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CASE REPORT

Acute Interstitial Nephritis, Hepatitis, Hemolysis Due to Rifampin: A Case Report

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ABSTRACT

Here we present the case of a patient suffering from nephrotoxicity, hepatotoxicity, and hemolysis due to rifampin. In this case, nephrotoxicity, hemolysis, and hepatitis presented simultaneously, which was not reported previously. The patient was a 71-year-old woman treated with rifampin in 2014. One week after the treatment, the patient had hepatitis, acute kidney injury, and hemolysis. Liver and renal function tests were impaired. The patient was severely ill, lethargic, pale, edematous, with generalized icterus. After discontinuation of rifampin, hemodialysis, and blood transfusion, after 50 days all the symptoms gradually disappeared and no other treatment was needed.

Key Words: Hemolysis, Hepatitis, Interstitial Nephritis, Rifampin

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INTRODUCTION

Rifampicin is a medicine Rifampicin, also known as rifampin, is an antibiotic used to treat several types of bacterial infections. This includes tuberculosis, leprosy, and brucellosis. It leads to adverse reactions, such as nephrotoxicity, sometimes resulting in acute renal failure, hemolysis, and hepatotoxicity. Hemolysis and febrile episodes are associated with rifampicin-dependent antibodies in the serum [1].

CASE PRESENTATION

Herein, we presented a case of a 71-year-old woman, who was diagnosed with brucellosis, referring to the Valiasr Hospital of Arak University of Medical Sciences in 2014. The patient was treated with daily administration of doxycycline 100 mg and rifampin 600 mg. One week after the commencement of the treatment, she developed fever, weakness, headache, decreased appetite, nausea and vomiting, generalized abdominal pain (more severe in the right upper quadrant), constipation, yellowish skin and sclera, orange urine color, decreased urine output, oliguria, and then anuria. In the physical examination, the patient had a blood pressure of 100/80 mmHg and body temperature of 37.2°C, and she was ill. Furthermore, the jugular venous pressure was elevated, and the sclera and skin of face and extremities were icteric

RESULTS

The cardiac examination revealed normal results, while the lung auscultation demonstrated fine crackles at the base of the lungs. The abdomen was distended in the shifting dullness test, and the extremities were edematous (Table1).

At the first step, urinalysis was reported abnormal then, red blood cell count (RBC), white blood cell count, and epithelial cells were evaluated. The immunological and virology examinations presented normal results, and urine culture was negative. Erythrocyte sedimentation rate was 101 mm/h. Furthermore, anti-glomerular basement membrane, Coombs Wright test, and 2ME wright test were negative. In the abdominal ultrasonography, no organomegally was detected. However, mild prehepatic ascities, enlargement of kidneys with increased cortical echogenicity, and decreased corticomedullary differentiation were observed.

During the hospital stay, the blood pressure was within 120/80-138/90 mmHg. In the second and third weeks of the hospitalization,

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Table 1. Changes of blood urea nitrogen, serum creatinine, hemoglobin, bilirubin, alanine transaminase, and aspartate aminotransferase

Parameters	Date								
	3/27	4/1	4/2	4/4	4/6	4/10	4/18	5/8	7/23
Blood urea nitrogen	107	78	75	43	26	52	54	-	-
Serum creatinine	7.1	7	7	5.5	4.7	4.2	2.8	1.47	1.1
Hemoglobin	6.9	10.4	10	9	7.9	10.2	10.3	10	14.5
Aspartate aminotransferase	132	72	29	-	-	-	-	26	25
Alanine transaminase	328	100	40	-	-	-	-	36	27
Bilirubin (total)	41.9	39.4	31.8	8.5	-	4.6	3.5	1.29	0.44
Bilirubin (direct)	22.3	22.1	21.4	4.6	-	2.4	1.99	0.72	0.15
LDH	3945	-	2794	-	1567	676	-	300	300

LDH: 3945; CBC= WBC: 36200 RBC: 2.3*106 Hb: 6.9 mg/dL

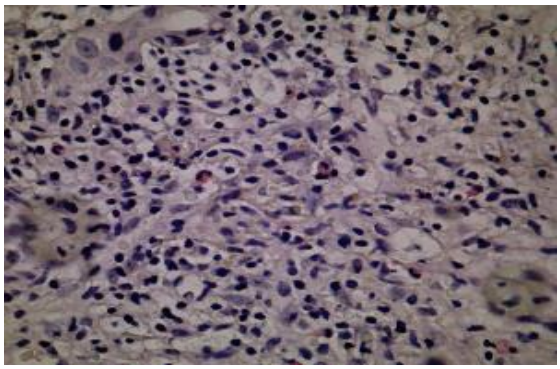

Figure 1. Acute interstitial nephritis with intense infiltration of lymphocytes plus scattered eosinophils associated with destruction of tubular units

the patient had two episodes of fever that ameliorated with ceftriaxone.

The patient was dialyzed eight times, and 5 units of packed cells were infused during hospital stay. The renal biopsy was performed after the patient became stable. The light microscopic examination revealed allergic interstitial nephritis with tubular necrosis. In addition, the immunofluresance microscopic examination demonstrated the local mesangial deposition of immunoglobulin (Ig) M. However, this was not observed for IgG, IgA, and IgE (figures 1, 2). The patient was hospitalized for three weeks, and discharged in a good condition. She had no more problems in the follow-up visits. Lab data examination was performed one and three months post-discharge. The blood urea nitrogen and creatinine were decreased.

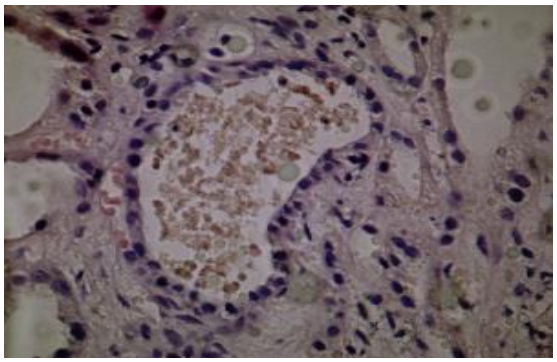

Figure 2. Acute tubular necrosis. The lumen contains a bilirubin cast. Adjacent tubules also disclose degenerative and regenerative changes

However, alanine transaminase/aspartate aminotransferase, total and direct bilirubin, erythrocyte sedimentation rate, white blood cell count, hemoglobin, and RBC were within the normal range, and the patient was in a good condition.

DISCUSSION

In this report, we described a patient, who suffered from nephrotoxicity, hepatotoxicity, and hemolysis, after the consumption of rifampin.

In the typical presentation, the patients taking rifampin might develop dizziness, chills, fever, myalgia, nausea, vomiting, lumbar pain, and a protracted course of oligoanuric renal failure (usually requiring dialysis therapy) within minutes to hours after the drug ingestion [2, 3].

But, several isolated cases of acute renal failure following rifampin therapy have been reported [3-8]. Some pathogenic mechanisms for the renal failure have been proposed, including intravascular hemolysis with hemoglobinuria, and its consequent nephrotoxicity. However, the role of intravascular hemolysis with hemoglobinuria has not uniformly confirmed in the literature [3, 9, 10]. The renal lesions are mostly tubular in nature. A variety of these lesions have been reported, including acute tubular necrosis, tubulointerstitial nephritis, light-chain proteinuria, and nonspecific glomerulonephritis [10].

The first case report of acute interstitial nephritis was published in the 1970s. In these studies, the renal biopsy revealed interstitial infiltrates in the patients receiving rifampicin for 21-71 days. These patients usually enjoyed the recovery of renal function after the discontinuation of the drug. Due to this temporal relationship, an immune-mediated or direct nephrotoxicity of rifampicin was postulated [11, 12].

The drug-induced acute interstitial nephritis can be managed though the immediate discontinuation of the offending agent and the

use of corticosteroids [13, 14].

However, in our case, we refrained from the administration of corticosteroids. Various mechanisms have been postulated for rifampicin-associated acute renal failure [15]. Nevertheless, it is difficult to determine the incidence of this condition among all the patients treated with this drug.

The renal damage is thought to result from allergic reactions to rifampicin or one of its metabolites that cause allergic interstitial nephritis. Immunogenicity of rifampicin has been indicated by the presence of rifampicin-dependent antibodies in serum, especially IgM [15, 16]. Nonetheless, the relationship between anti-rifampicin antibodies and the development of renal failure is not clear yet [17].

Rothwell and Richmond described a case of renal failure and jaundice occurring in a patient intermittently taking rifampicin (three doses of 450 mg over five weeks) for tuberculosis [18]. In the Medline database search, there were only two previous cases of hepatitis occurring in the patients treated with rifampicin in the absence of other hepatotoxic agents. Bachs et al. described two cases of rifampicin hepatitis in the women treated for primary biliary cholangitis [19].

Rifampin may cause hemolysis and hemolytic anemia in less than 1% of the people [20]. The hematological side effects of this drug include thrombocytopenia, leukopenia, hemolytic anemia (in less than 1% of the patients), and hemolysis, described as part of an immune-mediated reaction, which generally occur after interruptions in therapy [8].

In our patient, one week after the onset of rifampin administration, blood urea nitrogen and Cr increased, and the results of liver function tests became abnormal. In addition, RBC mass and hemoglobin reduced. After stopping rifampin consumption, hemodialysis, and blood transfusion, all the symptoms relieved, and the patient became stable. The renal biopsy revealed allergic interstitial nephritis with tubular necrosis. Furthermore, the immunofluorescence findings demonstrated local mesangial IgM deposit. In our case, all symptoms of nephrotoxicity, hemolysis, and hepatitis occurred simultaneously that have not been previously reported.

CONCLUSION

In this patient, after discontinuing the medication and starting hemodialysis and infusion of packed cells, all the symptoms gradually relieved so no other treatment activity was needed. In such patients, in addition to hepatic damage consideration, nephrotoxicity and blood tests must be evaluated, and if needed, other treatment activities should be initiated.

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CONFLICTS OF INTEREST

The authors declared no conflicts of interest.

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