

Acute Renal Failure—A Complication of New Multidrug Regimen for Treatment of Leprosy¹

Narendra M. Dedhia, Alan F. Almeida, Umesh B. Khanna,
Bharati V. Mittal, and Vidya M. Acharya²

The World Health Organization (WHO) recommends rifampin (600 mg once a month) in both multibacillary and paucibacillary cases (¹⁴), following pioneering work done by Opromolla (⁹). Hypersensitivity reactions such as "flu" syndrome (⁵) and renal failure (^{1, 3, 8, 13, 16}) are reported in association with intermittent or discontinuous rifampin therapy. Over 50 cases of rifampin-induced interstitial nephritis and subsequent renal failure have been reported following Poole's original report (¹¹).

We report here a case of rifampin-induced acute renal failure in a leprosy patient.

CASE REPORT

A 37-year-old male presented in 1982 with hypopigmented patches on both elbows and left leg and received dapsone therapy for his diagnosed leprosy. In November 1983, rifampin 600 mg once a week was started. After the thirtieth dose, the patient developed fever, myalgia, and arthralgia for which he received symptomatic therapy. The symptoms recurred after the next two doses and rifampin was discontinued, resulting in abatement of the symptoms. Rifampin was reintroduced in a dosage of 600 mg once a month when, on regular follow up, he was found to be smear positive. Following this, he had recurrence of fever, arthralgia, and myalgia lasting for two days. The next dose after a month resulted in the development

of a high-grade fever, myalgia, abdominal pain, vomiting, giddiness, and arthralgia. In the next 24 hr, a progressive oliguria was noted. He was managed conservatively initially but, as his blood urea nitrogen and creatinine levels progressively rose, he was referred to the nephrology unit of King Edward VII Memorial Hospital, Bombay, India, for further management.

On admission, he was drowsy, had mild tachycardia, blood pressure levels of 170/90 mm of Hg, and was in congestive heart failure. The rest of the clinical examination revealed hypopigmented, hypoesthetic patches on the elbows and left leg, and a minimally tender hepatomegaly.

Investigations revealed a low hemoglobin (9.9 g%), a polymorphonuclear leukocytosis with no eosinophilia, proteinuria (2+), and microscopic hematuria (50–70 RBC/Hpf). Coagulation studies were normal. Blood urea nitrogen (216 mg/dl) and plasma creatinine (17.5 mg/dl) were markedly elevated. An ultrasound examination of the kidneys was normal.

During the four weeks that elapsed before renal biochemical parameters normalized, the patient required seven hemodialysis sessions. A renal biopsy revealed an acute interstitial nephritis with a cellular infiltrate composed of mononuclear cells and eosinophils in association with regenerating proximal tubular epithelium (recovering acute tubular necrosis). A liver biopsy showed normal architecture with a focal ballooning of hepatocytes, and mild nuclear polyploidy with a few binucleated forms. There were foci of collections of lymphocytes and histiocytes in the parenchyma, forming microgranulomas. No typical lepromatous granulomas were seen.

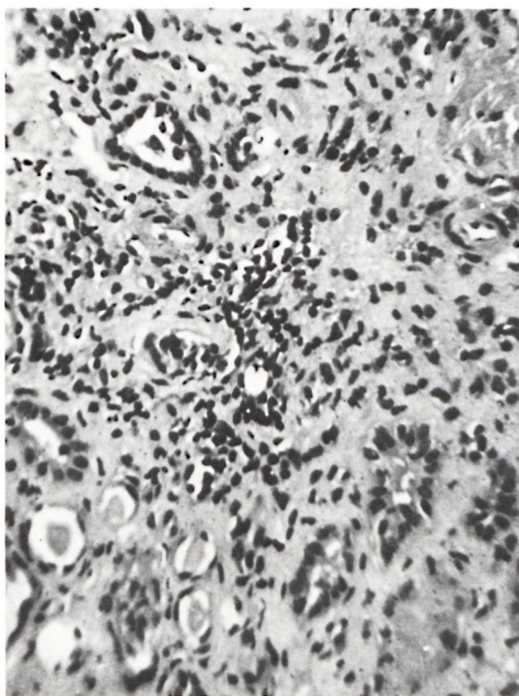
DISCUSSION

Hypersensitivity reactions and rifampin-induced acute renal failure (⁵) are reported

¹ Received for publication on 3 February 1986; accepted for publication in revised form on 24 April 1986.

² N. M. Dedhia, M.D., Registrar in Nephrology; A. F. Almeida, M.D., N.N.A.M.S., Reader in Nephrology; U. B. Khanna, M.D., D.N.B., Lecturer in Nephrology; B. V. Mittal, M.D., Reader in Nephrology; V. N. Acharya, M.D., F.A.M.S., Professor and Head, Department of Medicine and Division of Nephrology, Seth Gordhandas Sunderdas Medical College and King Edward VII Memorial Hospital, Parel, Bombay 12, India.

Reprint requests to Dr. Acharya.



THE FIGURE. Photomicrograph of kidney showing tubulo-interstitial lesion due to rifampin (H&E $\times 400$).

in association with high-dose biweekly or once-weekly rifampin therapy or when rifampin administration has been discontinuous. However, acute renal failure has also occurred in patients on continuous rifampin therapy (¹²).

Renal involvement usually presents with fever, gastrointestinal symptoms, myalgia, and arthralgia, as seen in our patient. Occasionally, there may be no precipitating symptoms (³). Rifampin is commonly cited as a drug causing interstitial nephritis (⁷). The other described lesions include acute tubular necrosis and, occasionally, renal cortical necrosis with permanent renal damage (²). The renal histology most commonly shows a tubulo-interstitial lesion with mononuclear and eosinophilic cellular infiltrate, as seen in our case.

Drug-induced, acute renal failure in leprosy is associated with dapsone (¹⁷) and with rifampin (⁶) administration. The occurrence of acute renal failure with an intermittent dosage schedule (once weekly or biweekly) has an immunological basis, and circulating rifampin-dependent antibodies in high titers are detected (¹). Continuous rifampin therapy also could result in renal failure,

probably due to interstitial nephritis subsequent to a direct nephrotoxicity of the drug (¹²). The occurrence of renal failure in a once-a-month dosage regimen, although rare, has been reported (⁶).

The recommended use of rifampin in leprosy employs the once-monthly dose. None of the reported studies have had serious side effects or hypersensitivity (^{4, 10, 15, 18}). However, fever and abdominal symptoms have been described in two cases (^{15, 18}).

Our patient developed renal failure following a hypersensitivity reaction while on a once-monthly rifampin schedule. However, even before being placed on this schedule, he had manifested adverse effects of rifampin when receiving rifampin once a week.

SUMMARY

A leprosy patient who developed acute renal failure on multidrug therapy is reported. The patient had initially received a once-weekly dose of rifampin and after he had stopped taking the drug for a time, was given rifampin on a once-monthly dose schedule. He recovered completely from his acute renal failure. Kidney biopsy showed interstitial nephritis with mononuclear and eosinophilic cellular infiltrates.

RESUMEN

Se describe el caso de un paciente quien recibiendo tratamiento con múltiples drogas desarrolló una falla renal aguda. Inicialmente el paciente había recibido una dosis por semana de rifampina, después suspendió el tratamiento durante un tiempo para continuar posteriormente con una dosis de rifampina cada mes. El paciente se recuperó completamente de su falla renal aguda. Una biopsia de riñón mostró nefritis intersticial aguda con infiltrado mononuclear y eosinofílico.

RÉSUMÉ

On rapporte ici le cas d'un malade de la lèpre qui a développé une décompensation rénale aiguë au cours de la polychimiothérapie. Ce malade avait d'abord été traité par une dose hebdomadaire de rifampicine; il avait alors interrompu la prise de ce médicament pendant un certain temps; il avait été ensuite à nouveau soumis à la rifampicine en dose mensuelle. Le malade a été entièrement rétabli de sa décompensation rénale aiguë. La biopsie du rein a montré une néphrite interstitielle avec des infiltrats à cellules mononucléaires et éosinophiles.

REFERENCES

1. CHAN, W. C., GABRIEL, S. M., YU, D. and YU, R. Y. H. Renal failure during intermittent rifampicin therapy. *Tubercle* **56** (1975) 191-198.
2. COCHRAN, E. M., MOORHEAD, P. J. and PLATTS, M. Permanent renal damage with rifampicin. *Lancet* **1** (1975) 1428.
3. CORDONNIER, D. and MULLER, J. M. Acute renal failure after rifampicin. *Lancet* **2** (1972) 1364-1365.
4. GIRDHAR, B. K. and DESIKAN, K. V. "Pulsed" rifampicin therapy in leprosy. A clinical study. *Lepr. India* **51** (1979) 475-480.
5. GIRLING, D. I. and HITZKE, K. L. Adverse reaction to rifampicin. *Bull. WHO* **57** (1979) 45-49.
6. NESSI, R., BONOLDI, G. L., REDAELLI, B. and DIFILIPPO, G. Acute renal failure after rifampicin: a case report and survey of the literature. *Nephron* **16** (1976) 148-159.
7. OPROMOLLA, D. V. A. First results of the use of Rifamycin SV in treatment of lepromatous leprosy. *Int. J. Lepr.* **31** (1963) 552.
8. OPROMOLLA, D. V. A., TONELLO, C. J. S., MCDUGALL, A. C. and YALWALKAR, S. J. A controlled trial to compare the therapeutic effects of dapsone in combination with daily or once-monthly rifampin in patients with lepromatous leprosy. *Int. J. Lepr.* **49** (1981) 393-397.
9. POOLE, G., STRADLING, P. and WORLLEDGE, S. Potentially serious side effects of high-dose twice-weekly rifampicin. *Br. Med. J.* **3** (1971) 343-347.
10. POWER, D. A., RUSSELL, G., SMITH, F. W., SIMPSON, J. G., MCLEOD, A. M., FRIEND, J. A. and CATTO, G. R. Acute renal failure due to continuous rifampicin. *Clin. Nephrol.* **20** (1983) 155-159.
11. RAMGOPAL, V., LEONARD, C. and BHATHENA, D. Acute renal failure associated with rifampicin. *Lancet* **1** (1973) 1195-1196.
12. REES, R. J. W. Chemotherapy of leprosy for control programmes. Scientific basis and practical application. *Lepr. Rev.* **54** (1983) 81-88.
13. REES, R. J. W., PEARSON, J. M. and WATERS, M. F. Experimental and clinical studies on rifampicin in treatment of leprosy. *Br. Med. J.* **1** (1970) 89-92.
14. SHAH, B. V., ALAMEIDA, A. F., KHANNA, U. B. and ACHARYA, V. N. Rifampicin induced acute renal failure. *J. Assoc. Physicians India* (in press).
15. WARRINGTON, R. J., HOGG, G. R., PARASKEVAS, F. and TSE, K. S. Insidious rifampin-associated renal failure with light-chain proteinuria. *Ann. Intern. Med.* **137** (1977) 927-930.
16. WATERS, M. F., REES, R. J., PEARSON, J. M., LAING, A. B., HELMY, H. S. and GELBER, R. H. Rifampicin for lepromatous leprosy: nine years' experience. *Br. Med. J.* **1** (1978) 133-136.