Acute Hemolysis and Oligoanuric Acute Renal Failure Caused by Interrupted

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Citation

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Abstract

A 38-year-old patient was treated with relapsing pulmonary tuberculosis with reinstitution of rifampicin (RFP) after a medication-free interval of l8 years. One week after initiation of treatment the patient developed acute severe hemolytic anemia and oligoanuric acute renal failure (ARF) necessitating dialysis. ARF following intermittent or discontinous and interrupted RFP therapy is a relatively infrequent clinical observation. Many pathogenetic mechanisms for the renal failure have been proposed, including intravascular hemolysis with hemoglobinuria and its consequent nephrotoxicity. Interrupted and intermittent therapy with RFP should be avoided and non-compliant patients should be given alternative treatment when possible.

INTRODUCTION

RFP is a widely used antituberculous drug. Administered daily, only minimal side-effect occur. A number of adverse effects, e.g., flu-like syndromes, hemolysis, acute renal failure (ARF), hepatotoxicity, and thrombocytopenia have been described with its use. ARF and acute hemolysis secondary to RFP occur either with intermittent RFP therapy or after restoration of drug therapy cycles.

Regarding the pathogenesis of the ARF renal biopsy consistently revealed tubular lesions. Intravascular hemolysis leading to ARF following RFP therapy is extremely rare. Although intravascular hemolysis with hemoglobinuria may play a role, it is not uniformly present. For both complications the prognosis is fair.

CASE REPORT

A 38-year old man who had antituberculous treatment for 8 months 18 years before applied to a state hospital with the complaints of productive coughing and night sweating. A sputum smear was positive for acid-fast bacteria. With the diagnosis of relapsing tuberculosis quartet drug therapy (isoniazid 300m/d, rifampicin 600 mg/d, pyrazinamide 2 g/d, ethambutol 1 g/d) was started. One week later the patient developed nausea, vomiting, decreased amount of urination and icterus. Then he applied to our institution and hospitalized. Physical examination revealed yellow skin and sklera, pale conjunctiva, 0,5 cm in size tender two submandibular lympadenomegaly (LAM), bilatreal inguinal LAMs like beads on a string , findings of dehydration, crepitating rales in right middle lung zones, 2 cm palpable liver. Abnormal laboratory tests were: leucocyte count: 63,000, hematocrit: 34.9, hemoglobin: 11.8 g/dL, haptoglobulin < 29 mg/dL, urea: 122 mg/dL, creatinine: 4.4 mg/dL, Na: 127 mEq/L, total biluribin: 16.3 mg/dL, direct biluribin: 9.6 mg/dL, ALT: 41 U/L, AST: 237 U/L, LDH: 4124 U/L, glucose: 324 mg/dL, üric acid: 15 mg/dL, Ultrasonography revealed hepatomegaly (175 mm). Peripheric smear didn't reveal microangiopathic hemolytic anemia morphology, there was eosonophilia and total Ig E levels were increased (828), reticulocyte count was 2.5 percent. Serologic markers for hepatitis were all negatif. Daily urine amount was 50 cc.

Based on the clinical findings we precluded that acute renal failure, intravascular hemolysis and hepatotoxicity were due to rifampicin. Due to technical considerations antirifampicin antibody level couldn't be measured and the patient refused to have a renal biopsy. After cessation of rifampicin urea and creatinin levels continued to increase and diuresis was still low necessitating hemodialysis. On the eight day of cessation diuresis began to increase but urea and creatinine were still high. Two weeks later the urea and creatinin levels also began to decrease while icterus and high biluribin levels were regressed. During the fift to sixth weeks acute renal failure was totaly resolved. Hemolytic component of rifampicin toxicity responded well to streoid treatment. Sputum smear was analyzed twice and was positive for acid-

fast bacili and Mycobacterium tuberculosis was confirmed by culture. The patient was discharged with reinstitution of antituberculous treatment with INH 300 mg/d, morphozide 2 g/d, ethambutol 1 g/d, thionamide 750 mg/d.

DISCUSSION

Several isolated cases of acute renal failure (ARF) following RFP therapy have been reported.([1,2,3,4,5,6,7]) There are approximately 60 cases of rifampicin induced renal failure being published. These cases commonly occur with intermittent drug therapy or after restoration of drug therapy cycles.([10]) Some cases have had antecedant intravascular hemolysis. A variety of pathogenic mechanisms for acute renal failure have been postulated.

In the typical presentation, within minutes to hours after RFP ingestion, dizziness, chills, fever, myalgias, nausea, vomiting, lumbar pain, and a protracted, course of oligoanuric renal failure that usually requires dialysis therapy develops. ([2,7,11])

Many pathogenetic mechanisms for the renal failure have been proposed, including intravascular hemolysis with hemoglobinuria and its cosequent nephrotoxicity. Altough intavascular hemolysis with hemoglobinuria may play a role, it is not uniformly present.([7,8,9]) Being mostly tubular a variety of renal lesions including acute tubuler necrosis, tubulointerstitial nephritis, lightchain proteinuria, and nonspesific glomerlonephritis have been reported.([9])

Some reports have documented hemolysis, direct and indirect positivity of the. Coombs test, and circulating antirifampicin antibodies. These antibodies have been detected in the direct antiglobulin test using anticomplement antisera. During intermittent rifampin therapy patients are more likley to develop rifampicin antibodies. Antirifampicin antibodies may form complexes with the antigens on tubular epithellim leading to tubular destruction. ([6,9,10])

Altough the precise pathophysilogic mechanisms are unknown in our patient, in the setting of intravascular hemolysis, hemoglobin toxicity to renal tubules is indoubtedy a contributing factor to renal failure. Rifampin was withdrawn and prednisone treatment instituted resulting in rapid resolution of the hemolysis, whereas hemodialysis was required for recovery of the renal function.

CORRESPONDENCE TO

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