Can Corticosteroids be Used as a First-Line Agent for Mercury-Related Glomerular Diseases?

To the Editor: Inorganic mercury exposure-related glomerular diseases are often reported in Asian countries. The half-life of inorganic mercury is about 50 days; with normal kidney function, complete elimination occurs within a few months of cessation of exposure. However, the complete remission of glomerular diseases may lag by a few more months. Chelation therapy with 2,3-dimercaptopropane-1-sulfonic acid shortens the complete remission time by faster elimination of mercury. Corticosteroids and cyclophosphamide are reserved only for severe manifestations which are not responding to chelation.[1] For mercury-related glomerulonephritis without other systemic toxicities, we used to follow an expectant line of management with renin-angiotensin blockade and statins because of the difficulty of procuring 2,3-dimercaptopropane-1-sulfonic acid.[2] We describe our experience with corticosteroids as the first line of management for mercury-related nephrotic syndrome ($n = 4$). Mercury exposure was defined as urine excretion >8 μg/d, measured by inductively coupled mass spectroscopy.[3] Three patients had membranous nephropathy (1 had chronicity on biopsy), and 1 had minimal change disease. The clinical and histopathological features are shown in Supplementary Table S1. None had other secondary causes for nephrotic syndrome. No extrarenal manifestations of mercury poisoning were present.

All patients were given 2 to 4 weeks of oral prednisolone 1 mg/kilogram body weight, tapered over the next 2 to 4 weeks. The referring physician started patient 1 on steroids, whereas for patients 2 to 4, steroids were started as soon as the diagnosis of mercury-related glomerular disease was made. Corticosteroid-treated patients had remission (defined as urinary protein-to-creatinine ratio <0.3 or urine protein nil) by the end of 4 weeks. The median time for entering remission with conservative management was considerably longer: 7 months (interquartile range 6, 16.5; $P = 0.016$); the individual patient details are already published.[2] Those patients who received steroids had more severe disease evidenced by lower glomerular filtration rate, lower serum albumin levels, and higher proteinuria and mercury levels. Despite having more severe disease, the median time for remission was faster in the steroid-treated group (Supplementary Table S2). The final glomerular filtration rate on follow-up was not different between the steroid and conservatively managed patients. Corticosteroids shortened the remission time in those with severe mercury exposure and severe nephrotic states with glomerular filtration rate reductions. The time for remission and glomerular filtration rate trends are given in Figure 1. There were no relapses of nephrotic syndrome on follow-up. The role of immunosuppression in mercury-related glomerulonephritis is quite unclear. The literature on the management of mercury-related glomerulonephritis is mainly from China, where chelation is the first line of treatment.[1,3,4] Previous reports did not observe any additional benefits of immunosuppression with 2,3-dimercaptopropane-1-sulfonic acid. Chelation increases urinary protein excretion in the initial cycles, possibly accounting for the lack of benefit of adding immunosuppression to chelation.[1] Mercury exposure is known to induce a state of inflammation as well as autoimmune responses that corticosteroids could suppress.[S1] The role of steroid therapy in mercury-related

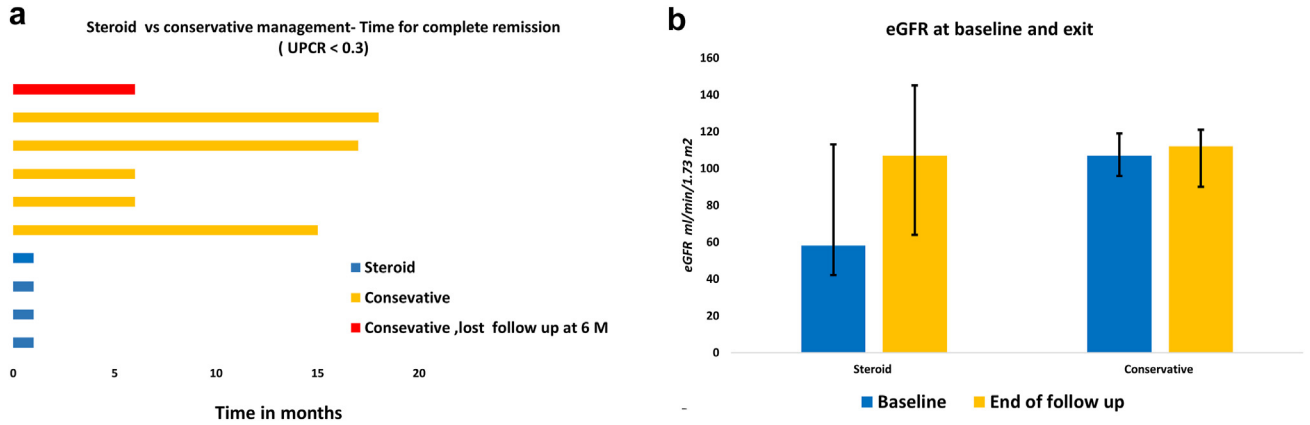

Figure 1. (a) Time taken for remission in steroid and conservatively managed patients. (b) GFR trends in steroid and conservatively managed patients. GFR, glomerular filtration rate

glomerulonephritis, without other organ toxicities, needs further exploration. A potential limitation of this report is the lack of data on antigens other than PLA2R; the putative antigen responsible for the disease remains unknown. Recently, neural epidermal growth factor-like 1 protien (NELL-1) has been proposed as a potential target antigen in indigenous medicine-related MN.[S2] Identifying the antigen and detecting the antibody levels might help to guide therapy in the future.

DISCLOSURE

All the authors declared no competing interests.

SUPPLEMENTARY MATERIALS

Supplementary File (PDF)

Supplementary References.

Table S1. Characteristics of steroid-treated patients.

Table S2. Characteristics of steroid-treated patients versus those managed conservatively.

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