CLINICAL VIGNETTE

A Biopsy Proven Concurrent Vancomycin Related Acute Tubular Necrosis and Infection Related Glomerulonephritis

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Introduction

Acute kidney injury is a frequent complication of severe sepsis.[1] Commonly employed interventions used to manage severe sepsis also have risks of renal toxicity that can exacerbate sepsis induced renal injury. We present a case of acute kidney injury and oliguria that developed as a result of the compounded effects of infection related glomerulonephritis and vancomycin nephrotoxicity in the setting of severe sepsis and receipt of intravenous contrast that exhibited rapid resolution after removal of vancomycin with hemodialysis.

Case

A 23-year-old generally healthy woman with no significant past medical history presented to the hospital with severe right upper extremity cellulitis associated with fever that had developed over the week prior to presentation. One day prior to presentation she had developed a maculopapular rash that began on the bilateral wrists and spread to her torso and subsequently the thighs. She denied any other significant symptoms. At presentation she was found to have severe sepsis with fever of 103.3ºF, tachycardia, lactic acidosis, and neutrophilic leukocytosis. Her renal function was normal with creatinine of 0.96 mg/dL. She initially received empiric vancomycin and piperacillin/ tazobactam. A CT scan with contrast of the right upper extremity performed the day of admission excluded evidence of drainable abscess or complicated soft tissue infection. A CT chest angiogram with contrast on day two of admission given persistent tachycardia and elevated D-dimer resulted as negative for pulmonary embolism. On day three of admission her serum creatinine was 0.68 mg/dL and vancomycin trough 3.9 mcg/mL so vancomycin dose was adjusted to achieve a goal trough of 15 to 20 mcg/mL. On day four of admission she was clinically much improved with resolving cellulitis and improvement in the maculopapular rash, however, her serum creatinine increased to 1.1 mg/dL and vancomycin trough was 46.3 mcg/mL so vancomycin was held. On day five of admission her serum creatinine had increased to 4.65 mg/dL and vancomycin levels remained elevated at 35.8 mcg/mL. Her ANA was elevated to 1:160 and so she received an empiric dose of 30 mg IV methylprednisolone out of concern for vasculitis associated AKI and rash. On day six she was again febrile to 102ºF, the serum creatinine increased to 5.62 mg/dL, and she developed oliguria and underwent renal biopsy. On day seven she continued to have mild fever to 100.8ºF and rising serum creatinine up to 6.4 mg/dL with persistently elevated vancomycin levels at 34.4 mcg/mL. She started HD primarily for vancomycin removal. On day eight she exhibited significant improvement in urine output and underwent HD without ultrafiltration. Over the subsequent week of hospitalization, she exhibited continued improvement with resolution of the sepsis and cellulitis, and improvement in renal function back to baseline. She was then discharged to home in excellent condition. The final result of the renal biopsy showed resolving sub-epithelial deposits (Figure 1), mild glomerular foot process effacement (Figure 2), and mesangial deposits (Figure 3) suggestive of low-grade infection related glomerulonephritis along with focal flattening and acute injury of tubular cells with vacuolopathy (Figure 4) likely related to vancomycin toxicity.

Discussion

Infection-related glomerulonephritis (GN) is an immune mediated glomerulonephritis caused by bacterial infections. Since infection is usually ongoing at the time of GN diagnosis, the term infection-related glomerulonephritis (IRGN) has been introduced.[1] In contrast to pediatric post-streptococcal glomerulonephritis which usually resolves, sporadic adult IRGN can lead to chronic kidney disease or even end-stage renal disease, which highlights the need for early identification and management.[2] Patients with adult IRGN often present in the setting of acute or recent infection with new onset hematuria and proteinuria or nephrotic syndrome with edema and reduced kidney function.[3]

Treatment of IRGN includes a combination of eradicating the acute infection as well as management of the complications of acute nephritis including diuretics, antihypertensive medications, renin-angiotensin blockade, and in some cases renal replacement therapy.[4] The role of immunosuppressive therapy in adult bacterial IRGN has not been reported in a randomized prospective clinical trial and current studies have not found a beneficial effect of steroids on outcome.[2,4]

Vancomycin related nephrotoxicity has been reported since 1956.[5] Risk factors associated with vancomycin nephrotoxicity include prolonged therapy for >21 days, loop diuretics[6], doses greater than or equal to 4 grams per day[7], and trough concentrations greater than 15 mg/L.[8]

The first step in management of vancomycin related nephrotoxicity is discontinuation of the vancomycin, after which most cases of vancomycin related nephrotoxicity spontaneously improve. However, as seen in this case report, patients with very high plasma vancomycin levels or with conditions that are compounded by severely impaired renal function, may not respond to discontinuation of the drug alone. Prolonged supratherapeutic vancomycin exposure can result in prolonged renal injury and increased risk of permanent renal damage. In such cases, timely aggressive drug removal is indicated to help relieve the nephrotoxic effect and aid in recovery of renal function. High-flux hemodialysis can eliminate the large molecule of vancomycin with a reported removal rate of up to 79%.[9]

This case illustrates a complex situation wherein vancomycin related nephrotoxicity was superimposed on IRGN in the setting of severe sepsis and receipt of intravenous contrast that together resulted in kidney failure with oliguria. This case also highlights the importance of close monitoring of vancomycin levels and aggressive intervention with hemodialysis to remove the insulting agents when indicated.

We followed our patient in clinic three months after hospital discharge and she continued to have normal kidney function with no evidence of any recurrent infection or sequela.

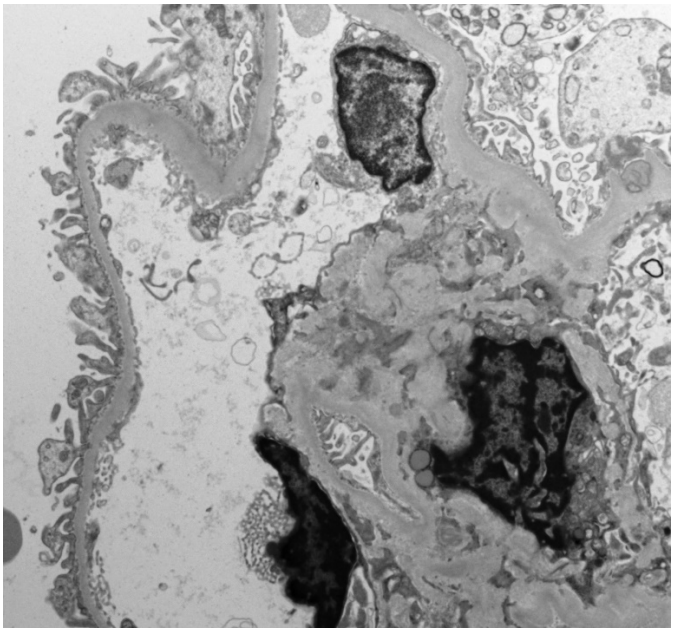

Figure 1: Resolving sub-epithelial mesangial deposits.

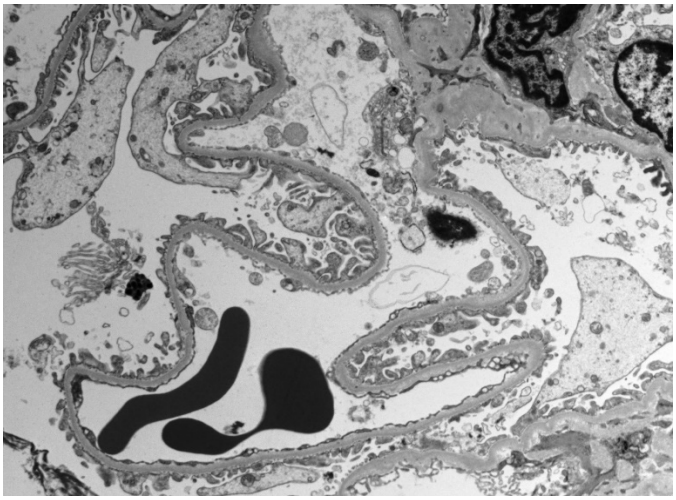

Figure 2: Mild food processes effacement.

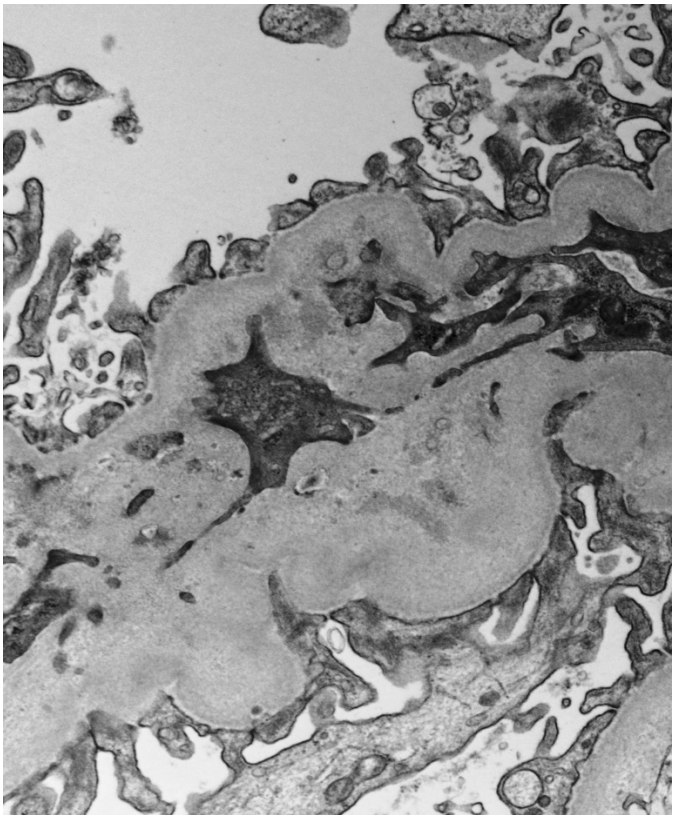

Figure 3: Partly and completely cleared mesangial deposits.

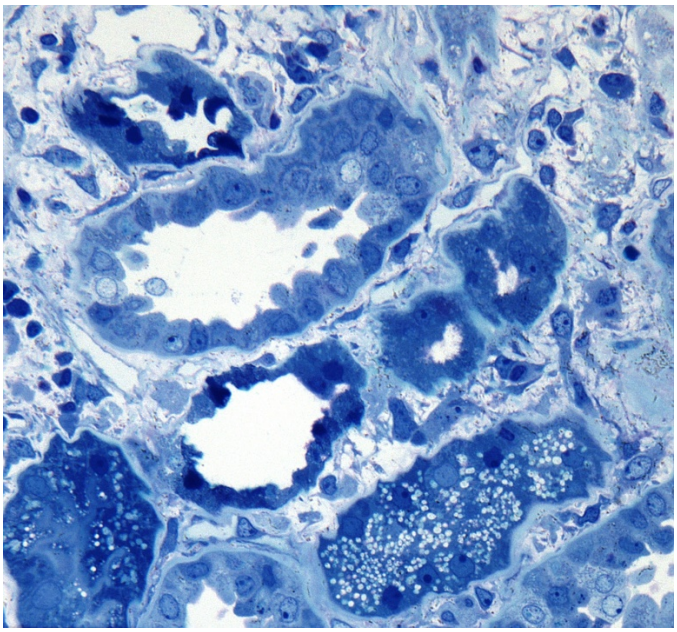

Figure 4: Acute tubular injury with tubular cell isometric vacuoles.

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