



Acute Kidney Injury Due to Inferior Vena Cava Stenosis After Liver Transplantation: A Case Report About the Importance of Hepatic Vein Doppler Ultrasound and Clinical Assessment

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Abstract

Rationale: Acute kidney injury (AKI) is a frequent complication after liver transplantation. In some patients, prompt intervention targeted at a specific etiology is of paramount importance.

Presenting concerns of the patients: A 25 years old man with advanced liver cirrhosis caused by sclerosing cholangitis and autoimmune hepatitis underwent orthotopic liver transplantation. One month after surgery, severe AKI developed in conjunction with recurrent ascites and lower extremity edema. Notable clinical findings included a persistently low urinary sodium excretion, a bland urinary sediment, and an abnormally monophasic hepatic vein waveform on Doppler ultrasound.

Diagnoses: Inferior vena cava stenosis.

Interventions: Angioplasty with stent installation.

Outcomes: Rapid improvement of renal function after stent installation.

Lessons learned: The following case illustrates the importance of integrating clinical cues, ultrasound features, and laboratory findings. The combination of AKI associated with lower extremity edema, abnormal monophasic hepatic vein flow on Doppler ultrasound, and a low urinary sodium excretion after liver transplantation should evoke the possibility of inferior vena cava stenosis as the etiologic factor.

Abrégé

Fondement: L'insuffisance rénale aiguë (IRA) est une complication survenant fréquemment à la suite d'une greffe hépatique. Pour certains patients, une intervention rapide et ciblée sur l'étiologie spécifique s'avère d'une importance capitale.

Présentation du cas: Un homme âgé de 25 ans atteint d'une cirrhose hépatique avancée causée par une cholangite sclérosante et une hépatite auto-immune a subi une greffe hépatique orthotopique. Un mois après l'intervention, le patient a développé une sévère IRA conjointement à des ascites récurrentes et un œdème des membres inférieurs. Parmi les principales manifestations cliniques figuraient la persistance d'une faible excrétion urinaire du sodium, la présence de sédiments urinaires neutres et une forme d'onde anormalement monophasique pour la veine hépatique à l'échographie Doppler.

Diagnostic: Sténose de la veine cave inférieure

Intervention: Angioplastie avec implantation d'une endoprothèse vasculaire

Résultats: Amélioration rapide de la fonction rénale à la suite de l'implantation de l'endoprothèse vasculaire

Enseignements tirés: Ce cas illustre l'importance d'intégrer les indicateurs cliniques, les informations obtenues à l'échographie et les résultats de laboratoire. L'IRA survenant à la suite d'une greffe hépatique, lorsqu'elle est associée à de l'œdème des membres inférieurs, à des ondes anormalement monophasiques de la veine hépatique à l'échographie Doppler, de même qu'à une faible excrétion urinaire de sodium, devrait évoquer la possibilité d'une sténose de la veine cave inférieure comme facteur étiologique.

Keywords

acute kidney injury, liver transplantation, hepatorenal reflex, venous congestion, Doppler ultrasound, hepatic vein Doppler

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What was known before

Inferior vena cava stenosis is a rare complication of liver transplantation and can lead to acute kidney injury (AKI).

What this adds

This case illustrates how this reversible cause of AKI can be suspected at the bedside.

Introduction

Acute kidney injury (AKI) is a frequent complication after liver transplantation. Early AKI (<72 hours), defined per the Kidney Disease: Improving Global Outcomes (KDIGO) criteria,¹ occurs in half of patients and is associated with reduced graft and patient survival.² Among them, 6.5% still require renal replacement therapy after 3 months. Multiple coexisting etiologic factors have been identified such as hemodynamic instability during surgery, the severity of the underlying liver disease, the need for blood transfusion, and the introduction of calcineurin inhibitor after transplantation.² Late-onset AKI is less clearly defined and occurs in a smaller proportion of patients.³ Regardless of the timing of onset, persistent renal dysfunction after liver transplantation is associated with a higher risk of end-stage kidney disease.⁴

Clinicians involved in the care of patient with AKI after liver transplantation are confronted with the multitude of possible etiologies. One of the main concerns in this setting is to avoid missing the opportunity to intervene when a reversible factor is involved. Other than the traditional tools used in the evaluation of AKI, specific clinical clues may be sought by the astute clinician. We report a case where the integration of clinical, ultrasound imaging and laboratory information coupled with an understanding of physiology led to the identification of inferior vena cava (IVC) stenosis as rare cause of late-onset AKI after liver transplantation. The patient gave written permission for the publication of this report, which is waived from institutional review board approval.

Case Presentation

A 25 years old man with advanced liver cirrhosis (Child-Turcotte-Pugh class C) caused by sclerosing cholangitis and autoimmune hepatitis was admitted for hypotension due to

hypovolemia induced by diuretics and nadolol use. He had ascites, esophageal varices, and splenomegaly with resultant anemia and thrombocytopenia. This patient was also known for iatrogenic Cushing syndrome, a previous episode of pancreatitis, osteopenia, and hypothyroidism. He had a model for end-stage liver disease (MELD-Na) score of 27 before surgery. He was not known for chronic kidney disease (serum creatinine = 65 $\mu\text{mol/L}$, estimated glomerular filtration rate [eGFR] > 60 mL/min/1.73m²) prior to surgery.

The patient underwent orthotopic liver transplantation 5 days after admission. The caval replacement technique was performed, in which the donor IVC is implanted in the recipient using end-to end cavocavostomy. Surgery was complicated by significant blood loss of 1.5 L and prolonged intraoperative hypotension. He developed AKI (KDIGO stage 2: >100% increase in serum creatinine) after the surgery (Figure 1) but renal function subsequently partially improved with serum creatinine between 130 and 155 $\mu\text{mol/L}$ during the month following surgery. Routine post-operative Doppler ultrasound evaluation of the liver showed normal flow in the hepatic artery and in the portal vein but abnormal monophasic hepatic venous flow.

Thirty-five days after surgery, kidney function deteriorated with a sudden doubling in serum creatinine in the 230 to 260 $\mu\text{mol/L}$ range. During this period, problematic ascites required repeated therapeutic paracentesis. Measurement of albumin and total protein at the time of the first paracentesis revealed a high serum-to-ascite albumin gradient (15 g/L vs 31 g/L, gradient: 16 g/L) and low total protein (23 g/L) suggestive of ascites related to portal hypertension.⁵ The patient also developed lower extremity edema. Despite repeated albumin 25% administration (a total of 525 g was administered) and crystalloid infusion, urinalysis showed low sodium and chloride levels compatible with significant renal sodium reabsorption (<20 mmol/L). Serum tacrolimus levels were maintained between 5 and 8 ng/mL (see Supplementary Material for details). No significant proteinuria or hematuria was present, and the urinary sediment was bland. Renal echography was normal including Doppler ultrasound study showing a resistive index of 0.62 with normal flow in the renal artery and vein.

The lack of improvement in renal function led to the decision to perform a renal biopsy at day 45 after surgery. Renal histology showed extramembranous deposits with granular deposits of immunoglobulin G and A in addition to complement deposition (C3 and C1q). Those findings

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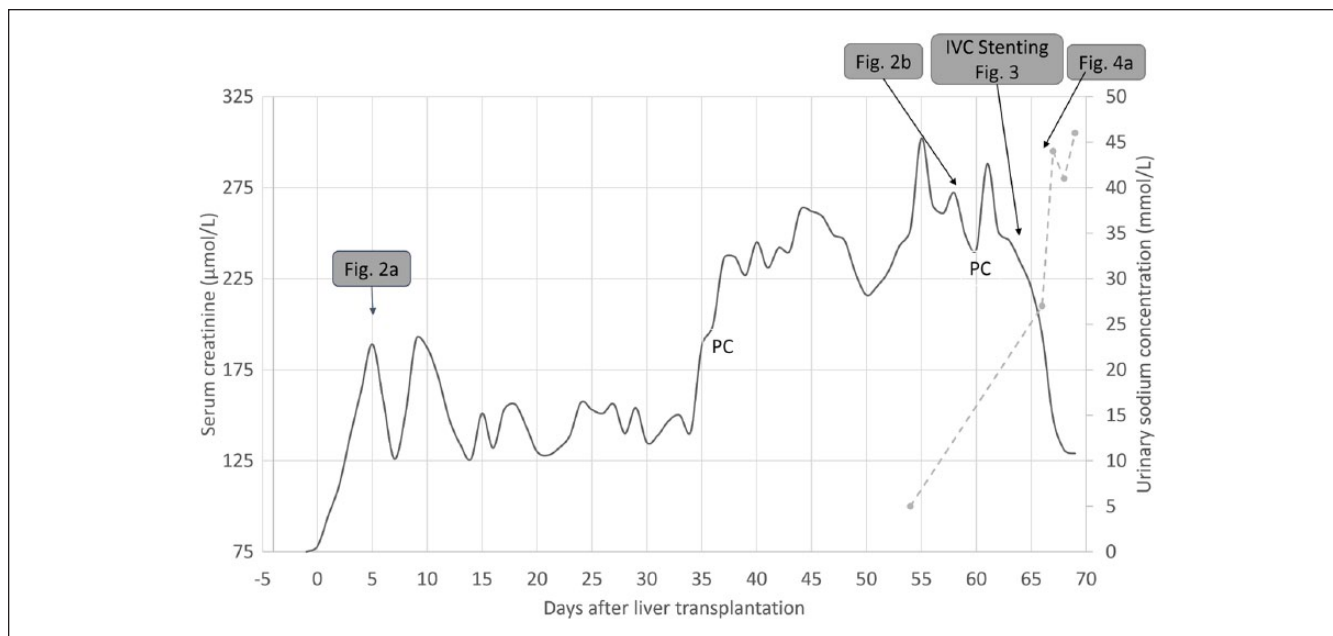


Figure 1. Evolution of serum creatinine (plain line) after orthotopic liver transplantation.

Note. Dotted line represents urinary sodium concentration. PC = paracentesis to drain ascites; IVC = inferior vena cava.

could have been compatible with membranous nephropathy, a condition reported in conjunction with autoimmune hepatitis.⁶ However, in the absence of significant proteinuria, the immunosuppression was not increased in response to this finding.

The continued presence of significant ascites accumulation and persistent kidney dysfunction led to a repeated Doppler ultrasound evaluation which still revealed monophasic hepatic vein flow (Figure 2a). A stenosis of the IVC was suspected at this time. On day 65, caval venogram by a right femoral vein approach was performed with the use of carbon monoxide to prevent further renal function deterioration. A severe stenosis of the distal cavocaval anastomosis located downstream of the hepatic veins associated with a trans-stenotic gradient of 12 mm Hg was demonstrated (Figure 2b). Vena cava angioplasty followed by stent placement (20 mm × 50 mm Gianturco Z-stent (Cook medical, Bloomington, Indiana) was performed (Figure 2c) with good angiographic result and no residual gradient or complication.

Following this intervention, a rapid improvement in serum creatinine was seen with a decrease from 220 µmol/L to 131 µmol/L within 48 hours. During this period, urinalysis revealed a progressive increase in sodium concentration. Doppler ultrasound evaluation of the liver showed normalization hepatic veins flow, both 24 hours after angioplasty and 7 days after (Figure 2d). Significant improvement in the patient clinical status was noted with reduced ascites accumulation and lower limb edema. After hospital discharge, 92 days after surgery, serum creatinine was 110 µmol/L (eGFR: >60 mL/min/1.73m²).

Discussion

This case illustrates a rare but reversible cause of AKI after liver transplantation. Inferior vena cava stenosis occurs in 1% to 2% of patients undergoing liver transplantation with caval replacement, and renal insufficiency is an associated finding in about 50% of cases.^{7,8} Although obstruction to venous return is a known cause of hemodynamic instability, it is rarely considered in the differential diagnosis in the setting of pre-renal AKI. However, a significant impedance to venous return can have profound consequences on renal hemodynamics. In this case, if we consider that the cardiac output was left unaffected by the decrease in cardiac preload, there are 2 mechanisms that could have resulted in renal dysfunction. First, the elevation in venous pressure is known to be detrimental to kidney function. Animal studies have shown that an increase in the renal venous pressure results in an acute decrease in glomerular filtration, even when the arterial pressure remains constant.^{9,10} In addition, the increase in central venous pressure seems to be the main factor associated with worsening in renal function in congestive heart failure patients.¹¹ Second, in the setting of an IVC stenosis located distal to the origin of the hepatic veins, the increase in hepatic vein pressure lead to post-hepatic portal hypertension. It has been shown that portal vein distension activates stretch receptors triggering a local reflex system.¹² This neurally mediated mechanism might lead to the stimulation of renal sympathetic nerves resulting in vasoconstriction, renin release, and sodium reabsorption.^{13,14} In support of this hypothesis, it has been shown that interrupting this network, either by section of the anterior hepatic nerve^{15,16} or sympathetic block,¹⁷ abolishes

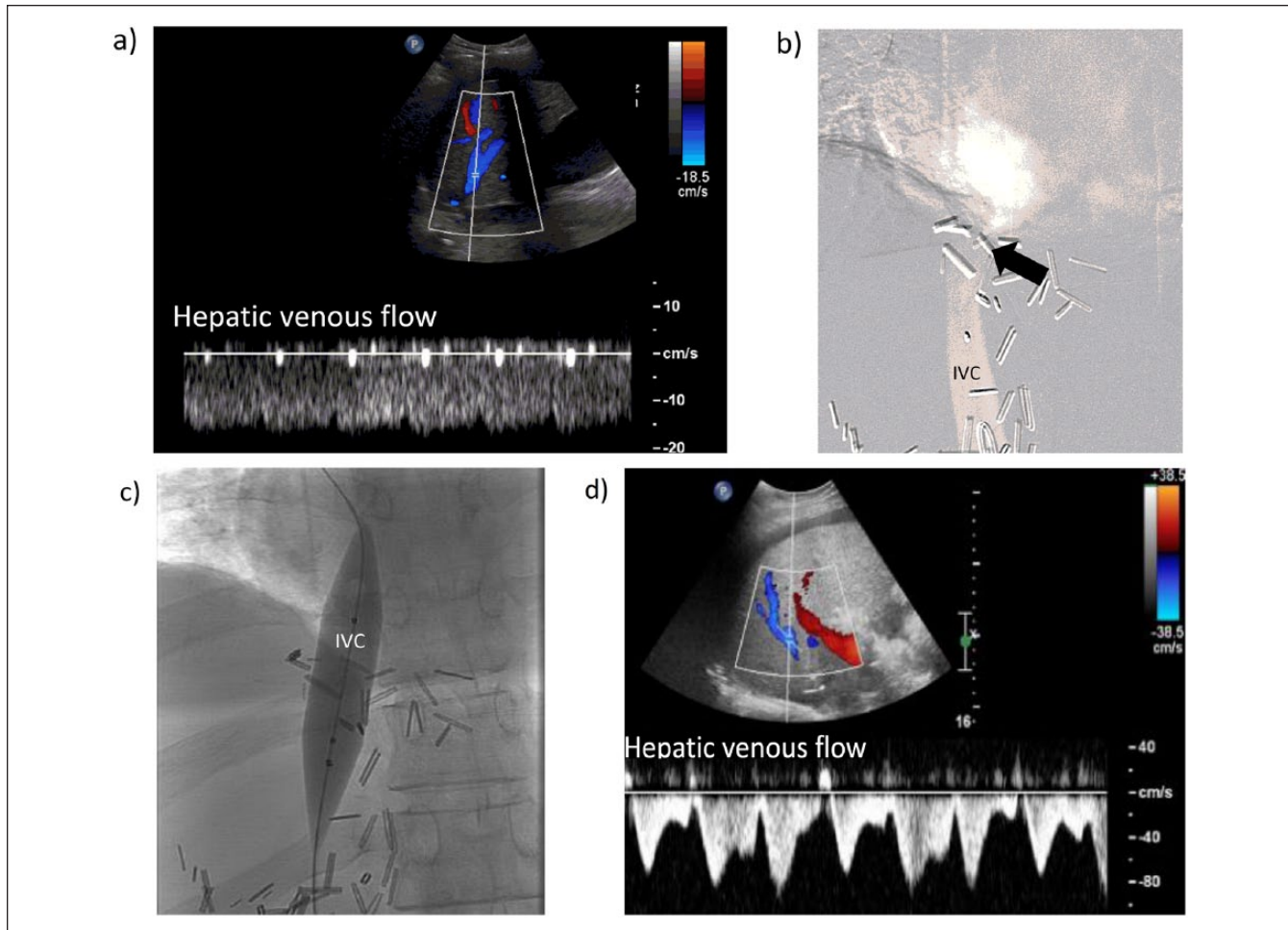


Figure 2. (a) Doppler ultrasound evaluation of the hepatic venous flow 58 days after surgery. (b) Carbon monoxide angiogram 65 days after liver transplantation showing a stenosis (arrow) of the distal cavocaval anastomosis. A significant pressure gradient of 12 mm Hg was measured across the stenosis. (c) Balloon dilatation and subsequent stent placement (not shown). (d) Doppler ultrasound evaluation of the hepatic vein flow at 24 hours after stent placement. Note. IVC = inferior vena cava.

this response. In the presented case, the development of recurrent ascites and the splenomegaly with concurrent persistent low urinary sodium may illustrate this phenomenon.

In this case, a 1-month delay occurred between the appearance of severe AKI and the diagnosis followed by the intervention to treat the etiology of renal failure. This case highlights the difficulty to clinically suspect this pathology. However, an abnormal hepatic venous flow was documented 5 days after surgery. Hepatic venous flow is usually used to diagnose diastolic right ventricular failure.¹⁸ However, its assessment has also been used in the setting of undifferentiated shock to diagnose an obstruction to venous return.¹⁹ Although a significant obstruction between the hepatic vein and the right atrium is present, the pressure variations during the cardiac cycle in the right atria or the central venous pressure waveform are not transmitted to the hepatic vein and the normal triphasic pattern is lost (Figure 3). Doppler ultrasound of the hepatic vein can be performed with minimal training using a basic

ultrasound machine. We therefore hypothesize that ultrasound might be used by a clinician trained in point-of-care ultrasound or by the radiologist to rule-out an obstruction to venous return proximal to the hepatic veins in patients with AKI. Previous data suggest that a triphasic pattern excludes the possibility of significant outflow obstruction, but a monophasic pattern might lack specificity to confirm the diagnosis.²⁰

Conclusion

This case illustrates IVC stenosis as a rare cause of AKI after liver transplantation. Renal dysfunction associated with ascites and lower extremity edema in the post-transplant period should prompt consideration for this diagnosis. Furthermore, an abnormal monophasic hepatic vein flow on Doppler ultrasound is a hallmark of hepatic venous outflow obstruction and might alert the attending clinician to this diagnostic possibility.

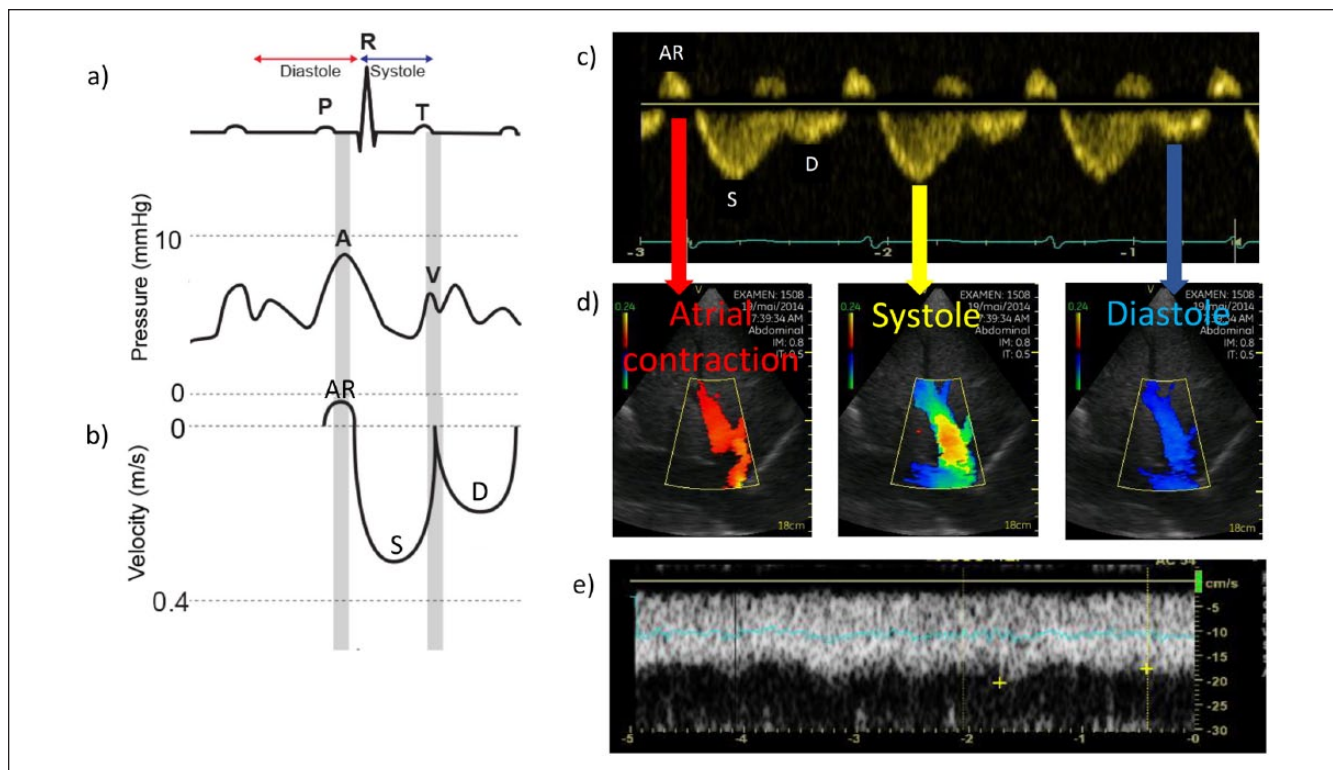


Figure 3. Interpretation of hepatic venous flow. Right atrial pressure variations during the cardiac cycle (a) are usually transmitted to the hepatic vein producing a triphasic waveform (b) which can be observed both on pulse wave Doppler (c) and on color Doppler (d) ultrasound. A monophasic waveform (e) is noted when a hemodynamically significant outflow obstruction is present between the hepatic vein and the right atria.

Note. A = a wave; V = v wave; AR = atrial reversal; S = systolic component; D = diastolic component; IVC = inferior vena cava.

Author Contributions

WBS was involved in data collection and article preparation. WBS, AYD, MNP, LB, JE, LL, and BW were involved in analysis and interpretation. AYD was involved in supervision. Each author contributed important intellectual content during article drafting or revision and accepted accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

This case report is waived from institutional review board approval.

Consent for Publication

The patient gave written permission for the publication of this report.

Availability of Data and Materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: AYD was a Speaker and received honoraria for Medtronic, CAE Healthcare and Masimo. The other authors have no conflict of interest to declare.

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Supplemental Material

Supplemental material is available for this article online.

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