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CASE REPORT

The Renal Failure That Vanished

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A 35-year-old African American female presented to her primary care provider with a 4-day history of progressive nausea, vomiting, and generalized malaise. The patient had been in her usual state of health prior to the onset of these symptoms and had no history of prior hospitalization. She denied any fevers, chills, abdominal pain, or change in diet prior to the onset of her symptoms. She also had no recent exposure to sick contacts, human immunodeficiency virus (HIV) risk factors, or history of recent travel. One week prior to her presentation, the patient had been prescribed rifampin for treatment of chronic hidradenitis suppurativa. She had been taking rifampin for 5 days until she developed her current symptoms. The patient was not taking any other medications and had no other medical problems.

On presentation, the patient was afebrile and her vital signs were within normal limits. She was alert and oriented with no scleral icterus. Cardiopulmonary exam was within normal limits. Her abdomen was nondistended with diffuse nonlocalizing tenderness, normal bowel sounds, and no signs of acute abdomen. No hepatomegaly was noted, and stool was negative for occult blood. No rashes or joint abnormalities were noted on exam, but multiple nodulocystic lesions were noted bilaterally in her axillae. Laboratory findings on presentation were most notable for a blood urea nitrogen level of 38 mg/dL, a creatinine of 5.3 mg/dL, and a calculated fractional excretion of sodium of 2.6%. Urine analysis revealed no significant hematuria, proteinuria, or red blood cell casts, but did demonstrate white blood cells, white blood cell casts, and eosinophils. Blood cultures drawn on admission were negative and the patient had a normal leukocyte count.

The patient was admitted to the general medicine service and the causes of her acute renal failure were explored. She was treated with intravenous fluids because a component of prerenal azotemia was initially suspected. Rifampin was discontinued. Despite significant hydration, the patient remained oliguric. She was challenged with high-dose loop diuretics for 3 days but still remained oliguric. Renal ultrasound showed moderately echogenic, large 16-cm kidneys bilaterally, with no evidence of hydronephrosis or renal calculi. Laboratory evaluation for diabetes and infiltrative disease of the kidneys such as HIV, amyloidosis, and nonspecific gammopathies were negative. The patient's creatinine level steadily increased and eventually peaked at 14.2 mg/dL. When the patient began to develop shortness of breath, lower extremity edema, and abdominal distension on hospital day 4, hemodialysis was initiated. On hospital day 6, the patient underwent a renal biopsy (Figure 1) that demonstrated patchy inflammatory infiltrates with scattered eosinophils and evidence of interstitial edema and tubulitis. Congo red staining was negative for amyloid and no immune deposits were noted. A diagnosis of acute interstitial nephritis (AIN) was made and the patient was started on high-dose prednisone.

Over the 48 hours following initiation of prednisone therapy, the patient's urine output gradually began to improve and the patient was producing over 2 liters of urine per day. In addition, the patient's axillary cystic lesions became less inflamed and painful. The patient was discharged home with plans to continue hemodialysis as an outpatient. Three days after discharge, when the patient presented for hemodialysis, her creatinine was noted to be 1.2 mg/dL. Due to her improved creatinine and maintenance of good urine output, hemodialysis was discontinued. The patient was slowly tapered off her prednisone over the next several weeks. One month later her creatinine was 0.9 mg/dL. She had required no further hemodialysis since her hospitalization.

Discussion

AIN is an uncommon but significant cause of acute renal failure, and accounts for 2% to 3% of all renal biopsies performed.[1] AIN is thought to be an immune-mediated process, and drug-induced hypersensitivity is the most common cause of AIN. Nonsteroidal anti-inflammatory drug (NSAID) use, antibiotics, proton pump inhibitors, and several other medications have been implicated in the pathogenesis of AIN. Rifampin is a medication that has a known association with AIN, with most cases being described in regions where treatment of endemic tuberculosis is common. The majority of cases of rifampin-induced AIN occur in the setting of drug reexposure, due to an immunologically-mediated process that causes tubulointerstitial injury.[2]

Patients with drug-induced AIN typically present with oliguria secondary to an acute decline in renal function. The

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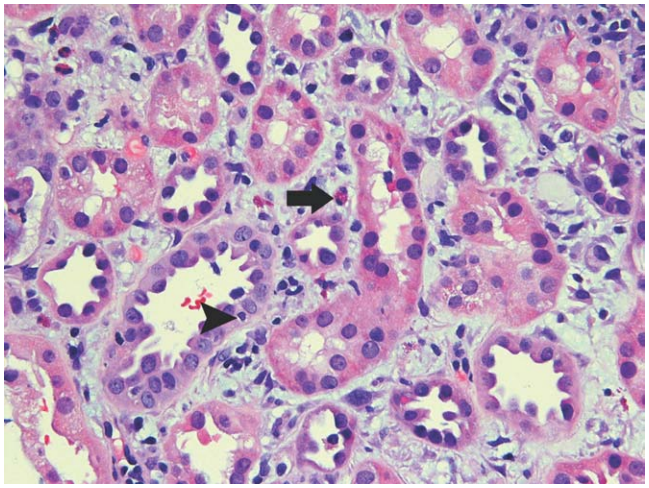

FIGURE 1. Renal biopsy with hematoxylin and eosin stain demonstrating acute interstitial nephritis. Prominent interstitial inflammation with interstitial edema and scattered eosinophils (arrow). Occasional lymphocytes (arrowhead) intermixed among tubular epithelial cells consistent with tubulitis.

classic clinical "triad" of fever, rash, and arthralgias is uncommon, and all 3 occur in only 30% of all cases.[3] More commonly, patients typically present with vague flu-like and gastrointestinal symptoms, including fever, abdominal pain, nausea, and vomiting. Urinalysis may be helpful, but hematuria occurs in less than one-half of all cases, and sterile pyuria is common but not always present. It has been suggested that the presence of eosinophiluria may lead to high suspicion of AIN, but the sensitivity and specificity of eosinophiluria are low, at 40% and 72%, respectively.[3] Thus, renal biopsy is often performed to make a confirmatory diagnosis of AIN in the appropriate clinical setting. Histopathologically, the presence of inflammatory infiltrates in the renal tubules and interstitium with conservation of the glomerular structures is visualized.[2,3]

A large number of patients who present with AIN may require temporary renal replacement therapy; however, most patients have been observed to recover full renal function. Despite this, review of the literature shows that many patients may have persistent elevations in their serum creatinine. Corticosteroid therapy, although controversial, has commonly been initiated in patients whose renal function does not improve with conservative therapy. To date there are no prospective randomized clinical trials, and data guiding optimal management in AIN is sparse. Some studies have demonstrated no benefit in corticosteroid therapy in lowering serum creatinine levels in patients with AIN,[4] but others have observed a significantly increased risk of interstitial fibrosis and failure to return to baseline creatinine in those patients that received delayed treatment with corticosteroids more than 1 week after the withdrawal of the offending agent.[5]

The patient described in our case did not present with the classic symptoms noted in AIN. Yet she had evidence of eosinophiluria, which increased our suspicion for AIN. Although other potential etiologies of this patient's acute renal failure were considered, given her negative serologic studies and the results of her renal biopsy, AIN was considered the leading diagnosis. Since AIN was recognized early in this patient, the offending medication was discontinued promptly, prednisone therapy was initiated appropriately, and the renal failure that had developed quickly vanished.

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