidney pathology when HRS and massive ascites occur.

Case Report

A 40-year-old man with acute liver failure was admitted to our hospital. He had undergone coronary artery bypass grafting because of angina pectoris 3 years ago. He had no previous history of renal and liver disease. He had no-smoking history and drank socially. He was previously hospitalized elsewhere for septic shock due to acute epiglottitis. He recovered from septic shock, but he had unrecoverable liver dysfunction and his hepatic spare ability had decreased. Therefore, he was transferred to our hospital 30 days after the disease onset. On admission, he had severe jaundice and massive ascites and showed flapping tremor; however, his consciousness was lucid. He was severely obese (body weight: 120 kg, body mass index: 41.5). Physical examination showed a high fever of 38.2°C, pulse of 72 beats/min, and blood pressure of 116/70 mm/Hg. Laboratory results showed decreases of prothrombin time (38%), albumin (2.1 g/dL), and cholinesterase (49 IU/L), and increases of white blood cell count (22 300/μL), total bilirubin (26.4 mg/dL), creatinine (2.1 mg/dL), C-reactive

protein (CRP) (4.1 mg/dL), and NH_3 (121 μg/dL) (Table 1). Computed tomography of the abdomen showed massive ascites (Figure 1A), and the intraperitoneal and retroperitoneal organ, especially right renal vein, were compressed by the ascites (Figure 1B). We diagnosed him with sepsis-associated late-onset hepatic failure and AKIN stage 2. We appropriately performed general care and maintained proper circulation, breathing, and fluids. Moreover, we performed plasma exchange and administered fresh frozen plasma and albumin to support his liver function. However, his liver dysfunction did not recover and the kidney function worsened. Serum creatinine increased to 4.1 mg/dl and urine volume gradually decreased. Then, we started noradrenaline for HRS 20 days after admission. We palliatively performed large-volume paracentesis (LVP) with an upper limit of 5 L, and urine volume increased after the LVP. However, IAP was continuously high at 20 mmHg even after LVP, indicating he had severe ACS. He died 30 days after admission.

We performed an autopsy after obtaining consent from his family. At the time of death, the amount of abdominal ascites had reached 10 L, even though LVP was performed a few days before. The liver weighed 1973 g with no signs of severe atrophy. There was significant accumulation of neutrophils and severe cholestasis in the bile duct. In the portal area, there was bridging fibrosis and aggregation of Kupffer cells. The primary cause of hepatic failure was thought to be sepsis-associated liver injury.

There were signs of congestion in the kidneys – weight 301 g in the right kidney and 345 g in the left kidney – upon dissection (Figure 2). Regarding bilateral renal congestion, there were bile casts and advanced erythroid fullness in the renal tubules. There was also swelling in the renal tubules. There was no change in the glomerulus and collecting tubule and no renal fibrosis (Figure 3). When we measured bladder pressure after LVP, it was 20 mmHg, which is in the range of intraabdominal hypertension (IAH). IAH was due to massive ascites. Additionally, we thought that the observed renal congestion was due to renal vein compression, which was caused by a large quantity of abdominal ascites. Thus, we concluded that this patient had HRS-1 and ACS at the same time.

Discussion

Although liver diseases cause irreversible renal dysfunction, such as hepatitis C virus-induced cryoglobulinemia, membranoproliferative glomerulonephritis, HRS causes reversible renal failure [8,9]. HRS is difficult to clinically distinguish from primary renal failure. According to the definition of HRS from the International Ascites Club (IAC) proposed in 2007, HRS is divided into 2 types (1 and 2) based on prognosis and clinical characteristics [2].

Table 1. Laboratory data on admission.

(CBC)						
WBC	22300/µl	(Chemistry)		ANA	<40	
Neut	87%	T-bil	26.4 mg/dl	AMA	(−)	
Eo	2.90%	D-bil	20.5 mg/dl	HBsAg	(−)	
Baso	0.40%	AST	107 IU/l	anti-HBs	(−)	
Mon	3.20%	ALT	46 IU/l	anti-HCV	(−)	
Lymph	37.40%	ALP	446 IU/l	(Urine examination)		
RBC	352×10^4/µl	LDH	621 IU/L	Specific gravity	1.018	
Hb	12.2 g/dl	CHE	256 IU/l	pH	6	
Ht	40.30%	γ-GT	83 IU/l	Protein	30 mg/dl	
Plt	12.4×10^4/µl	TP	7.1 g/dl	Occult blood	10–19/HP	
		Alb	2.1 g/dl	Ketone	(−)	
(Coagulation)		CRP	4.14 mg/dl			
PT	38%	T-Cho	145 mg/dl			
APTT	60.0 sec	TG	107 mg/dl			
fibrinogen	227 mg/dl	BUN	65 mg/dl			
		Cr	2.09 mg/dl			
		NH3	121 µg/dl			

Alb – albumin; ALP – alkaline phosphatase; ALT – alanine aminotransferase; ANA – antinuclear antibody; AMA – antimitochondrial antibody; APTT – activated partial thromboplastin time; AST – aspartate aminotransferase; BUN – blood urea nitrogen; CBC – complete blood count; CHE – cholinesterase; Cr – creatinine; CRP – C-reactive protein; D-bil – direct bilirubin; Hb – hemoglobin; Ht – hematocrit; LDH – lactate dehydrogenase; Plt – platelets; PT – prothrombin time; RBC – red blood cells; T-bil – total bilirubin; T-chol – total cholesterol; TP – total protein; WBC – white blood cells; γ-GT – γ-glutamyltransferase.
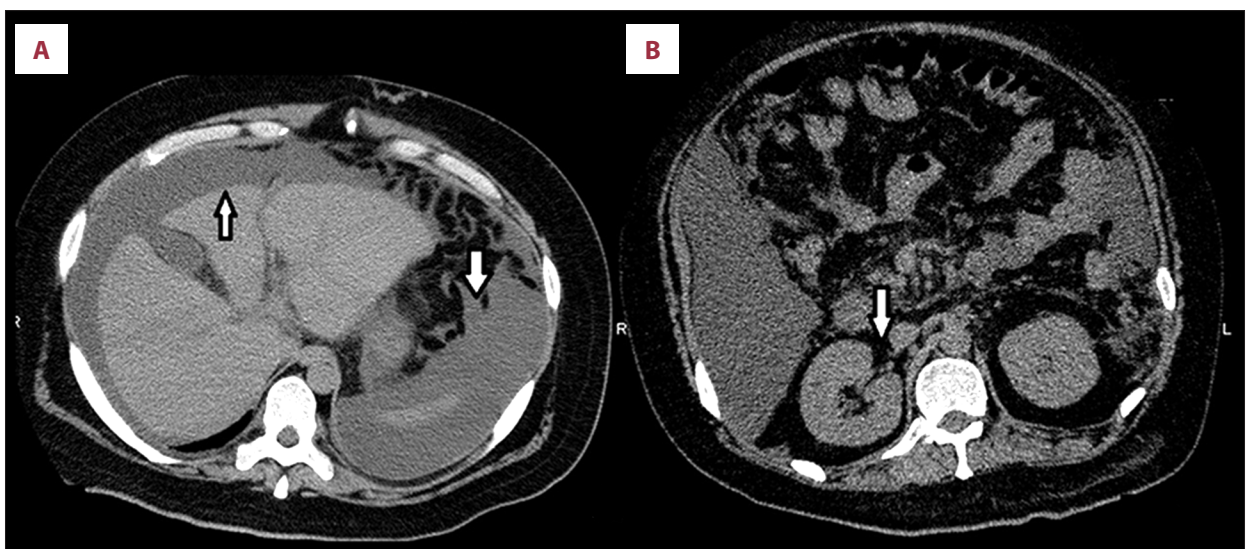

Figure 1. Computed tomography of the abdomen. (**A**) Massive ascites and obesity was observed (arrow). (**B**) The pelvic viscera was compressed by the ascites (arrow).

Figure 2. Macroscopic findings of the kidney. Macroscopic findings showed bilateral renal congestion.

Figure 3. Microscopic findings of the kidney. Microscopic findings showed swelling in the renal tubules. There was no change in the glomerulus and collecting tubule and no renal fibrosis. There were bile casts and advanced erythroid fullness in the renal tubules.

The patient had no reaction to rehydration therapy and albumin administration, and he had no previous history of renal dysfunction. He had recovered from bacteremia and his blood pressure was maintained. Clinically, he was originally diagnosed as HRS-1. We did not find major evidence of renal tubule necrosis in the autopsy; otherwise, we found some bile casts caused by elevation of serum bilirubin, which affect renal function. To maintain effective plasma circulation, an albumin infusion is first performed. In addition, albumin treatment is combined with terlipressin as the first-line treatment, or midodrine and noradrenaline are used as alternatives [10]. We administrated noradrenaline, which was permitted by health insurance. However, regardless of treatment choice, the effect is temporary, and a liver transplant is the only treatment that can extend patient survival. The 3-year survival rate after a liver transplant of an HRS-1 patient is reported to be 65% [11]. Various factors concern the etiology of HRS, and the definition is corrected as needed. Wong et al. reported new diagnostic criteria of HRS in cirrhosis patients, jointly proposed by the IAC and Acute Dialysis Quality Initiative. In the new criteria, HRS-1 and HRS-2 are both incorporated in AKI and chronic kidney disease (CKD) [12]. AKI is a relatively frequent problem, occurring in approximately 20% of hospitalized patients with cirrhosis [13]. In the autopsy of this case, both kidneys showed severe renal congestion. ACS is defined as hypoperfusion and ischemia of intraabdominal viscera and structures caused by raised IAP. It causes lethal conditions, with acute renal, acute respiratory, and acute circulatory failure. Cade et al. reported a significant increase in urine flow rate and Ccr after reduction in IAP, from 22 to 10 mmHg, with paracentesis in patients with cirrhosis [14]. ACS is diagnosed upon measuring IAP by the pressure transducer and is often found in decreased eGFR in the presence of ascites in the early stage [15]. IAP in a normal individual ranges from slightly sub-atmospheric to approximately 6.5 mmHg. Recent studies demonstrated that even at the relatively low IAP of 10–15 mmHg, significant alterations 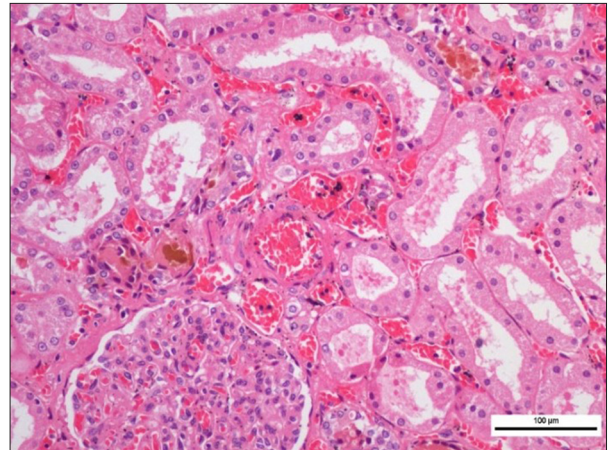in organ function are still observed. In this state, renal vein pressure and renal vascular resistance are significantly elevated [16]. It is suggested that compression of renal vein is vital in the development renal dysfunction [17]. IAH is the significant pathological mechanism and independent risk factor in the occurrence and development of HRS.

Conclusions

There are effective treatments of ascites to control IAP according to pathophysiology. Currently, tolvaptan effectively treats hepatic edema and ascites-related clinical symptoms in liver cirrhosis patients who do not respond sufficiently to conventional diuretics [18]. In the case of acute liver failure and a terminal cirrhosis patient, the final lifesaving effort is a liver transplant, but while the patient waits for the opportunity, renal dysfunction becomes a high-risk factor affecting survival [19].

In liver cirrhosis, because of the dynamic change of blood flow that may cause rupture of esophageal varices and fall in blood pressure, LVP is often avoided. Renal function is reversible for HRS patients as aforementioned, but in the case of liver cirrhosis, there may be advanced renal insufficiency when massive ascites exists. Thus, we have to take into consideration ACS and ACS-mediated renal dysfunction. For HRS patients, maintenance of renal function is critical to improve the MELD score and patient survival. Currently, ACS is not mentioned in the definition of HRS, but we think, from this case, that the prevention of ACS at an early stage is crucial for prevention of HRS.

Conflict of interest

None declared.

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