Clinical Images in Nephrology and Dialysis

Case Answer

A 43-year-old woman with a 20-year history of SLE and a 13-year history of lupus nephritis was referred to our hospital for evaluation of worsening proteinuria. During the past 20 years, the patient had experienced multiple flares of SLE, including central nervous system lupus and biopsy-proven renal flares, and hence, had received several pulses of intravenous methylprednisolone and cyclophosphamide. Four years before presentation, kidney biopsy to investigate increased urinary protein excretion of 6 g/d demonstrated both active and chronic glomerular lesions of lupus nephritis, including mesangial proliferation; wire-loop lesions; and numerous deposits in the subendothelial, inframembranous, subepithelial, and mesangial areas. After another pulse therapy, mycophenolate mofetil 1000 mg was added to prednisolone 10–15 mg/d. Azathioprine therapy was attempted but discontinued due to pancytopenia. Tacrolimus was given for a short period but discontinued due to worsened glucose control. She had been using insulin for 7 years for steroid-induced diabetes. Physical examination was notable for bilateral lower leg edema. Urinary protein excretion was 8 g/d. Serum creatinine level was 1.27 mg/dl, albumin was 2.3 g/dl, and hemoglobin A1c was 8.5%. The eGFR was 37.5 ml/min per 1.73 m² according to the estimating equation for Japanese population (1). A repeat kidney biopsy was performed.

Light microscopy revealed glomerular insudative lesions, arteriolar hyalinization, and mesangial proliferation (Figure 1A) but no active lesions of lupus nephritis. Immunofluorescent microscopy showed linear IgG deposition along the glomerular basement membrane and scarce granular deposition (Figure 1B). Electron microscopy demonstrated foot process effacement, thick glomerular basement membrane (420–730 nm in width; wider than 395 nm) (2), and a limited number of deposits, which were tiny and some of which were lucent (Figure 1C). These findings were diagnostic of diabetic nephropathy superimposed on chronic lesions of lupus nephritis. Treatment strategy was switched from strengthening immunosuppression to strict glycemic control and management of diabetic complications. However, unfortunately, the patient died from sudden cardiac arrest before the first follow-up visit after kidney biopsy.

When proteinuria worsens in a patient with lupus nephritis, a repeat kidney biopsy remains the gold standard to diagnose whether it is due to a lupus flare or caused by a different comorbid kidney disease (3). In the presented patient, investigating the renal pathology not only contributed to understanding the etiology of proteinuria but also, had the potential to suggest her systemic comorbidities, which presumably needed appropriate intervention. Although rarely featured in the literature, the risk of diabetic complications, including diabetic nephropathy, should be kept in mind in patients with SLE and long-term corticosteroid exposure.

Teaching Points

- In patients with lupus nephritis, repeat kidney biopsies remain the gold standard to diagnose the etiology of worsening proteinuria. Determining whether it is due to a lupus flare or caused by a different comorbid kidney disease has a substantial effect on the clinical management thereafter.
- Diabetic nephropathy is on the differential diagnosis list of worsening proteinuria in patients with SLE and long-term corticosteroid exposure. Discovering diabetic nephropathy not only changes the clinical approach to the patients’ kidney disease but may also affect the management and outcomes of other vascular complications associated with diabetes mellitus.

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Author Contributions

Y. Oda was responsible for data curation and investigation; Y. Ubara provided supervision; Y. Oda wrote the original draft; and J. Hoshino and Y. Ubara reviewed and edited the manuscript.

Disclosures

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Yasuhiro Oda,1 Junichi Hoshino,1,2 and Yoshifumi Ubara1,2


Correspondence: Yasuhiro Oda and Yoshiitumi Ubara, Nephrology Center, Toranomon Hospital Kajigaya, 1-3-1 Kajigaya, Takatsu, Kawasaki, Kanagawa 213-8587, Japan. Email: yasuhirooda3@gmail.com and ubara@toranomon.gr.jp
Figure 1. | Histology of the kidney biopsy specimens demonstrated diabetic nephropathy superimposed on chronic lesions of lupus nephritis. (A) Light microscope image (periodic acid–Schiff staining) shows glomerular insudative lesions, arteriolar hyalinization, and mesangial proliferation. Original magnification, ×400. (B) Fluorescent microscope image demonstrates linear IgG deposition along the glomerular basement membrane but scarce granular deposition. Original magnification, ×400. (C) Electron microscope image reveals foot process effacement, thick glomerular basement membrane, and a limited number of small deposits, some of which are lucent.

References