Acute Renal Failure as a Complication of Mediterranean Spotted Fever

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days later the serum creatinine level was 9.5 mg/dl and urea 290 mg/dl. Proteinuria was 1.5g/24h with persistence of erythrocytes in the urinary sediment. Immunological tests for cryoglobulin, antinuclear antibodies, circulating immunocomplexes, rheumatoid factor, complement, ant basement membrane antibodies, and anticytoplasmic antibodies were normal or negative. Serology for hepatitis B and C, and human immunodeficiency virus was also negative. Echography ruled out an obstructive pathology or any other specific renal characteristic. A renal biopsy was performed and hemodialysis was started and applied on five occasions. Renal histopathology showed normal glomeruli, marked interstitial fibroedema with an inflammatory component, and necro-

Dear Sir,

Herein we report a case of acute renal failure as a complication of Mediterranean spotted fever. Severe renal failure has exceptionally been described in the literature; the pathogenesis of this disorder remains speculative.

The patient was a 76-year-old male that became acutely ill 2 days before admission. Initially he had fever (39.5°C), chills, headache, and generalized arthromyalgias; 2 days later a diffuse maculopapular exanthema was evident, and he was admitted to the hospital.

He was in good general condition. The blood pressure was 130/80 mm Hg, the heart rate 95/min, and the temperature 39°C; the patient was well oriented and without any clinical sign of dehydration. A generalized maculopapular exanthema was noted, with a 2-cm necrotic plaque in the right hypochondria.

The laboratory findings were as follows: white blood cell count 7,200/mm³ (83% neutrophils), hematocrit 44%, platelets and coagulation tests were normal, urea 74 mg/dl, creatinine 2.6 mg/dl, Na 130 mEq/l, K 4 mEq/l, serum hepatic enzymes were slightly elevated, creatine kinase 103 U/l. The urinary sediment contained 30 erythrocytes and 2-3 leukocytes, no casts were noted, protein was 2+. The rest of his blood chemistry was normal. A thorax radiography showed no abnormalities.

With the suspicion of Mediterranean spotted fever, which was subsequently confirmed serologically (the *Rickettsia conorii* antibody titer increased using an indirect immunofluorescence assay), we started chemotherapy with doxycycline. The maculopapular

exanthema, fever, and the general symptoms rapidly improved, but his renal function worsened with normal urine output. His central venous pressure was in the normal range. Six

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Fig. 1. Interstitial fibroedema with a mixed inflammatory component and tubular damage. HE. $\times 200$.

sis with some hemoglobin casts in the tubular lumen (fig. 1). Vasculitis was not observed. The immunofluorescence examination was negative.

Ten days later his renal function started to improve, and hemodialysis was discontinued; the serum creatinine level being 3.4 mg/dl and urea 198 mg/dl. Four months later, he had normal renal function; the serum creatinine value being 1.4 mg/day and urea 46 mg/dl. The urinary sediment was normal.

Mediterranean spotted fever is a common infectious disease in endemic areas; the prognosis is usually benign [1-5]. Asymptomatic kidney disorders, such as minimal proteinuria, microhematuria, and mild renal failure, are relatively common consequences of *R. conorii* infection. These abnormalities are re-

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ported in up to 50% of the patients [2-5]. Major renal involvement such as acute renal failure has only rarely been described [6-8]. When present, it has been usually associated with dehydration, high fever, and vomiting in critically ill patients. A vasculitic syndrome has sometimes been suspected [2, 9], as seen in other tissues, but it has never been histologically documented in the kidney. In the exceptional cases reported in whom histopathological examinations were performed, only tubulointerstitial involvement has been demonstrated [6, 7]. In our patient prerenal causes of acute renal failure have been ruled out; he had no dehydration, arterial hypotension, hemolysis, rhabdomyolysis, or other known nephrotoxic factors. Immunofluorescence staining and serological tests ruled out an immunomediated mechanism.

As with the 2 previously reported cases [6, 7], we could only demonstrate tubulointerstitial involvement; no specific vascular lesions were observed. The pathological changes described in rickettsial diseases in other tissues are vascular, being especially common in skin, muscles, heart, lung, and brain [10]. The vascular damage is described as scattered along the arteries, veins, and capillaries. The process is patchy with areas of congestion and edema. This patchy affection makes it difficult to rule out definitively vascular involvement on the basis of a small kidney biopsy specimen.

Rickettia rickettsii and *Rickettsia diaporica* are included in the etiologic classification of interstitial nephritis [11]; not specifically mentioned is *R. conorii*, the etiological cause of Mediterranean spotted fever. Although the pathogenesis of acute renal failure in rickettsiosis remains putative, and further pathology examinations are needed to clarify the typical histopathological pattern in spotted fever diseases affecting the kidney, we propose that *R. conorii* should be considered in the differential diagnosis of acute interstitial nephritis, and rickettsiae must also be suspected on the basis of microhematuria, mild proteinuria, and renal failure which these patients frequently present.

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