Capillary Leak Syndrome Following Immune Checkpoint Inhibition: A Unique Cause of Acute Kidney Injury

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Introduction

Immune checkpoint inhibition (ICI) is associated with acute kidney injury (AKI) via direct cytotoxicity including allergic interstitial nephritis (AIN), acute tubular necrosis (ATN), and glomerulopathy.

ICI uncommonly causes capillary leak syndrome (CLS) — increased capillary protein permeability leading to hypotension, anasarca, and intravascular volume depletion. The mechanism proposed for CLS is T-cell stimulation of cytokines that induce vascular endothelial leak.

Case

A 71-year-old male with a history of metastatic Hurthle cell tumor on pembrolizumab immunotherapy presented with recurrent falls due to hypotension. Last immunotherapy session was 8 weeks prior to admission, the patient presented to an outside facility for anasarca and hypotension resulting in antihypertensive discontinuation. Patient returned home with worsened anasarca associated with a 35 lb. weight gain over 6 weeks.

At our hospital, he was administered IV fluids due to persistent hypotension (total 6 L). Urinalysis showed no hematuria and low-grade proteinuria. Urine studies (two separate collections) showed urine sodium < 5 mmol/L, urine Cl < 10 mmol/L, and elevated urine creatinine, suggesting renal underperfusion.

Worsened anasarca prompted diuresis attempts, yet urine output (UO) remained low. Uremia developed requiring 4 hemodialysis sessions without fluid removal.

We report a case of CLS following pembrolizumab (Keytruda) therapy resulting in severe prerenal AKI that was reversed with IV immunoglobulin (IVIG) treatment and albumin infusion.

Results

Right heart catheterization to assess volume status showed low bi-ventricular filling pressures and low cardiac output (Table 1). CLS was suspected and albumin 25 grams was started for 3 days. IVIG was administered after receiving preauthorization (Gammagard administration) Cr was 3.09 mg/dL. Delay of IVIG was due to preauthorization by insurance.

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Discussion

ICI are known to uncommonly cause CLS.

- CLS results in end-organ injury, generally through endothelial disruption and hypoperfusion.

- Our case is a rare and under-recognized form of AKI in checkpoint inhibitor use.

- Reported cases of CLS have not shown improvement with steroid use.

- Prenatal azotemia arose from intravascular volume depletion leading to decreased renal perfusion.

- CLS and AKI reversed with IVIG and albumin therapy.

- Steroids were not administered in our patient.

- Albumin infusions (25 grams IV for 5 doses) were provided when the diagnosis of CLS was suspected, following the right heart catheterization.

- IV crystalloid fluid resuscitation did not restore intravascular depletion.

- IVIG may be considered as treatment in immunotherapy induced CLS as a way to minimize T cell activation.

- The patient made renal recovery back to baseline and did not need long term dialysis.

References

