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Illuminating and Instructive Clinical Case

Human Albumin-enriched Peritoneal Dialysis: A Novel Approach to Manage Refractory Ascites and Kidney Dysfunction in Decompensated Advanced Chronic Liver Disease

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Abstract

For individuals with decompensated advanced chronic liver disease (dACLD), the onset of refractory ascites (RA) represents a dramatic event. In this setting, a relevant proportion of RA patients develop kidney dysfunction, as well as hepatorenal syndrome-acute kidney injury, with limited therapeutic and survival chances. An 81-year-old woman with dACLD-RA was admitted with severe ascites and stage IV chronic kidney dysfunction. On the second day, hepatorenal syndrome-acute kidney injury occurred, requiring standard medical therapy. Intravenous human albumin (HA) and terlipressin administration were compromised by poor venous access and severe respiratory dysfunction. After excluding transjugular intrahepatic portosystemic shunt and transplantation due to age and comorbidities, peritoneal dialysis (PD) was initiated, leading to renal recovery and ascites resolution. Two weeks later, she was readmitted due to the unfeasibility of accessing peripheral veins for the intravenous administration of HA, which was essential to support circulatory function, preserve oncotic balance, and properly manage both RA and chronic kidney dysfunction. A novel PD+HA protocol was therefore started, with intraperitoneal infusion of HA-enriched dialysate to allow a positive albumin gradient from dialysate to blood. Over 12 months, serum albumin levels increased, and clinical stability and improved nutritional status were observed, with no additional hospitalizations or complications. This is the first case describing the application of HA-enriched PD in managing a dACLD patient with RA and kidney dysfunction. HA-enriched PD may represent a promising strategy in complex dACLD care by guaranteeing frequent and small-volume paracentesis and preservation of oncotic pressure without dialytic albumin loss.

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Introduction

In the natural history of liver cirrhosis, the transition to decompensated advanced chronic liver disease (dACLD) marks a critical prognostic turning point, dramatically increasing mortality.[1] In this context, ascites denotes the most frequent liver-related event (LRE), also representing the *praeludium* to further decompensating episodes frequently observed in patients developing refractory ascites (RA).[2]

RA is defined by resistance to standard diuretic therapy with early recurrence of abdominal fluid after large-volume paracentesis (LVP), constituting a challenging scenario that commonly undermines the disease course.[3,4] In this context, portal hypertension and systemic inflammation synergistically determine splanchnic vasodilation with reduced effective arterial volume, thereby sustaining kidney dysfunction.[3,4] A significant proportion (~20%) of RA-affected patients develop hepatorenal syndrome (HRS)-acute kidney injury (AKI), contributing to a higher risk of hospitalization and worsening outcomes in dACLD,[2] highlighting the urgent need for personalized strategies. For this purpose, a recent expert symposium established novel diagnostic criteria with stratified recommendations for managing cirrhotic patients presenting with kidney dysfunction.[5] Upon confirmation of HRS-AKI, vasoconstrictor therapy, with terlipressin as the preferred initial agent, should be promptly initiated alongside the administration of intravenous (i.v.) human albumin (HA) to restore effective arterial volume.[5] In non-responders to the albumin-vasoconstrictor approach, transjugular intrahepatic portosystemic shunt (TIPS), and renal replacement therapy (i.e., dialysis) may represent a bridge to liver transplantation in selected individuals, although inconclusive evidence does not support the routine adoption of TIPS in the management of HRS-AKI.[4] Nevertheless, the concrete chances of survival remain dramatically poor.[4]

In contrast to hemodynamic (i.e, hypotension) and hem-

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Table 1. Laboratory findings on admission

Complete blood count		Biochemical features	
RBC (mm^3)	2,740,000	AST (U/L)	46
Hb (g/dL)	7.3	ALT (U/L)	43
WBC (mm^3)	1,920	ALP (U/L)	123
Neutrophiles (mm^3)	1,190	GGT (U/L)	74
Lymphocytes (mm^3)	740	Creatinine (mg/dL)	2.1
PLT (mm^3)	140,000	Bilirubin (mg/dL)	1.1
Coagulation		Total protein (g/dL)	5.4
PT (%)	105	Albumin (g/dL)	2.9
INR	1	Glucose (mg/dL)	187
Fibrinogen (mg/dL)	482	CRP (mg/dL)	2
Hepatic function		ESR (mm/h)	41
CPT	B8	Na^+ (mEq/L)	137
MELD-Na	16	K^+ (mEq/L)	4.2

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPT, Child-Pugh-Turcotte score; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Gamma-GT, gamma-glutamyl transferase; Hb, hemoglobin; INR, International normalized ratio; K^+, potassium; MELD-Na, Model for End-stage Liver Disease–Sodium; Na^+, sodium; PLT, platelets; PT, prothrombin time; RBC, red blood cell count; WBC, white blood cell count. Altered parameters are reported in bold.

orrhagic complications characterizing hemodialysis, peritoneal dialysis (PD) represents a valid alternative, providing hemodynamic stability and obviating the need for anticoagulant drugs. Moreover, PD offers constant drainage of ascites, playing a potentially pivotal role in RA-affected individuals with kidney dysfunction. Despite these possible benefits, PD is scarcely used because there is a perception that using PD may lead to excessive albumin loss and increase the risk of peritonitis and malnutrition, worsening the prognosis of these patients.[5]

Due to its relative pleiotropic effects,[6] HA administration represents a cornerstone in the management of dACLD.[4] In this setting, long-term i.v. HA administration has emerged as a disease-modifying treatment, contributing to reduced complications and better overall prognosis.[6] However, the current routine i.v. HA injection is associated with practical challenges, including poor peripheral venous access, infusion-related phlebitis, and the need for close clinical monitoring.[7]

Alternatively, administration of HA via intraperitoneal infusion during PD may offer potential benefits beyond the sparing of i.v. access and the possibility of small paracentesis; indeed, this approach theoretically allows a positive albumin gradient from dialysate to blood, therefore maintaining oncotic pressure and dependent hemodynamic stability. We tested this hypothesis for the first time in a patient shared between the gastroenterology and nephrology groups at the Academic Hospital of the University Vanvitelli in Naples, Italy. This hypothesis was generated and tested in a patient with severe dACLD and RA.

Case presentation

An 81-year-old female patient affected by dACLD, complicated with clinically significant portal hypertension (CSPH), was admitted to our department in April 2024 for severe ascites.

Upon presentation to the hospital, the patient was non-icteric, showing preserved vital parameters.

Metabolic dysfunction-associated steatotic liver disease and chronic hepatitis C virus infection (diagnosis: October 2017; sustained virological response achievement after antiviral treatment with a direct-acting antiviral regimen: July 2023) defined the mixed etiology dACLD of liver disease. Alcohol consumption was excluded by using the Alcohol Use Disorders Identification Test questionnaire. Other extrahepatic comorbidities included chronic obstructive pulmonary disease and severe chronic kidney dysfunction (CKD stage IV; eGFR: 21.7 mL/m/1.73m^2).

The investigation of past hepatologic medical history revealed, in November 2023, the occurrence of grade 3 ascites confirmed by ultrasound, requiring a first hospital admission. On that occasion, endoscopy revealed esophageal varices (small varices, F1, without red spots); non-selective beta-blocker-based primary prophylaxis (i.e., oral carvedilol, progressively titrated to the dosage of 12.5 mg/day) of acute variceal bleeding was started. After this first LRE, in the following months, despite proper medical therapy and multiple LVPs, ascites remained poorly controlled and frequently recurred, meeting the RA criteria,[3,4] and requiring hospitalization for paracentesis every four weeks in the last 12 months.

On admission, physical examination evidenced a tense and distended abdomen with an everted umbilical scar. A qualified nutritionist performed a complete evaluation, including the assessment of body composition through Bioelectrical Impedance Analysis. Significant malnutrition (reduced protein intake <1.5 mg/kg/day), simultaneously with dysgeusia and severe appetite impairment, respectively assessed by using the modified version of the validated chemotherapy-induced taste alteration scale questionnaire, calculating the "Dysgeusia Total Score" and a visual analog scale for appetite impairment, was evidenced.[8] Moreover, a reduced skeletal muscle mass index (4.9 kg/m^2), consistent with severe sarcopenia according to the European Working Group on Sarcopenia in Older People criteria, as well as frailty denoted by an elevated Liver Frailty Index (LFI ≥ 4.5),[8] was highlighted.

Laboratory tests showed normochromic/normocytic anemia (hemoglobin level of 7.3 g/dL), requiring immediate blood transfusion, elevated reticulocyte count, reduced platelet count (140,000/μL), low serum albumin levels (2.9 g/dL), and increased serum creatinine (2.1 mg/dL; estimated GFR: 21 mL/m/1.73 m^2 by CKD-EPI equation) (Table 1).

On day one, LVP was also performed, with removal of approximately 3.5 liters of yellow-citrine ascitic fluid. Cell count

and microbiological examination of the removed fluid subsequently ruled out PBS/bacterial ascites (polymorphonuclear count < 250/mm^3; culture: negative), and the chemical-physical test confirmed transudative ascites (Serum-Ascites Albumin Gradient – SAAG >1.1 g/dL), thus confirming the relative CSPH-related genesis.

Finally, the patient's liver function was assessed by determining the Child-Pugh Turcotte score (B8) and the Model for End-Stage Liver Disease–Sodium score (16), collectively denoting moderately advanced hepatic dysfunction.

On the second day, due to a significant rise in serum creatinine (2.7 mg/dL), simultaneously with a contraction of urinary output (<0.5 mL/h/12 h), the ongoing diuretic therapy and beta-blocker administration were discontinued. According to recent recommendations,[5] intravascular volume expansion was properly initiated by administering i.v. HA (1.5 g/kg of 20% HA) over the following 24 h, without observing improvement in serum creatinine levels (2.5 mg/dL) or urinary output (persistence of urinary output <0.5 mL/h/12 h), thus configuring, after excluding other causes of acute kidney dysfunction, the criteria for HRS-AKI.

On the third day, therefore, vasoconstrictor therapy (terlipressin by continuous i.v. infusion at the initial dose of 2 mg/day), in combination with the infusion of HA (i.v. 20% HA administration), was started.[5] Notably, significant challenges arose due to inadequate peripheral venous access, resulting in repeated, often unsuccessful cannulation attempts. Considering the elevated risk of catheter-related infections in this frail and immunocompromised patient, central venous catheterization was deemed clinically inappropriate due to the high risk of infection.

On the fourth day, the underlying chronic obstructive pulmonary disease, simultaneously with the presence of a moderate right-sided pleural effusion (confirmed on bedside ultrasound), determined a clinical worsening of the patient's respiratory function (oxygen saturation falling from 96% to 88% on room air), requiring the suspension of vasoconstrictor therapy, considering the relevant risk of terlipressin-induced respiratory decompensation.[4] In this phase, oxygen supplementation, fluid management, and close monitoring of respiratory and renal function were intensified.

Aiming to provide second-line therapeutic choices, TIPS placement and liver transplantation were evaluated and subsequently excluded, given the patient's unfavorable risk profile: advanced age (>80 years), presence of malnutrition and sarcopenia, persistent renal function impairment, and severe extra-hepatic comorbidities.

Therefore, also considering kidney-related manifestations, PD-based renal replacement therapy was considered, and, thanks to the close collaboration with the nephrology team, a joint multidisciplinary strategy was devised to address both the patient's persistent uremic symptoms and RA. Consequently, a Tenckhoff catheter was successfully placed in the peritoneal cavity (Fig. 1A), and after 72 h, PD was initiated using a single icodextrin dwell.

This approach enabled a remarkable improvement in renal function, obtaining reversal of AKI within the following 72 h (on the tenth day: serum creatinine levels: 2 mg/dL; urinary output: 1.2 mL/h/12 h), in association with effective and progressive ascitic fluid removal (14 liters in total over a few days).

After one week of stabilization and multidisciplinary monitoring, the patient was discharged on a home-based PD regimen specifically tailored to relative renal needs. Moreover, according to current guidelines and evidence,[4,6] the i.v. HA administration (dosage 40g/week, i.e., 20%/twice/week) was recommended to be continued in the home setting.

Two weeks later, she was readmitted due to ongoing difficulties in accessing peripheral veins for the i.v. administration of HA, clinically crucial to support circulatory function, preserve oncotic balance, and properly manage RA. Notably, blood tests at readmission showed a marked reduction in serum albumin levels (2.6 g/dL) and a slight re-increase in serum creatinine levels (2.3 mg/dL). Therefore, after obtaining informed consent for this off-label procedure, the intraperitoneal administration of HA ("HA-enriched PD" = "PD+HA") was proposed as an innovative and multidisciplinary therapeutic approach. In particular, a home-performable PD+HA protocol was developed, consisting of the sterile addition of two vials (100 mL each) of 20% HA solution to 800 mL of icodextrin-based dialysate, yielding a final concentration of 40 g/day of albumin. The dwell time was set to 12 h, with administration scheduled every other day (Fig. 1B). Supplementary File 1 reports complete details of the "PD+HA" protocol.

The patient was discharged after five days, and a 12-month multidisciplinary follow-up with a hepatologist and nephrologist (currently ongoing) was planned. Relevantly, sustained clinical stability was reported in the weeks following discharge, with approximately 0.5 liters of ascitic fluid being consistently removed in the home setting every other day before the instillation of the PD+HA dwell. Remarkably, no PD-related complications (e.g., peritonitis, tunnel infections) were reported; no further LREs occurred, and the patient did not require LVP or hospitalizations. eGFR and residual diuresis remained stable over time without the need to increase dialysis dose. Similarly, blood pressure has consistently been controlled by diuretic titration based on body weight monitoring.

PD+HA contributed positively to the maintenance of oncotic pressure (serum albumin levels increased, with values constantly ≥3 g/dL), effective plasmatic volume, as testified by the improved renal function, and better nutritional status with relief of abdominal distension and dysgeusia, increased appetite, daily protein intake, and skeletal muscle mass index (Fig. 1C).

The patient has not been hospitalized since the start of the new approach and is currently (last visit July 2025) under monthly follow-up in an outpatient nephrology and gastroenterology clinic (two visits on the same day).

Discussion

In the natural history of liver cirrhosis, the transition to dACLD represents a dramatic crossroads, dramatically burdening prognosis.[1,2] In particular, acute decompensation, characterized by a sudden onset of complications such as severe ascites, hepatic encephalopathy, and gastrointestinal bleeding, often requires hospitalization with a significant risk of acute-on-chronic liver failure.[1,2] Importantly, a higher incidence of further decompensation episodes, liver transplantation, and death, regardless of the Model for End-Stage Liver Disease score, has been reported after acute decompensation.[1,2]

The recently introduced concept of *"recompensation"*, achieved through aetiological treatment, improved liver function, and sustained resolution of decompensation (for at least 12 months), has redefined the dACLD "classic" prognostic trajectories.[1] However, despite this encouraging evidence, ascites resolution with off-diuretics over one year remains utopian in the case of RA.[3,4] In this clinical context, portal hypertension and systemic inflammation act synergistically to induce splanchnic vasodilation, resulting in a diminished effective arterial blood volume that perpetuates renal dysfunction.[3,4] Notably, up to 20% of RA-affected patients develop

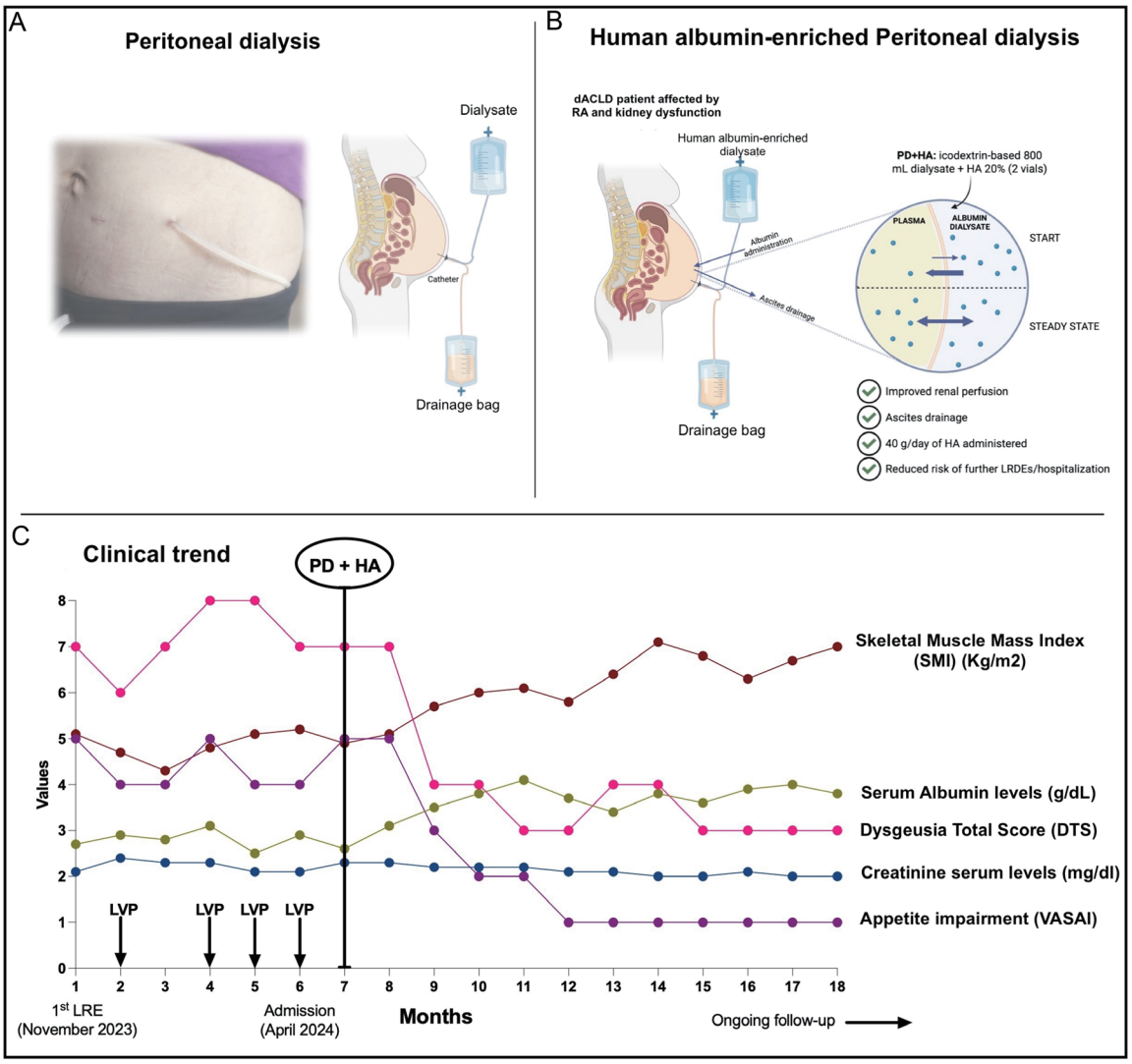

Fig. 1. Peritoneal dialysis (PD) and human albumin-enriched PD. (A) Positioning of the Tenckhoff catheter and starting peritoneal dialysis. The catheter was surgically positioned within the peritoneal cavity to facilitate abdominal infusion of dialysis solution and to enable its subsequent drainage following the diffusion of waste products. (B) Main principles of the "PD + HA" approach and relative clinical benefits. (C) Clinical, biochemical, and nutritional course (before and after PD + HA). RA, refractory ascites; HA, human albumin; dACLD, decompensated advanced chronic liver disease; LRDEs, liver-related decompensating events; PD + HA, human albumin-enriched peritoneal dialysis; LVP, large volume paracentesis.

HRS-AKI, contributing to worsening prognosis, higher risk of hospitalization, and elevated mortality (estimated one-year rate between 30%–50%).[1,2]

Accordingly, in this case report, despite successful hepatitis C virus-antiviral therapy, the persistence of metabolic dysfunction-associated steatotic liver disease-related manifestations fueled liver disease progression, CSPH worsening, grade 3 ascites recurrence, and RA onset requiring multiple LVPs and hospitalizations, as well as HRS-AKI occurrence. The patient's frailty, poor venous access, and respiratory comorbidities complicated the administration and tolerance of standard treatments, reflecting the urgent need for individualized, multidisciplinary approaches in this setting.

In this scenario, PD emerged as a feasible and effective strategy, enabling gradual ascitic fluid removal and progressive renal recovery, thus permitting discharge with the indication to continue i.v. HA administration. Indeed, hypoalbuminemia has been revealed as a predictor of mortality in CKD-affected patients and an independent risk factor for peritonitis in PD.[9] On the hepatologic side, HA administration represents a cornerstone in the therapeutic management of dACLD patients, representing, *de facto,* a disease-modifying drug.[6] In this sense, long-term HA therapy has been demonstrated to improve survival rates, reduce complication rates, and overall contribute to a more favorable prognosis in dACLD.[4,6] However, these benefits have been documented exclusively with i.v. HA administration, which may pose logistical challenges, including limited peripheral venous access, infusion-related phlebitis, and the requirement for close monitoring. Nevertheless, PD is not commonly used due to concerns about excessive albumin loss and the perception of an increased risk of peritonitis and malnutrition, potentially leading to worse patient outcomes.[8,9] However, by enriching the dialysate with an appropriate dose of albumin, it is possible to reverse the concentration gradient, enabling the use of the peritoneum as a route for albumin administration.

Regarding this, the possibility of adopting intraperitoneal albumin administration has already been reported by other evidence, revealing, among various scenarios, the potential benefits derived from this alternative strategy in managing PD patients with hypoproteinemia, reducing peritonitis risk, and, more recently, facilitating the targeted delivery of cancer therapy for the local treatment of peritoneal metastasis.[9,10] Anyway, to the best of our knowledge, this is the first case reporting the administration of HA via alternative intraperitoneal infusion in the specific hepatological setting of dACLD complicated by RA and kidney dysfunction. Importantly, in this case, PD+HA emerged as an innovative approach that offered a tailored solution for maintaining oncotic balance and volume status, avoiding the burden of i.v. access. This novel strategy, by ensuring simultaneously adequate HA supplementation, proper ascites drainage, and CKD control, minimized procedural risks, improved nutritional status, and ultimately avoided hospitalizations.

In this sense, considering cost-benefit implications, although intraperitoneal HA administration entails substantial drug usage with relative costs, the potential to reduce hospitalization rates, complications from repeated LVP, and challenges in i.v. access management may render this approach a cost-effective alternative in selected patients, warranting further economic evaluation and analysis in large-scale studies.

Conclusions

In the era of Precision Medicine, the reported experience emphasizes the crucial importance of a multidisciplinary strategy integrating hepatology and nephrology expertise to personalize treatment plans, proposing a potential revolutionary paradigm shift in dACLD-RA care, as well as opening the door to future investigations to validate this novel strategy and establish standardized criteria for patient selection and monitoring.

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Conflict of interest

The authors have no conflict of interests related to this publication.

Author contributions

Guarantor of the article (MR, SB, MD), conceptualization (MR, SB, MD, CG, FDN, PV, CN, LDN, AF), methodology, investigation, writing the original draft (MR, SB, MD, CG, FDN, PV, CN), formal analysis (CG, FDN, PV, CN), data curation, and supervision (LDN, AF). All authors approved the final version of the manuscript.

Ethical statement

The patient has provided written informed consent for participation in the study and the publication of the relevant data in the present research. Anonymized consent is proposed as a supplementary file (Supplementary File 2). This study received ethical approval from the Institutional Review Board of the University of Campania "Luigi Vanvitelli" in Naples (Approval Number: 0021377/i-22) and was performed in accordance with the Declaration of Helsinki (as revised in 2024)

Data sharing statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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