Methods. Renal biopsy specimens from 112 patients with ANCA-associated pauci-immune glomerulonephritis were investigated using direct immunofluorescence, light and electron microscopy. For direct immunofluorescence, IgG, IgA, IgM, C3c and C1q staining on fresh frozen renal tissue were routinely performed immediately after a renal biopsy. Complement deposition was defined as the presence of C3c or C1q for at least 1+ in a 0–4+ scale. Clinical and histopathological data between patients with and without complement deposition were compared.

Results. In direct immunofluorescence microscopy, C3c and C1q could be detected in glomerular capillary wall and/or mesangium in the specimens of 37/112 (33.0%), 7/112 (6.3%) patients, respectively. Compared with patients without C3c deposition, patients with C3c deposition had a higher level of urinary protein ($P < 0.01$) and poorer initial renal function ($P < 0.05$).

Conclusion. Complement deposition was not rare in renal histopathology of human ANCA-associated pauci-immune

References
glomerulonephritis, which was associated with more severe renal injury.

Keywords: ANCA; complement; pauci-immune; vasculitis

Introduction

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a group of autoimmune disorders, including Wegener's granulomatosis (WG), microscopic polyangiitis (MPA), Churg-Strauss syndrome (CSS) and renal-limited vasculitis (RLV), characterized by necrotizing small-vessel vasculitis with autoantibodies directed against neutrophil cytoplasmic constituents, in particular proteinase 3 (PR3) and myeloperoxidase (MPO). Kidney is one of the most vulnerable organs. The histopathological hallmark of ANCA-associated glomerulonephritis is ‘pauci-immune’ necrotizing crescentic glomerulonephritis, characterized by little or no glomerular staining for immunoglobulins in renal histology by immunofluorescence microscopy examination.

Though the pathogenesis of ANCA-associated glomerulonephritis has not been fully elucidated, recent studies in animal models suggested that complement activation via an alternative pathway was one of the important contributing factors in the development of anti-MPO antibody-associated systemic vasculitis in mice [1,2]. In human ANCA-associated glomerulonephritis, several studies had suggested that complement deposition could be detected in renal histopathology [3–13]. For instance, Brouwer et al. suggested that in patients with WG, complement was found in 70% patients with more severe forms of glomerulonephritis and in 30% patients with mild/moderate glomerulonephritis [9]. Therefore, it would be of interest to further investigate the clinical and pathological significance of complement deposition in renal histopathology of patients with ANCA-associated pauci-immune glomerulonephritis.

Methods

Patients

Patients with ANCA-associated pauci-immune glomerulonephritis, diagnosed from 1997 to 2007 in the Renal Division and Institute of Nephrology, Peking University First Hospital, were enrolled in this retrospective study. A Renal biopsy was performed at the time of diagnosis. ‘Pauci-immune’ was defined as ‘the intensity of glomerular immunoglobulin (including IgG, IgA and IgM) staining by direct immunofluorescence assay in renal sections was negative to 1+ staining on a scale of 0–4+’. All the patients met the criteria of Chapel Hill Consensus Conference definition for ANCA-associated vasculitis [14]. Patients with anti-glomerular basement membrane (anti-GBM) disease, post-infectious glomerulonephritis, other underlying diseases that cause secondary vasculitis, such as systemic lupus erythematosus, rheumatoid arthritis, Sjogren’s syndrome, malignancy, drug-induced vasculitis and Behet’s disease, were excluded clinically. Clinical and pathological data were extracted for analysis. No repeat biopsies were included. Informed consent was obtained from each patient when the renal biopsy was performed. The research was in compliance of the Declaration of Helsinki.

Detection of ANCA and anti-GBM antibodies

All the sera were tested for ANCA and anti-GBM antibodies at the time of presentation before immunosuppressive treatment was instituted. ANCA tests were performed by both indirect immunofluorescence (IIF) assay and antigen-specific ELISAs. Standard IIF assays were performed according to the manufacturer (EUROIMMUN, Lübeck, Germany). In antigen-specific ELISAs, two highly purified known ANCA antigens, PR3 and MPO, purified as previously reported [15], were used as solid phase ligands. Anti-GBM antibodies were detected by ELISA using highly purified bovine non-collagenous NC1 domain of α3 (IV) NC1 as solid phase ligands as previously reported [16].

Renal histopathology

Renal specimens were evaluated using direct immunofluorescence, light and electron microscopy.

For direct immunofluorescence, the specimens were embedded on OCT compound (Miles Laboratories, Elkhart, IN, USA) and frozen in an acetone-dry ice mixture. The frozen sections were cut into 2–3 μm on a cryostat and stored at −80°C until use. These sections were rinsed in a 0.01 mol/L phosphate-buffered saline (PBS), pH 7.4, fixed in absolute acetone for 10 min, and incubated for 30 min at room temperature with fluorescein isothiocyanate-conjugated rabbit anti-human IgG, IgA, IgM, C1q, C3c or fibrinogen antisera (Dakopatts, Copenhagen, Denmark). The stained sections were rinsed by PBS and examined under a fluorescence photomicroscope (Zeiss Axiophot, Oberkochen, Germany).

For light microscopy, paraffin sections were stained with silver, periodic acid-Schiff (PAS), haematoxylin & eosin (H&E) and trichrome, and were forwarded to two pathologists. Both pathologists scored the biopsies separately, blinded to patients’ data and the scores of the other observer, according to a previously standardized protocol for scoring renal biopsies of patients with ANCA-associated vasculitis [17–19]. In short, each glomerulus was scored separately on the presence of fibrinoid necrosis, crescents (cellular/fibrous and segmental/circumferential), glomerulosclerosis (local/segmental/global), granulomatous reactions, as well as a number of other lesions. The presence of glomerular lesions was calculated as the percentage of the total number of glomeruli in a biopsy. Interstitial and tubular lesions were scored semiquantiatively on the basis of the percentage of the tubulointerstitial compartment that was affected: interstitial infiltrates (‘−’ for 0%, ‘+’ for 0–20%, ‘++’ for 20–50%, and ‘+++’ for >50%), interstitial fibrosis (‘−’ for 0%, ‘+’ for 0–50%, ‘++’ for >50%) and tubular atrophy (‘−’ for 0%, ‘+’ for 0–50%,
‘++’ for >50%’). Vascular lesions were scored as presence or absence. Furthermore, all the kidney biopsies were also scored according to an activity index (AI) and chronicity index (CI) as previously described [20]. All specific histologic lesions were semiquantitatively graded on a scale of 0–3 (absent, mild, moderate and severe, respectively). Necrosis, cellular crescents and fibrous crescents were weighed by a factor of 2. The maximum possible scores for AI and CI were 24 and 18, respectively. Differences in scoring between the two pathologists were resolved by re-reviewing the biopsies and coming to a consensus.

Statistics

Differences of quantitative parameters between groups were assessed using the t-test (for data that were normally distributed) or non-parametric test (for data that were not normally distributed). Differences of semiquantitative results were tested using the Mann–Whitney U-test. Differences of qualitative results were compared using the chi-square test. They were considered significant if the P-value was less than 0.05. Analysis was performed with the SPSS statistical software package (version 11.0, Chicago, IL, USA).

Results

Demographic features

One hundred and sixty-five patients with ANCA-associated glomerulonephritis received renal biopsy. Eighteen of them were excluded because of drug-induced ANCA-associated glomerulonephritis. Among the remaining 147 patients, 35 were excluded because the intensity of glomerular immunoglobulin staining by direct immunofluorescence assay in renal sections was equal to or more than 2+ (including 20 patients whose IgM staining was equal to or more than 2+ in renal sections). So, in total there were 112 patients diagnosed with ANCA-associated pauci-immune glomerulonephritis. None was serum anti-GBM antibodies positive. Sixty patients were male and 52 patients were female, with an average age of 58.1 ± 13.6 years. Ninety-four of the 112 patients (83.9%) were pANCA positive, and all the sera could recognize MPO. Eighteen patients (16.1%) were cANCA positive, and all the sera could recognize PR3. Of the 112 patients with AAV, 39, 64, 1 and 8 patients were classified as WG, MPA, CSS and RLV, respectively.

Complement deposition in renal histopathology

In direct immunofluorescence microscopy, C3c could be detected in the specimens of 37/112 (33.0%) patients. Fifteen (15/37, 40.5%), seventeen (17/37, 45.9%) and five (5/37, 13.5%) were graded as 1+, 2+ and 3+ of C1q staining on a scale of 0–4+, respectively. C3c deposition was found in glomerular capillary wall, mesangium and arterioles in 32/37, 28/37 and 1/37, respectively. However, C1q could be detected in the specimens of 7/112 (6.3%) patients only. Five (5/7, 71.4%), one (14.3%) and one (14.3%) were graded as 1+, 2+ and 3+ of C1q staining on a scale of 0–4+, respectively. C1q deposition was found in glomerular capillary wall and mesangium in 7/37 and 5/37, respectively. Among the seven patients with C1q deposition, C3c could also be detected. In the direct immunofluorescence assay in renal sections of these seven patients, IgG, IgA and IgM staining were all negative in two patients; IgG, IgM and IgA were 1+ on staining in two, one and three patients, respectively. The electron microscopy assay showed that electron-dense deposits were absent in the specimen in five patients, and the other two had very mild electron-dense deposits.

Renal manifestations

Of the 37 cases (37/112, 33.0%) with C3c deposition in renal histopathology, all had haematuria. The median level of urinary protein was 1.8 (range 0.0–10.0) g/24 h. The level of initial serum creatinine at presentation was 491.2 ± 305.9 µmol/L (range 77.0–1167.7 µmol/L). The median level of estimated glomerular filtration rate (eGFR) was 9.9 (range 2.70–101.6) mL/min/1.73 m². Eighteen cases (18/37, 48.6%) were dialysis dependent on diagnosis. Of the seven cases (7/112, 6.25%) with C1q deposition in renal histology, all had haematuria. The median level of urinary protein was 2.58 (range 0.72–6.65) g/24 h. The level of initial serum creatinine at presentation was 518.0 ± 221.0 µmol/L (range 170.0–700.0 µmol/L). The median level of eGFR was 6.5 (range 5.1–30.9) mL/min/1.73 m². Five cases (5/7, 71.4%) were dialysis dependent on diagnosis.

Compared with the 75 patients without C3c deposition in renal histopathology, patients with C3c deposition had higher levels of urinary protein [median and range, 1.8 (0, 10.0) g/24 h versus 0.93 (0, 13.4) g/24 h, P < 0.01], higher initial serum creatinine (491.2 ± 305.9 µmol/L versus 354.8 ± 320.8 µmol/L, P < 0.05) and lower eGFR at presentation [median and range, 9.9 (2.70–101.6) mL/min/1.73 m² versus 24.1 (1.87, 153.6) mL/min/1.73 m², P < 0.05]. The proportion of dialysis dependence at presentation was also significantly higher in patients with C3c deposition than that in those without (48.6% versus 28.0%, P < 0.05). There was no significant difference on renal manifestations between patients with and without C1q deposition in renal histopathology (Table 1).

Renal histopathology

An average of 24.4 ± 13.0 glomeruli were obtained in the 112 renal biopsies. Of the 37 cases with C3c deposition in renal histopathology, 25.5% ± 26.0% (0–90.9%) of the glomeruli were normal, and 63.7% ± 27.2% (0–100%) of the glomeruli had crescents formation. The mean and median percentage of global sclerosis was 4.3% and 0.0% (range 0–34.9%), respectively. All the 37 patients had interstitial infiltrates, and 8/37 (21.6%), 19/37 (51.4%) and 10/37 (27.0%) scored as mild (+), dense (+++) and very dense (+++), respectively. Twenty-four of the 37 (64.9%) patients had interstitial fibrosis, and 2/37 (5.4%) and 22/37 (59.5%) scored as focal (+) and diffuse (+++), respectively. Tubular atrophy was present in 34/37 (91.9%) biopsies, and 4/37 (10.8%)
had a significantly lower percentage of normal glomeruli than those without (AI: 3.80 ± 2.17 versus 5.89 ± 2.97, CI: 4.60 ± 3.44 versus 5.55 ± 3.16, respectively).

**Table 1.** Comparison of clinical and laboratory features of patients with and without C3c or C1q deposition in renal histology

<table>
<thead>
<tr>
<th>Parameter</th>
<th>With C3c deposition (n = 75)</th>
<th>Without C3c deposition (n = 75)</th>
<th>With C1q deposition (n = 7)</th>
<th>Without C1q deposition (n = 105)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.1 ± 14.7</td>
<td>59.1 ± 13.1</td>
<td>54.1 ± 11.7</td>
<td>58.4 ± 13.8</td>
</tr>
<tr>
<td>MPO-ANCA/PR3-ANCA</td>
<td>33/4</td>
<td>61/14</td>
<td>7/0</td>
<td>87/18</td>
</tr>
<tr>
<td>WG/MPS/CSS/RLV</td>
<td>13/17/1/6</td>
<td>26/47/0/2</td>
<td>3/3/0/1</td>
<td>36/61/1/7</td>
</tr>
<tr>
<td>Fever</td>
<td>24 (64.9%)</td>
<td>49 (65.3%)</td>
<td>4 (57.1%)</td>
<td>69 (65.7%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>25 (67.6%)</td>
<td>43 (57.3%)</td>
<td>6 (85.7%)</td>
<td>62 (59.0%)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>20 (54.1%)</td>
<td>30 (40.0%)</td>
<td>4 (57.1%)</td>
<td>46 (43.8%)</td>
</tr>
<tr>
<td>Muscle pain</td>
<td>10 (27.0%)</td>
<td>25 (33.3%)</td>
<td>2 (28.6%)</td>
<td>33 (31.4%)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>15 (40.5%)</td>
<td>31 (41.3%)</td>
<td>4 (57.1%)</td>
<td>42 (40.0%)</td>
</tr>
<tr>
<td>Skin rash</td>
<td>6 (16.2%)</td>
<td>16 (21.3%)</td>
<td>2 (28.6%)</td>
<td>20 (19.0%)</td>
</tr>
<tr>
<td>Pulmonary involvement</td>
<td>23 (62.1%)</td>
<td>48 (64.0%)</td>
<td>2 (28.6%)</td>
<td>69 (65.7%)</td>
</tr>
<tr>
<td>Ophthalmic</td>
<td>10 (27.0%)</td>
<td>18 (24.0%)</td>
<td>2 (28.6%)</td>
<td>26 (24.8%)</td>
</tr>
<tr>
<td>Otic</td>
<td>17 (45.9%)</td>
<td>27 (36.0%)</td>
<td>5 (71.4%)</td>
<td>39 (37.1%)</td>
</tr>
<tr>
<td>Upper respiratory tract</td>
<td>10 (27.0%)</td>
<td>18 (24.0%)</td>
<td>3 (42.9%)</td>
<td>25 (23.8%)</td>
</tr>
<tr>
<td>Nervous system</td>
<td>7 (18.9%)</td>
<td>12 (16.0%)</td>
<td>2 (28.6%)</td>
<td>17 (16.2%)</td>
</tr>
<tr>
<td>Urinary protein (g/24 h)</td>
<td>1.8 (0, 10.0)</td>
<td>0.93 (0, 13.4)**</td>
<td>2.58 (0.72, 6.65)</td>
<td>3.00 (0, 13.4)</td>
</tr>
<tr>
<td>Initial Scr (µmol/L)</td>
<td>491.2 ± 305.9</td>
<td>354.8 ± 320.8**</td>
<td>518.0 ± 221.0</td>
<td>391.4 ± 326.0</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73 m²) (median and range) sliced by sexa</td>
<td>9.9 (2.70, 101.6)</td>
<td>24.1 (1.87, 153.6)*</td>
<td>6.5 (5.1, 30.9)</td>
<td>20.8 (1.87, 153.6)</td>
</tr>
<tr>
<td>Dialysis dependent at presentation</td>
<td>18 (48.6%)</td>
<td>21 (28.0%)*</td>
<td>5 (71.4%)</td>
<td>34 (32.3%)</td>
</tr>
<tr>
<td>Low serum complement 3</td>
<td>2 (5.4%)</td>
<td>5 (6.7%)</td>
<td>2 (28.6%)</td>
<td>5 (4.8%)</td>
</tr>
<tr>
<td>BVAS</td>
<td>21.4 ± 5.39</td>
<td>20.3 ± 5.26</td>
<td>19.4 ± 5.59</td>
<td>20.7 ± 5.30</td>
</tr>
</tbody>
</table>

*P < 0.05, **P < 0.01, compared with the ‘with C3c deposition’ group.

and 30/37 (81.1%) scored as focal (+) and diffuse (++), respectively.

Compared with the 75 patients without C3c deposition in renal histopathology, patients with C3c deposition had a significantly lower percentage of normal glomeruli (25.5% ± 26.0% versus 43.7% ± 32.2%, P < 0.01) and a significantly higher percentage of crescent formation (63.7% ± 27.2% versus 44.4% ± 30.9%, P < 0.01) (Table 2). Interstitial infiltrates and tubular atrophy were more prevalent and severe in patients with C3c deposition than in those without (P < 0.01, P < 0.05, respectively) (Figure 1).

Parameters of renal histopathology of patients with and without C1q deposition are listed in Table 2 and Figure 1. There was no significant difference between the two groups.

The AI and CI were not significantly different between patients with C3c deposition and those without (AI: 6.03 ± 2.75 versus 5.65 ± 3.07, CI: 5.88 ± 3.22 versus 5.29 ± 3.13, respectively), nor between patients with C1q deposition and those without (AI: 3.80 ± 2.17 versus 5.89 ± 2.97, CI: 4.60 ± 3.44 versus 5.55 ± 3.16, respectively).

**Table 2.** The percentages of various glomerular lesions

<table>
<thead>
<tr>
<th>Glomerular lesion</th>
<th>With C3c deposition (n = 37)</th>
<th>Without C3c deposition (n = 75)</th>
<th>With C1q deposition (n = 7)</th>
<th>Without C1q deposition (n = 105)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal glomeruli</td>
<td>25.5 ± 26.0</td>
<td>43.7 ± 32.2*</td>
<td>8.6 (0, 81.0)</td>
<td>33.3 (0, 100)</td>
</tr>
<tr>
<td>Crescent</td>
<td>63.7 ± 27.2</td>
<td>44.4 ± 30.9*</td>
<td>32.6 (6.1, 61.5)</td>
<td>50.0 (1.6, 100)</td>
</tr>
<tr>
<td>Cellulara</td>
<td>43.3 ± 32.8</td>
<td>45.4 ± 38.6</td>
<td>36.2 (0, 87.9)</td>
<td>10.6 (0, 96.2)</td>
</tr>
<tr>
<td>Fibrousa</td>
<td>26.9 ± 29.1</td>
<td>31.6 ± 35.8</td>
<td>0.0 (0, 39.7)</td>
<td>0 (0.7, 35.7)</td>
</tr>
<tr>
<td>Glomerular sclerosis</td>
<td>0.0 (0, 34.9)</td>
<td>0.0 (0, 37.5)</td>
<td>0.0 (0, 12.5)</td>
<td>0 (0.37, 5)</td>
</tr>
</tbody>
</table>

*P < 0.01, compared with the ‘with C3c deposition’ group.

Extra-renal manifestations

Extra-renal manifestations at presentation are listed in Table 1. There was no significant difference between patients with and without C3c deposition, or patients with and without C1q deposition. Among the 112 patients, there were 7 patients (7/112, 6.25%) having slightly low serum C3. The level of serum C3 among these seven patients was 0.55 ± 0.04 g/L (normal range, 0.60–1.50 g/L).

**Discussion**

Recently, it has been suggested in an animal model that complement activation was involved in the pathogenesis of ANCA-associated pauci-immune glomerulonephritis [1,2]. In human AAV, several studies had suggested that complement deposition in kidney was not rare, as reviewed in Table 3. However, the relationship between complement deposits and the clinical or pathological findings had not been fully investigated.
Table 3. Reports in literatures of patients with AAV with complement deposition in renal histopathology

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>No. of cases</th>
<th>Disease</th>
<th>Complement deposition (no. of patients and complement components)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hu et al. [3]</td>
<td>1977</td>
<td>1</td>
<td>WG</td>
<td>1C3</td>
</tr>
<tr>
<td>Pinching et al. [5]</td>
<td>1983</td>
<td>13</td>
<td>WG</td>
<td>8C3</td>
</tr>
<tr>
<td>Lanham et al. [6]</td>
<td>1984</td>
<td>5</td>
<td>CSS</td>
<td>3C3</td>
</tr>
<tr>
<td>Grotz et al. [7]</td>
<td>1991</td>
<td>11</td>
<td>WG</td>
<td>10C3</td>
</tr>
<tr>
<td>Andrassy et al. [8]</td>
<td>1992</td>
<td>20</td>
<td>WG</td>
<td>4C3c and C3d</td>
</tr>
<tr>
<td>Brouwers et al. [9]</td>
<td>1994</td>
<td>20</td>
<td>WG</td>
<td>10C3</td>
</tr>
<tr>
<td>Allmaras et al. [10]</td>
<td>1997</td>
<td>3</td>
<td>RIV and IgA nephropathy</td>
<td>3C3c and C3d</td>
</tr>
<tr>
<td>Haas et al. [11]</td>
<td>2000</td>
<td>6</td>
<td>AAV (with IgA deposits)</td>
<td>6C3</td>
</tr>
<tr>
<td>Neumann et al. [12]</td>
<td>2003</td>
<td>45</td>
<td>AA V</td>
<td>2C3, 7C1q</td>
</tr>
<tr>
<td>Haas et al. [13]</td>
<td>2004</td>
<td>126</td>
<td>AA V</td>
<td>71C3, 10C1q</td>
</tr>
</tbody>
</table>

**Fig. 1.** Differences of tubulointerstitial lesions between patients with AAV with and without C3c deposition. \*P < 0.05, \*\*P < 0.01, compared with the ‘with C3c’ group.

In the current study, C3c and C1q deposition were detected in renal histology of some patients with ANCA-associated pauci-immune glomerulonephritis. It is to date one of the largest studies to investigate complement deposition in kidneys. The possible clinical and histological significance of complement deposition was also systematically analysed. It was found that about one-third of the renal biopsy specimen had glomerular complement deposition in routine direct immunofluorescence. This proportion fell into the ranges of previous studies [3–13]. However, since renal complement deposition is not rare in patients with ANCA-associated glomerulonephritis with immune complex deposits [12,13], patients with AAV recruited in the current study were limited in those with the feature of ‘pauci-immune’.

Among the human complement system, C3 plays a central role and is the most abundant complement protein in serum. C3 supports the activation of all the three pathways of complement activation, i.e. the classical, alternative and lectin pathway, resulting in the conversion of C3 to C3a and C3b [21]. C3c localization in glomeruli indicates ongoing immune deposit formation and complement activation [22]. C1q deposition indicates the activation of the classical pathway.

The current study suggested that patients with C3c deposition had more severe renal lesions than those without C3c deposition. In laboratory tests, patients with C3c deposition had higher levels of urinary protein and poorer initial renal function than those without. In renal histopathology, patients with C3c deposition had higher percentage of crescent formation and more severe interstitial infiltrate and tubular atrophy than those without, though the total AI or CI were not significantly different. Since C3c localization in glomeruli indicates ongoing complement activation, it might also suggest ongoing glomerular inflammation and thus contribute to severe renal lesions. It was hypothesized that complement activation amplified neutrophil influx, neutrophil activation and vessel damage, resulting in the aggressive necrotizing inflammation of ANCA-associated vasculitis [1].

The proportion of patients with C1q deposition was relatively low. Interestingly, however, all the seven patients with C1q deposition were MPO–ANCA positive and these C1q depositions were not related to the presence of immune complexes. It indicated that the classical pathway of complement activation might also occur, at least in some patients with MPO–ANCA-associated pauci-immune glomerulonephritis. Activation of the classical pathway is initiated by immune complex. However, there was little immune complex in these renal specimens of human ASV. In experimental animal models, immune complex deposition could be detected in renal vasculature at the early stage of ANCA-associated glomerulonephritis. After the inflammatory reaction was initiated, complements as well as immune
complex were degraded rapidly by some enzymes released from polymorphonuclear leukocytes [23–25]. These findings might explain the lack of immune complex in these patients. Whether the classical pathway activation of complement system plays a role in human ANCA-associated glomerulonephritis needs further investigation.

Previous studies have found that IgM and/or C3 could be commonly found in sclerotic lesion [26,27]. In the current study, the relatively low proportion of IgM and C3 deposition might result from the low proportion of sclerotic lesion in our patients.

Although a number of renal biopsy specimens in the current study had glomerular complement deposition, whether complements are trapped or de novo produced in kidneys is not yet clear.

In conclusion, complement deposition was not rare in renal histopathology of human ANCA-associated pauci-immune glomerulonephritis, which was associated with more severe renal injury. The role of complement played in human AAV needs further investigation.

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Conflict of interest statement. None declared.

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