Silent Lupus Nephritis with Fingerprint Deposits

Akihiro Tojo, Kenjiro Kimura, Yasunobu Hirata, Hiroaki Matsuoka and Tsuneaki Sugimoto

A 26-year old woman with diffuse active lupus nephritis showed no proteinuria. Electron microscopy revealed a typical fingerprint pattern in glomerular subendothelial electron dense deposits. Out of 21 renal biopsy cases of lupus nephritis, we found fingerprint deposits in 4 cases (19%) including the present case. All of the cases showed diffuse proliferative glomerulonephritis with overt proteinuria, except the present case. To our knowledge, the present case is the first reported case of active lupus nephritis, where fingerprint deposits were found, with normal urinalysis.

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Introduction

Organized glomerular electron dense deposits with a fingerprint pattern are well known in lupus nephritis. In 1967, Grishman et al (1) first demonstrated the characteristic deposits in 3 out of 41 biopsy cases with lupus nephritis (7%). Since then only a few cases (2-7) have been reported to have fingerprint deposits in lupus erythematosus. The nature of this lesion is still unknown. In this report we present a case of lupus nephritis with normal urinalysis, where electron microscopy revealed typical fingerprint deposits. We also re-evaluated previous renal biopsy cases of lupus nephritis and tried to elucidate the clinical and pathological features of these fingerprint deposits.

Case Report

A 26-year-old woman was hospitalized for slight fever, arthralgia, and erythema in the extremities. She was healthy until the onset of hypersensitivity to sunburn with severe rash and bulla in the face and extremities two years before admission. These symptoms disappeared in response to large doses of oral steroid therapy. Two years later, she complained of muscle weakness and hypertension while taking 15mg prednisolone a day, and was then admitted to our hospital.

Routine urinalysis showed no abnormalities. The urinary protein excretion was less than 150mg per 24 hours. However, the urinary microalbumin (5.0mg/dl, normal range; less than 3.2mg/dl) and N-acetyl-beta-D-glucosaminidase (NAG) activity (10.9 U/l, normal range; 0.97-4.17 U/l) were slightly increased. The hemoglobin level was 11.5 g/dl, and the white blood cell count was 6400/mm³. The blood creatinine was 0.7 mg/dl, and the creatinine clearance was 100 mg/min. The erythrocyte sedimentation rate (ESR) was 50 mm/h. The serum complement levels were low (CH50; 17.4, C3; 34, C4; 9), and the serum IgG was 1639mg/dl, IgA 506mg/dl, and IgM 54mg/dl. Speckled type antinuclear antibody was positive (×40). The anti-double strand (ds) DNA antibody and the mixed type cryoglobulin (IgG and IgM) were positive, whereas the anti-Sm and anti-RNP antibodies were negative. From these clinical features, the patient was diagnosed as lupus erythematosus according to the ARA criteria (8). As microalbuminuria was detected, renal biopsy was performed. Subsequently, the patient was treated with oral prednisolone 30mg a day, combined with cyclophosphamide 100mg a day. The treatment relieved her clinical symptoms, and returned the urinary albumin excretion, ESR and the serum complements levels to the normal range.

Histology of Renal Biopsy Specimen

Light microscopy

The renal biopsy specimen was fixed in 95% ethanol and 1% acetic acid, dehydrated and embedded in paraffin. Three μm thick sections were cut. Sections were stained with hematoxlyn-eosin and periodic acid-Schiff. The renal biopsy tissue contained 16 glomeruli without global sclerosis. Most of the glomeruli showed global mesangial
cell proliferation. The wire loop lesion and the karyorrhexis were observed in several glomeruli, which indicated active lupus nephritis (Fig. 1). The tubules showed focal atrophy and the interstitium showed focal lymphocytic infiltration. The arterioles showed moderate medial thickening.

**Immunohistochemical study**

With the peroxidase-anti-peroxidase (PAP) method, granular deposits were shown in mesangial and subendothelial areas, being most intense with IgG (Fig. 2), and moderate with IgM, C1q and C3, and least with IgA. IgG was also linearly positive along glomerular basement membrane.

**Electron microscopy**

Massive electron dense deposits were revealed in the mesangium and subendothelial area (Fig. 3a). At higher magnifications, the deposits in the subendothelial area were found to have a characteristic fingerprint pattern. The curved or straight electron dense bands were regularly arranged and consisted of lamellar structures (Fig. 3b).

**Discussion**

In the present case, diffuse active lupus nephritis was revealed despite normal urinalysis. The characteristic “fingerprint” pattern was found in subendothelial electron dense deposits. We have performed renal biopsies in 21 patients with lupus erythematosus, which were diagnosed using the ARA criteria (8). Among the 21, 4 cases (19%), including the present case, showed fingerprint deposits. Lupus erythematosus of these patients was highly active, with the ESR, antinuclear antibody and serum complements levels as markers of the disease activity (Table 1). Previously reported cases with fingerprint deposits (1, 4, 5) were also clinically active. Histologically, all 4 cases with fingerprint deposits showed diffuse proliferative lupus nephritis. Previously reported cases (1, 3–5) also demonstrated diffuse proliferative glomerulonephritis with wire loops or diffuse membranous nephritis with mesangial and endothelial proliferation (type IV or V in WHO classification). These cases were associated with overt proteinuria. To our knowledge, the present case is the first reported case of lupus nephritis with normal urinalysis where fingerprint deposits were found. We have experienced 2 cases of lupus nephritis without proteinuria and hematuria, but the findings of renal histology were rather slight without fingerprint deposits.

Although the fingerprint deposits have been reported in some types of chronic glomerulonephritis other than lupus nephritis, they are exceptional and the unique structure is still valuable in diagnosis of lupus nephritis (7, 9). Two cases reported by Alpers et al (3) were suggestive in this regard. They found fingerprint deposits in renal biopsy specimens from 2 patients without any clinical evidence of lupus erythematosus. Clinical signs and symptoms of lupus erythematosus appeared 2 and 5 years later, respectively, in these 2 patients. These cases may support the assumption that deposits with the fingerprint pattern may be specific markers for lupus erythematosus, even when overt clinical features are lacking. Thus fingerprint deposits might exist from early stages of this disease.

Grishman et al (1) first reported the fingerprint deposits in 3 out of 41 biopsy cases (7%) with lupus nephritis. Alpers et al (3) found the fingerprint deposits in 9 cases out of 177 lupus nephritis (5%). All 9 cases showed diffuse mesangial proliferation. However, Jenis and Lowenthal (6) reported that they found this characteristic deposit in 20% of lupus nephritis. This incidence is very similar to our experience (19%). More careful electron microscopic examination with higher magnification,
Lupus Nephritis with Fingerprint Deposits

Table 1. Clinical Features of Patients with Lupus Nephritis with Fingerprint Deposits

<table>
<thead>
<tr>
<th>Case</th>
<th>Age to biopsy</th>
<th>Plasma IgG mg/dl</th>
<th>CH50 U/ml</th>
<th>Urinary ANF g/day</th>
<th>Histology WHO classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>60 months</td>
<td>2806</td>
<td>29.4</td>
<td>×160</td>
<td>1.7 IVb</td>
</tr>
<tr>
<td>2</td>
<td>6 months</td>
<td>13.4</td>
<td>×640</td>
<td>10.0</td>
<td>IVc</td>
</tr>
<tr>
<td>3</td>
<td>4 months</td>
<td>3012</td>
<td>23.3</td>
<td>×320</td>
<td>0.13 IVc</td>
</tr>
<tr>
<td>4*</td>
<td>50 months</td>
<td>2484</td>
<td>17.4</td>
<td>×40</td>
<td>0.02 IVb</td>
</tr>
</tbody>
</table>

* the present case

The thickness of electron dense bands was 16.6 to 20.4 nm in our 4 cases (Table 2), which is slightly larger than those of Grishman et al (1) (10.5–15.0 nm) or Kim et al (4) (8–10 nm). The distance from the center of one band to the center of the next band measured 22.9 to 33.4 nm in our 4 cases, which is almost consistent with 22.5 to 29.0 nm in 3 cases reported by Grishman et al (1) and 19 to 21 nm in a case reported by Kim et al (4). The C57BL/6J mice, an experimental model of lupus erythematosus, showed the fingerprint deposits with curved lamellar lines separated by about 30 nm with a clear space of about 65 nm (10). The fingerprint pattern

Fig. 3. a) Electron-dense deposits in mesangial and subendothelial area (×3,000). b) Glomerular deposits showing characteristic fingerprint deposits (×60,000).
Table 2. Morphometry of Fingerprint Deposits

<table>
<thead>
<tr>
<th>Case</th>
<th>Thickness of bands (nm)</th>
<th>Distance of bands (nm)</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16.6 ± 0.5</td>
<td>22.9 ± 1.0</td>
<td>Subendothelium</td>
</tr>
<tr>
<td>2</td>
<td>16.6 ± 0.3</td>
<td>23.6 ± 0.4</td>
<td>Mesangium</td>
</tr>
<tr>
<td>3</td>
<td>20.4 ± 0.6</td>
<td>33.4 ± 0.6</td>
<td>Subepithelium</td>
</tr>
<tr>
<td>4*</td>
<td>18.8 ± 0.3</td>
<td>26.5 ± 0.6</td>
<td>Subendothelium</td>
</tr>
</tbody>
</table>

* the present case

differs in size and configuration slightly, which might indicate different compositions of deposits. The thickness of these electron dense bands are nearly equal to the length of immunoglobulin. However, the components of this characteristic fingerprint pattern have not been elucidated. Immunohistochemical studies showed that the immune deposits were stained not only with IgG but also with IgM, IgA, C1q and C3 in all of our 4 cases. Kim et al (4) reported that the fingerprint patterns were observed in the serum cryoprecipitates as well as in the glomerular deposits, and that the immunoglobulin composition of cryoprecipitates was identical with that of glomerular deposits. It is known that organized deposits similar to fingerprint deposits in lupus nephritis are observed in cryoglobulinemia (11-14). Furthermore, Feiner and Gallo (12) demonstrated that mixed IgG-IgM cryoglobulinemia shows deposits composed of curved cylindrical and annular structures and that deposits in IgG cryoglobulinemia are composed of numerous straight parallel fibrils aggregated into bundles. However, the size and shape of these structures seen in cryoglobulins are slightly larger than those in lupus nephritis. Finally, a direct or indirect relation of viral infection and the electron dense deposits has been suggested in lupus nephritis (7). Further studies are necessary to elucidate the components of the fingerprint deposits and the relation of the deposits to the pathogenesis of lupus nephritis.

In conclusion, we presented a patient with diffuse active lupus nephritis with fingerprint deposits despite normal urinalysis. The fingerprint deposits were observed in 19% of renal biopsy cases with systemic lupus erythematosus, and all of these patients showed diffuse active proliferative nephritis.

References