# Acute Renal Failure in Leprosy[1]

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Chronic renal failure is one of the common causes of death in leprosy ([1]). A wide variety of renal lesions including amyloidosis ([11]), chronic interstitial nephritis and glomerulonephritis ([8]) have been reported to be associated with leprosy. Recently proliferative glomerular lesions have been considered to be of immune complex origin ([12]). Development of acute renal failure in leprosy is an infrequent finding. Three patients having lepromatous leprosy were referred to us for the management of acute renal failure. Of these three, two had acute tubular necrosis and one showed the classical picture of rapidly progressive glomerulonephritis.

## REPORT OF CASES

**Case No. 1.** A 45 year old male had progressive skin disease for two years. He was investigated and diagnosed as a case of lepromatous leprosy and received dapsone (DDS, 4, 4'-diaminodiphenylsulfone) 100 mg weekly for four weeks and then increased to 300 mg per week. Two weeks later the patient noticed a change in the color of urine (dark brown) and became oliguric. The urinary output did not increase despite massive diuretic therapy (Furosemide 200 mg). He was referred to this hospital for further management.

The hematocrit was 25% and free plasma hemoglobin was 380 mg/100 ml. The total leukocyte count was 29,200 cell/mm$^3$ and erythrocyte sedimentation rate was 50 mm/hour (Westergren). The reticulocyte count was 8.5%. Peripheral smear showed crenated and fragmented red cells with Heinz body formation. Glucose-6-phosphate dehydrogenase (G6PD) activity was normal. Urinalysis showed eight to ten red cells, a few white blood cells and occasional hemoglobin casts per high power field. Pertinent serum investigations revealed blood urea nitrogen (BUN) of 125 mg/100 ml, creatinine 9.2 mg/100 ml, bilirubin 4.5 mg/100 ml with unconjugated fraction of 3.5 mg/100 ml, SGOT 11 IU, SGPT 15 IU, alkaline phosphatase 11 KAU. Serum electrolytes were within normal limits. Antistreptolysin-0 titer was 250 Todd units. Antinuclear antibody, rheumatoid factor, lupus erythematosus cell and direct Coomb's tests were negative. X-ray of the abdomen showed both kidneys to be of normal size. Initially he was treated with parenteral fluids and massive diuretic therapy. There was no increase in urinary output and he remained oliguric for 13 days. During this period three peritoneal dialyses were carried out. On the fifth day of oliguria, a percutaneous renal biopsy was performed. Renal histology revealed degenerated tubules, interstitial edema, infiltration of inflammatory cells and regenerating tubular epithelium (Fig. 1). On the 14th day, he passed into a diuretic phase and urinary output ranged between 1-3 liter/day. Two weeks later, laboratory investigations revealed a BUN of 15 mg/100 ml and a serum creatinine of 1.2 mg/100 ml.

**Case No. 2.** A 43 year old male was investigated as a case of lepromatous leprosy. One week before admission he developed a high grade fever which was associated with generalized body aches. Three days later he developed anuria (the patient did not receive dapsone therapy prior to the episode of anu-

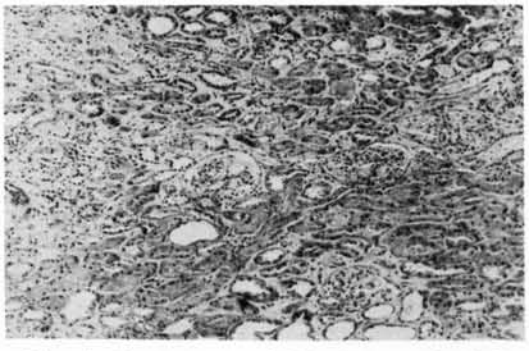

FIG. 1. Shown are variable degrees of tubular degeneration, pigment cases in the tubular lumina and interstitial edema. Glomeruli are normal. H & E, ×110.

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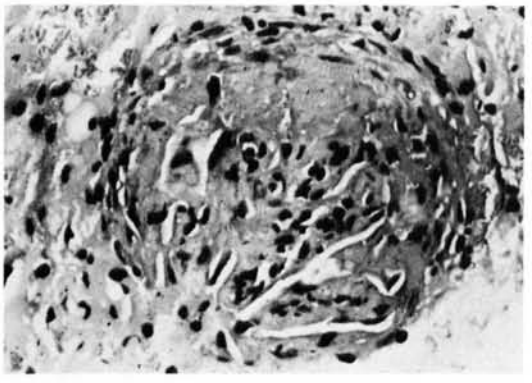

FIG. 2. Shown are a glomerulous with crescent at periphery, mesangial hyalinization and a few polymorphonuclear infiltrates. H & E, ×440.

ria or during the period of renal failure). Examination revealed a mild degree of anemia. He had puffiness of face and pedal edema. Pulse was 90/min. Blood pressure was recorded to be 160/106. Laboratory data revealed a hematocrit of 36%, total leukocyte count 9,000 cells/mm$^3$ and ESR 35 mm/hour. Blood peripheral smear did not reveal any abnormality. BUN and serum creatinine were 150 mg/100 ml and 11.5 mg/100 ml respectively. Serum bilirubin was 0.8 mg/100 ml. Serum electrolytes were within normal limits. Coagulation and complement studies were normal. Antistreptolysin-0 titer was 125 Todd units. A culture of material from skin lesion was negative for streptococci. Antinuclear antibody, lupus erythematosus cell and direct Coomb's tests were negative. X-ray of the abdomen showed normal sized kidneys.

The patient was dialyzed twice during the next week. Subsequently, the urinary output increased to 800-1000 ml/day. After the first peritoneal dialysis percutaneous renal biopsy was performed. Renal histology revealed mesangial and epithelial cell proliferation with exuberant crescent formation (Fig. 2). Out of 22 glomeruli included in the section, 20 showed the presence of crescents. Arterioles did not show any evidence of angiitis. As the BUN stabilized between 75-90 mg/100 ml on conservative therapy alone, he was discharged with the advice to take hematinics, aluminum hydroxide gel, 30 gm protein and a high carbohydrate diet.

**Case No. 3.** A 52 year old male was diagnosed as having lepromatous leprosy and was on treatment with dapsone 300 mg weekly. Four weeks later he was admitted to the local hospital with the history of repeated vomiting and oliguria. He was treated with parenteral fluids and massive doses of furosemide. There was no significant increase in urinary output so he was referred to this hospital. Physical examination revealed classical features of lepromatous leprosy. He was moderately anemic and had a mild degree of jaundice. Blood pressure was recorded to be 150/90. Laboratory data revealed a hematocrit of 18% and free plasma hemoglobin of 750 mg/100 ml. The total leukocyte count was 22,000 cells/mm$^3$ with a normal differential cell count. Reticulocyte count was 5.6%. Blood peripheral smear showed crenated and fragmented red cells with Heinz body formation. Erythrocytes were not deficient in G6PD. Serum biochemical investigations revealed a BUN of 150 mg/100 ml, creatinine 12 mg/100 ml, bilirubin 3.2 mg/100 ml with an unconjugated fraction of 2.8 mg/100 ml, SGOT and SGPT were 9 IU and 11 IU respectively. Serum alkaline phosphatase was 9 KAU. Antinuclear antibody, rheumatoid factor, lupus erythematosus cell and direct Coomb's were negative. Red cells and hemoglobin casts were present in the urine on the day of admission and the patient had renal biopsy within 24 hours. The biopsy specimen revealed varying degrees of tubular degeneration and regenerating tubular epithelium. The glomeruli did not reveal any abnormality.

After 15 days of oliguria he went into a diuretic phase (urinary output 2-4 liters). During the oliguric phase, four peritoneal dialyses were performed. Laboratory investigations carried out four weeks later showed BUN of 12 mg/100 ml and serum creatinine of 1.1 mg/100 ml.

## DISCUSSION

Both glomerular and interstitial lesions are known to occur in lepromatous leprosy ([8]). Proliferative glomerular lesions ([7]) are similar to poststreptococcal glomerulonephritis. Patients with leprosy and skin lesions are probably more susceptible to streptococcal skin infection and subsequent renal involvement. However, cases are on record where similar types of glomerular lesions ([7]) have been observed without any serological evidence of recent streptococcal infection. Immune complex deposition has been shown to occur in the dermis during ENL reaction ([13])

and in the glomeruli ([12]) in cases of lepromatous leprosy. Deposits of IgM at the dermo-epidermal junction in three cases of lepromatous leprosy have been observed ([2]) and one of them showed subendothelial and intramembranous deposits. All of these evidences suggest an immune-complex origin for glomerulonephritis. The second case in the present study had clinical and histological (crescents $> 70\%$) manifestations suggestive of classical, rapidly progressive glomerulonephritis. Systemic diseases such as lupus erythematosus and polyarteritis nodosa are associated in up to 40% of cases with such type of nephritic illness ([4]). Post-streptococcal etiology ([4]) is attributed occasionally. There was no clinical or serological evidence suggestive of SLE or post-streptococcal glomerulonephritis in the present case (Case No. 2). Vessels included in the renal biopsy specimen also did not show any evidence of arteritis. Leprosy is not ordinarily considered to be associated with this type of nephritic illness, however in the present case there is no other suggestion which could negate this possibility. Cases 1 and 3 developed acute renal failure as a result of development of acute tubular necrosis. Both the patients showed hematological evidence of intravascular hemolysis in the form of leukocytosis, reticulocytosis, raised plasma hemoglobin and suggestive peripheral smear. None of the patients were G6PD deficient. The common agent which could have produced intravascular hemolysis in both the cases was dapsone. Presence of Heinz bodies in the peripheral smear also indicated its oxidative activity. The hemolytic effect of dapsone even in the therapeutic doses is too well known ([5]). Negative direct Coomb's test suggested that hemolysis was not immune mediated. The mechanism of acute renal failure due to intravascular hemolysis is not clearly understood. Rodriguez-Erdman ([10]) considered the liberation of thromboplastin factors from the lysed red cells and the activation of intravascular coagulation as the chief pathogenetic mechanism responsible for renal lesions of acute tubular necrosis. Bywaters and Stead ([3]) considered tubular obstruction as a major factor. Phillips and Silvers ([9]), however, observed that obstruction by the products of hemolysis was unlikely to be the sole cause.

Drutz *et al* ([6]) have reported a patient who developed acute renal failure during ENL phase. However, the degree of renal insufficiency seemed to be a mild one as there was no mention of BUN levels and the patient did not require the help of dialysis therapy. None of the patients in the present study showed clinical or histological evidence of ENL reaction.

## SUMMARY

Three patients having lepromatous leprosy developed acute renal failure. Two patients completely recovered and one was left with a moderate degree of renal insufficiency. Renal tissue obtained by percutaneous biopsy revealed acute tubular necrosis in two and diffuse crescentic glomerulonephritis in the third case.

## RESUMEN

Tres pacientes con lepra lepromatosa desarrollaron insuficiencia renal aguda. Dos de los pacientes se recuperaron completamente y uno de ellos permaneció con un grado moderado de insuficiencia renal. Las biopsias percutáneas del tejido renal revelaron necrosis tubular aguda en dos casos y glomerulonefritis difusa en el tercer caso.

## RÉSUMÉ

Trois malades souffrant de lèpre lépromateuse ont développé une décompensation rénale aigue. Deux malades ont été complètement guéris. Chez le dernier, un degré modéré d'insuffisance rénale a persisté. Du tissu rénal obtenu par biopsie percutanée a révélé une nécrose tubulaire aigue chez deux malades, et une glomerulonéphrite diffuse en croissant chez le troisième.

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