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Acute Kidney Injury Associated with Rifampin-Based Treatment for Latent Tuberculosis Infection

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Summary

Treatment for latent tuberculosis infection (LTBI) is a key tuberculosis elimination strategy. Rare adverse reactions associated with LTBI treatment have been reported. We report the only case of acute kidney injury reported to CDC surveillance for adverse events related to LTBI treatment. This patient experienced rapid intravascular hemolysis resulting in heme pigment nephropathy; he was hospitalized and received 3 hemodialysis treatments, but recovered without sequelae. While adverse events related to LTBI treatment are rare, healthcare providers should maintain clinical vigilance and regularly counsel patients to facilitate prompt diagnoses and effective clinical management of affected patients.

Keywords

tuberculosis; rifampin; kidney injury; hemodialysis

CASE REPORT

A 32-year-old man who was born in Peru presented to an emergency department in the United States with nausea, vomiting, and dark urine. He had no previous medical history; his symptoms developed within hours after taking a dose of rifampin to treat latent tuberculosis infection (LTBI); this was the first dose he had taken after stopping rifampin for approximately 2 weeks. Approximately 4 months before presentation to the emergency department, he was diagnosed with LTBI after an 11-mm tuberculin skin test (TST) reaction; his chest radiograph was normal and he had no signs or symptoms of TB disease. At both the time of LTBI diagnosis and upon presentation to the emergency department, the patient denied use of any other drugs or medications. He had initiated treatment with a 4-month regimen of 600 mg of oral, daily, self-administered rifampin with instructions to abstain

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from alcohol during treatment. Approximately 2 weeks before symptom onset, after having completed 3 months of treatment, the patient discontinued rifampin in order to consume alcohol at a social event.

Upon presentation, the patient's temperature was 98.5°F, blood pressure was 146/93, heart rate was 58, and respiratory rate was 14. The patient appeared acutely ill; jaundice, scleral icterus, and lower abdominal tenderness were noted during physical examination. His blood urea nitrogen (BUN) (45 mg/dL; normal: 6–20 mg/dL) and creatinine (3.3 mg/dL; normal: 0.5–1.2 mg/dL) were elevated; his bicarbonate was 20 mmol/L (normal: 21–31 mmol/L). His alanine aminotransferase (136 U/L; normal: 10–60 U/L), aspartate aminotransferase (258 U/L; normal: 10–42 U/L), total bilirubin (16.8 mg/dL; normal: 0.3–1.2 mg/dL), and white blood cell count (19.6 K/mm^3 with 56% neutrophils, 41% bands, and 3% lymphocytes; normal: 5–10 K/mm^3) were elevated. His platelet count (154,000/cm^3) and creatinine kinase (152 U/L; normal: 52–336 U/L) were normal. Urinalysis revealed 4^+ proteinuria with 4^+ blood, 4^+ bilirubin, glycosuria, and 1–8 dirty brown fine granular casts per low-power field with no cellular casts. Serologic results for viral hepatitis (A, B, and C) were negative. Renal ultrasound demonstrated "bilaterally increased renal echogenicity compatible with medical renal disease without evidence of obstruction." The patient was hospitalized with a diagnosis of acute renal failure.

Upon hospitalization, intravenous fluids with sodium bicarbonate were started; his bicarbonate steadily decreased to 17 mmol/L during the first 3 days of hospitalization. He received a 3-day course of intravenous piperacillin-tazobactam for "possible urinary tract infection or biliary tract infection." Meanwhile, his BUN increased to 83 mg/dL and creatinine increased to 10.4 mg/dL. Furthermore, clinical signs of volume overload developed: increasing peripheral edema on physical exam; a new pleural effusion by computerized tomography; and cephalization of pulmonary vessels on chest radiography. His hemoglobin decreased from 17 g/dL to 13.8 g/dL during these first 3 hospital days; his serum haptoglobin was measured at <8 mg/dL (normal: 43–212 mg/dL), with an elevated plasma hemoglobin of 26.9 mg/dL (normal: 0.0–15.2 mg/dL), a positive direct Coombs test, a negative indirect Coombs test, and a positive direct antiglobulin test for anticomplement antibodies. These data, in the context of the subacute progression after restarting rifampin, prompted a diagnosis of warm, drug-induced, hemolytic anemia.

Because of worsening azotemia, (BUN 107 mg/dL, creatinine 14.6 mg/dL), along with nausea, anorexia, and fluid overload, the patient underwent hemodialysis on hospital day 4. Pathologic examination of a kidney biopsy specimen demonstrated "tubular degenerative changes with prominent heme-pigmented casts consistent with acute tubular injury." The patient was dialyzed on two more occasions — on hospital days 6 and 9. On hospital day 10, the anorexia started to resolve, his peripheral edema improved, and his net fluid balance was negative on hospital days 10, 11, and 12. On hospital day 13, the patient was discharged. Two weeks later, his symptoms had resolved and his laboratory values normalized. He required no further dialysis treatments.

Millions of people in the United States have LTBI and many have received treatment without complications;[1] nonetheless, rare adverse reactions have been reported since the

1970s. To understand LTBI treatment-associated serious adverse events (SAEs), defined as hospitalizations or deaths among persons undergoing treatment for LTBI, CDC formed the National Surveillance for Severe Adverse Events (NSSAE) in 2004 to capture SAEs associated with any LTBI treatment regimen.[2] While kidney injury among persons taking rifampin for treatment of TB and Hansen's disease has been reported, this is the first report of kidney injury associated with any LTBI treatment regimen to NSSAE.[3–5] The available information strongly suggests a rifampin-related event for this patient; nonetheless, this conclusion remains a diagnosis of exclusion because definitive laboratory testing was not available. Clinical guidelines for LTBI treatment recommend monthly assessments during therapy that include education regarding signs and symptoms of medication toxicity to ensure prompt diagnoses among affected persons.[6] To ensure rapid diagnosis and effective management of persons who experience adverse events, persons experiencing abnormal symptoms should immediately stop taking the medication and seek medical evaluation.[3]

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