

CASE REPORT

Forced diuresis oriented by point-of-care ultrasound in cardiorenal syndrome type 5 due to light chain myeloma—The role of hepatic venogram: A case report

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Abstract

Monitoring venous congestion by ultrasound assessment of hepatic venogram allowed individualized fluid management in severe cardiorenal syndrome type 5 due to light chain myeloma, preserving residual renal function and avoiding heart failure.

KEYWORDS

cardiorenal syndrome, forced diuresis, hepatic venogram, myeloma, point-of-care ultrasound

1 | INTRODUCTION

A 78-year-old woman was affected by severe cardiorenal syndrome type 5 due to light chain myeloma. Cast nephropathy and hypokinetic cardiomyopathy conditioned oliguria and heart failure. Monitoring venous congestion by ultrasound assessment of hepatic venogram oriented hydration and diuretic therapy, resolving heart failure and preserving residual diuresis.

Cardiorenal syndrome (CRS) is defined as pathophysiologic disorder of the heart and the kidneys, whereby acute or chronic dysfunction of one organ induces acute or chronic dysfunction of the other.¹ The less the cardiac and renal function and the narrower will be their mutual adaptation to changes in circulating volume.² Excessive hydration in the

presence of heart and renal injury may precipitate in venous congestion, fluid overload, and heart failure (HF). Thus, fluid management becomes challenging, whenever renal and heart function are both hampered by systemic diseases, as it happens in CRS type 5.³

Noninvasive grading of venous congestion by point-of-care ultrasound (POCUS) predicted the risk of acute kidney injury (AKI)⁴ and oriented diuretic therapy in CRS.⁵ In 2016, European Society of Cardiology categorized the clinical phenotypes of HF, according to signs of congestion and peripheral perfusion, represented by the combination of wet-dry and warm-cold patterns.⁶ POCUS may provide real-time estimation of venous congestion and its responsiveness to diuretics and ultrafiltration (UF), before other signs of wetness, dryness, or hypoperfusion appear.

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We recently purposed a simplified approach for daily assessment of venous congestion by POCUS, limited to interpretation of inferior vena cava (IVC) and hepatic veins (HV) venogram.⁷ Five patterns of HV venogram were described, ranging from the less (stage 0) to the most

congested (stage 4) one (Figure 1). Lower venous congestion in inspiration (I) than in apnea (A) was supposed to reflect favorable responsiveness to reduction in circulating volume, mimicked by increased venous return during inspiration (Figure S1). Strength of venous congestion was

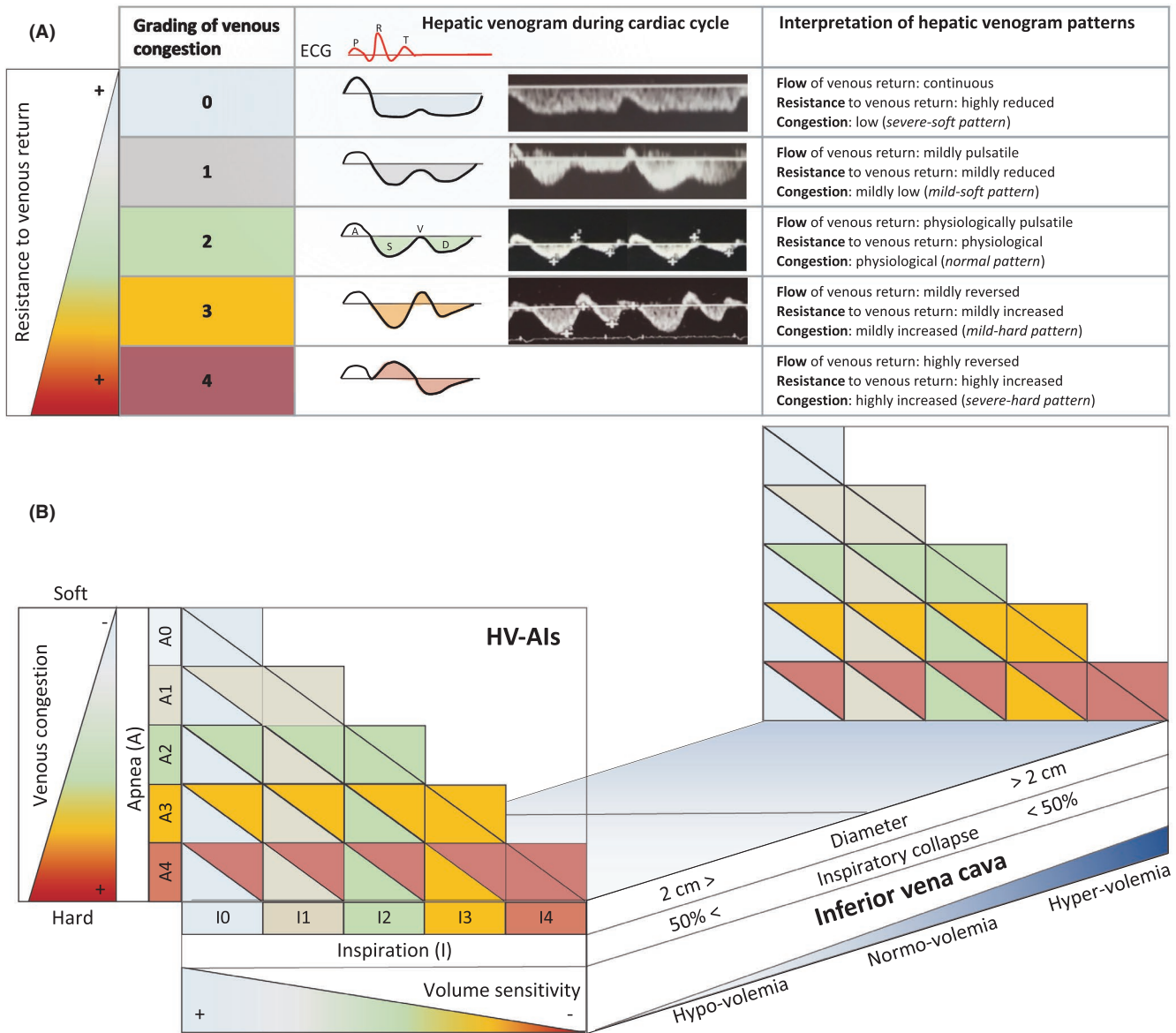


FIGURE 1 Classification of venous congestion by point-of-care ultrasound assessment of hepatic venogram and inferior vena cava. Notes A. Patterns of hepatic venogram are graded in 5 classes from 0 to 4, according to pulsatility and direction of venous flow. Normal pattern (Grade 2) is represented by negative and separated systolic (S) and diastolic (D) waves, with S being higher than D component. Progressive fusion of S and D waves is considered as secondary to reduced resistance to venous return, marker of reduced venous congestion (Grades 0-1, soft patterns). Progressively reversion of venous flow, represented by positive V and S waves, is considered as secondary to increased resistance to venous return, marker of increased venous congestion (Grades 3-4, hard patterns). Grade 4 did not appear in the present case, making ultrasonographic images unavailable for iconography. B. Pattern of hepatic venogram may vary between apnea (A) and inspiration (I) (Figure S1). Lower venous congestion during inspiration is taken as sign of sensitivity to reduction in circulating volume, mimicked by increased venous return induced by negative mediastinic pressure during respiratory cycle. HV-AIs derives by the combination of hepatic venogram in apnea and inspiration, leading to 15 classes, capable to merge the grade of venous congestion and its hypothetical response to volume reduction (volume sensitivity). The same HV-Ais classes might be hypothetically associated with different replenishment and collapse of IVC. Merging information, derived by HV-AIs and IVC, may help to discriminate venous congestion from circulating volume. ECG: electrocardiography, HV-AIs: Hepatic venogram-Apnea and Inspiration score

then categorized in 15 classes by the combination of HV venogram in apnea and inspiration,⁷ herein renamed as the Hepatic Veins-Apnea and Inspiration score (HV-AIs). Final classification ranged from the “softest” (not congested, HV-AIs A0-I0) to the “hardest” (highly congested, HV-AIs A4-I4) class (Figure 1). Harder patterns, associated with enlarged non collapsing IVC, were suggested to be partially related to expanded circulating volume (hard-hypervolemic patterns), while harder patterns in the presence of empty and collapsing IVC were referred to impaired heart function, independently from reduced circulating volume (hard-hypovolemic patterns) (Figure 1).⁷

Forced diuresis is encouraged to minimize renal damage in myeloma cast nephropathy.⁸ We report the case of an old woman affected by severe CRS type 5 due to light chain myeloma with cast nephropathy and hypokinetic cardiomyopathy, where forced diuresis was guided by daily POCUS assessment of HV-AIs and IVC, avoiding precipitation in fluid overload and HF.

2 | CASE REPORT

On December 2019, a 78-year-old Caucasian woman was admitted to emergency room due to persisting nausea. Clinical history was suggestive for arterial hypertension, dyslipidemia, thyroid struma, microvascular coronary disease with preserved left ventricular ejection fraction (LVEF), and normal renal function 9 months before. Usual medications included lysine acetylsalicylate, metoprolol, diltiazem, and esomeprazole.

At admission, vital signs and physical examination were unremarkable. Instrumental work up detected AKI (Figure 2), negative T waves on lateral leads at electrocardiography and normal aspect of thorax X-ray and abdominal ultrasound. Prerenal AKI was suspected, and intravenous (iv) hydration was started. Patient was transferred to Medicine ward.

On day 3, renal function was unchanged in the presence of iv hydration and unquantified diuresis. POCUS was performed, showing initial fluid overload (bilateral thorax B lines, IVC 2.36 cm, 47% inspiratory collapse). Parenchymal AKI was suspected. Hydration was reduced, and biochemical analysis for myeloproliferative and autoimmune disorders was prescribed. On day 4, diuresis reduced and HF appeared. POCUS revealed worsened fluid overload and venous congestion (pleural effusions, IVC 2.07 cm, collapse 22%, HV-AIs A3-I2) (Figure 2). Hydration was interrupted. Noninvasive ventilation and high dose furosemide were started. Methylprednisolone was empirically initiated, and patient was transferred to renal unit. On the same day, cardiac ultrasound showed hypokinetic cardiomyopathy, diastolic insufficiency, and pulmonary hypertension in the absence of

ventricular hypertrophy (LVEF 38%, E/A 1.27, pulmonary arterial pressure 60 mm Hg).

On day 5, diuresis increased, favoring 1 Kg negative fluid balance and mildly reduced venous congestion (IVC 1.75 cm, 50% collapse, HV-AIs A2-I1). Furosemide was tapered, leading to diuresis contraction and rebounded venous congestion on day 6 (IVC 2.54 cm, collapse 52%, HV-AIs A2-I2). Furosemide was then increased in association with single dose of potassium canrenoate and metolazone, achieving diuretic response within next 12 hours. On day 7, gas exchange, fluid overload, and venous congestion improved (IVC 1.56 cm, collapse 69%, HV-AIs A1-I1). To avoid dehydration, furosemide was interrupted. Diuresis suddenly slowed again.

Dependence from diuretics and narrow tolerance to increased circulating volumes suggested diagnosis of CRS type 5. Forced diuresis was initiated, for achieving both diuresis ≥ 1 mL/Kg/h and neutral fluid balance. Hydration and diuretics were thereafter oriented by twice daily POCUS.

Furosemide was restarted at halved dose in association with hydration. In the afternoon of day 7, increased venous congestion was detected (HV-AIs A3-I3), despite 150 mL/h diuresis, and mildly low circulating volume (IVC 1.64 cm, collapse 100%). Hydration and furosemide drip were halved. On day 8, neutral fluid balance was achieved, maintaining 100 mL/h diuresis, normal circulating volume, and reduced venous congestion (IVC 1.39 cm, collapse 53%, HV-AIs A2-I1). Furosemide and hydration were halved, leading to 40% diuresis reduction, rebounded venous congestion (HV-AIs A3-I3), and wet lungs. Diuresis increased once furosemide was augmented, achieving negative fluid balance and reduced venous congestion on day 9 (IVC 1.97 cm, collapse 100%, HV-AIs A2-I1). Hydration was increased, and furosemide was reduced. However, few hours later signs of hypovolemia and extremely reduced venous congestion appeared (IVC 1 cm, collapse 100%, HV-AIs A0-I0). Furosemide infusion was suspended, proceeding with unchanged hydration. Renal biopsy was performed on the same day.

Within next 48 hours, diuresis decreased and venous congestion worsened, requiring adjustment of hydration and low dose furosemide. Diuresis increased to 200 mL/h with signs of improved venous congestion (HV-AIs A3-I1), despite increased circulating volume (IVC 2.3 cm, collapse 50%). Hydration was increased to avoid further hypovolemia.

On day 13, results of renal histology (Figure 3) and biochemical analysis (kappa-free light chain (FLC) 5.190 mg/L, kappa Bence Jones 890 mg/L) suggested diagnosis of light chain myeloma with cast nephropathy. Bicarbonate hemodialysis was initiated due to persisting renal injury. Polymethyl methacrylate dialyzer (Toray BK-F 2.1) was adopted due to absorptive properties on FLC (Table S1),⁹ being high cutoff membranes unavailable at our institution. UF was not applied, to avoid renal underfilling.

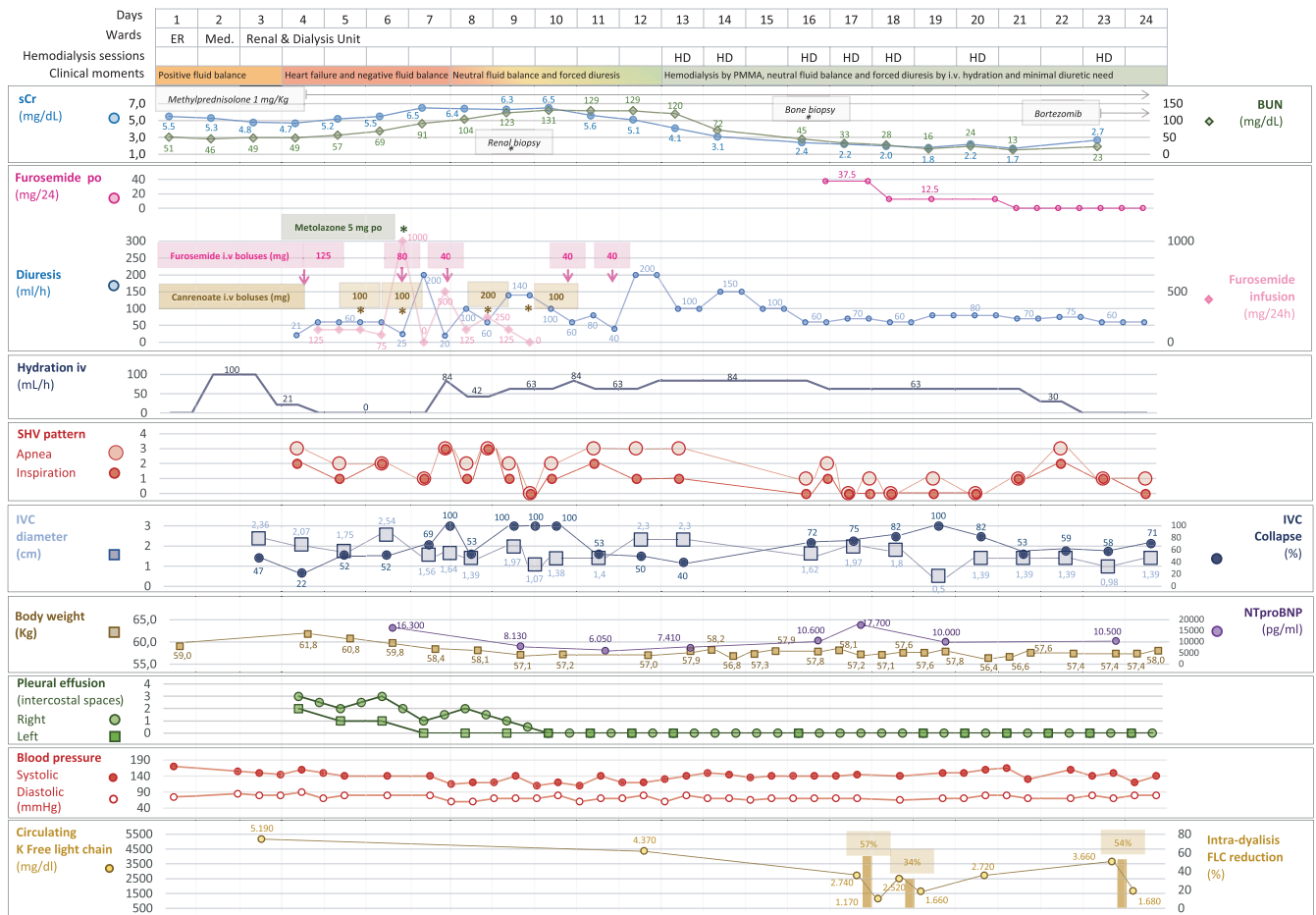


FIGURE 2 Trend for renal function, POCUS assessment of venous congestion, hydration, diuretic therapy, dialysis, body weight, kappa-free light chain, and NT-pro-BNP. Notes. Clinical course is divided into 4 clinical moments: 1) positive fluid balance, 2) heart failure and negative fluid balance, 3) neutral fluid balance and forced diuresis, and 4) hemodialysis with neutral fluid balance and minimal diuretic therapy. The first moment (days 1-3) was characterized by overhydration precipitating in heart failure. In the second moment (days 4-7), diuretics at high dose were required to achieve negative fluid balance (- 3 Kg) and to improve both pleural effusions and venous congestion. During third moment (days 8-12), forced diuresis by iv hydration and low dose diuretics was guided by POCUS, achieving resolution of fluid overload. Of note, HV-AIs resulted more sensitive than IVC to real-time adjustments of hydration and diuretic doses. The last moment (days 13-24) was characterized by the prosecution of forced diuresis with minimal diuretic dose. In this phase, hemodialysis by PMMA achieved FLC removal, up to 50% when accompanied by dialyzer substitution. BUN, blood urea nitrogen; ER, emergency room; FLC, free light chain; HD, hemodialysis; HV-AIs, Hepatic Venogram-Apnea and Inspiration score; Iv, intravenous; IVC, inferior vena cava; Med, Medicine ward; NT-pro-BNP, N-terminal probrain natriuretic peptide; PMMA, polymethyl methacrylate; Po, per os; POCUS, point-of-care ultrasound; sCr, serum creatinine

Hydration was continued from days 13-15, achieving slow reduction in diuresis toward 60 mL/h and neutral fluid balance. From day 16 to discharge, body weight and diuresis remained stable. Furosemide and hydration were suspended on days 21 and 22, respectively. Bone biopsy, performed on day 16, confirmed multiple myeloma (Figure S2). Bortezomib was initiated from day 23. Angiography excluded coronary disease on day 20.

Patient was discharged at home on day 24 without signs of venous congestion or fluid overload. HD was suspended on March 2020, due to improved renal function. On November 2020, ninth cycle of chemotherapy (bortezomib, melphalan, prednisone) was concluded, achieving partial improvement

of myeloma (kappa FLC 1.870 mg/L, kappa Bence Jones 345 mg/L) with stable chronic kidney disease (sCr 1.39, BUN 90, eGFR 36 mL/min). Cardiac ultrasound was unchanged on May 2020.

3 | DISCUSSION

Venous congestion received growing interest as risk factor for AKI during HF, independently from reduced cardiac output and renal underfilling.¹⁰⁻¹⁵ Furthermore, worsening renal function represents an independent risk factor for re-hospitalization as for cardiovascular morbidity and mortality

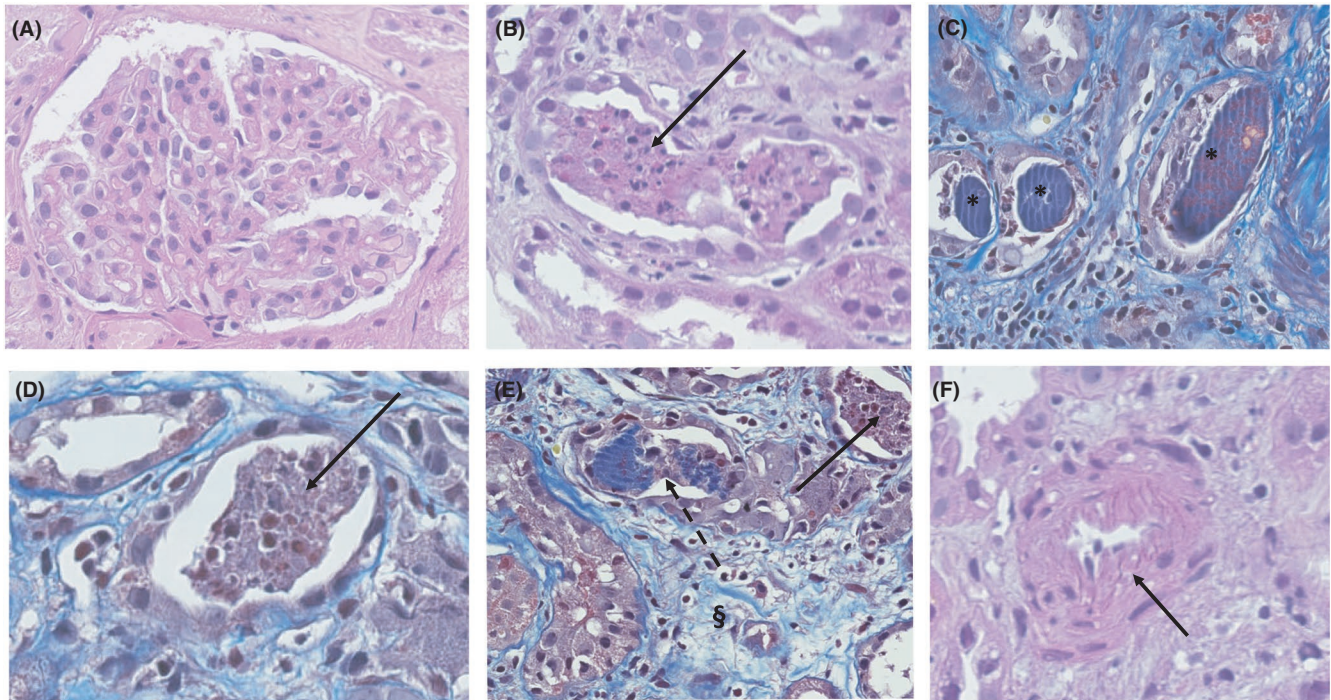


FIGURE 3 Renal Biopsy (optic microscopy). Notes. Renal biopsy, performed on day 9, was suggestive for myeloma cast nephropathy and light chain-induced interstitial nephritis. A: Normal glomerulus (HE). B: Tubular cast with polymorphonuclear inflammation (arrow) (HE). C: Proteinaceous casts (*) (MT). D: Tubular cast with polymorphonuclear inflammation (arrow) (MT). E: Proteinaceous casts (dotter arrow) with polymorphonuclear inflammation (arrow) and interstitial fibrosis (§) (MT). F: Moderate subintimal arteriolar sclerosis (arrow) (HE). Immunofluorescence showed linear staining for kappa light chains along tubular basement membranes, negative staining for IgA, IgG, IgM, C1q, and C3 (image not available). Rosso Congo staining was negative (image not available). HE: hematoxylin & eosin stain; MT: Masson trichrome stain

only whenever associated with residual volume overload.¹⁶ Thus, real-time assessment of venous congestion may provide prognostic benefits, by guiding resolution of the overhydrated conditions with limited risk of dehydration, renal underfilling, and worsening kidney function.

Point-of-care ultrasound was adopted for assessing venous congestion, reflected by pulsatile waveforms of hepatic, portal, and renal venograms.⁴ The Venous Excess UltraSound (VExUS) score was purposed, for grading systemic congestion by combination of IVC diameter and venous Doppler waveforms at aforementioned sites. VExUS independently predicted the risk of rehospitalization among patients admitted to intensive care unit after cardiac surgery⁴ and was further applied, for guiding fluid removal by dialysis and diuretics among adult patients affected by CRS and AKI.^{5,17}

In the present case, HV-AIs was applied daily during acute phase of CRS type 5 secondary to light chain myeloma. HV-AIs responded to changes in hydration and diuretics earlier than what observed for IVC. This was evident from days 7 to 10, when different patterns of venous congestion were detected by HV-AIs independently from total inspiratory IVC collapse (Figure 2). This is the first

description of repeated dose-response effects of intravenous hydration and diuretics on hepatic venogram up to date. Degree of renal disease and residual diuresis make the context of the present case highly different from the one previously published,⁷ where POCUS assessment of venous congestion was applied in an anuric hemodialysis affected by COVID-19. In the present case, monitoring venous congestion helped in resolving fluid overload, thereafter keeping neutral fluid balance with maintained diuresis independently from heart and renal insufficiency. This made UF unnecessary, protecting residual renal function during parenchymal AKI.

Although repeated measures provided clear response of HV-AIs to changing hydration, the accuracy and reliability of the score are limited by the absence of invasive hemodynamic assessment and single case description. Diagnosis of CRS type 5 is also weakened by the lack of endomyocardial biopsy or cardiac magnetic resonance, ascertaining light chain cardiomyopathy.¹⁸

In conclusion, the case supports the use of POCUS, for improving bedside care of renal patients.^{19,20} Noninvasive grading of venous congestion by HV-AIs may be considered a promising tool, for orienting fluid management in severe

CRS type 5. However, the aforementioned approach requires further investigation to be verified.

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Published with written consent of the patient.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in any part from the treatment process to writing the manuscript.

AUTHOR CONTRIBUTIONS

Lorenza Magagnoli: had the major role in data collection. Andrea Galassi: had major role in writing and editing the manuscript. All the authors were involved in the patient care. All the authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

No ethical issue in reporting of this case.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study. Para clinic data which are referred to in the case presentation are available on request from the corresponding author.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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