Incidence and clinical significance of anti-moesin autoantibodies in small-vessel vasculitis

Junya Murano,1,2 Kouju Kamata,1 Shokichi Naito,1 Tomoko Okamoto,1 Mariko Kamata,1,2 Chikako Okina,1 Takashi Sano,1 Yasuo Takeuchi,1 Togo Aoyama1

1 Department of Nephrology, Kitasato University School of Medicine
2 Department of Internal Medicine, Kitasato University Graduate School of Medical Sciences

Background: Newly discovered anti-moesin autoantibodies may damage vascular endothelial cells resulting in vasculitis. We, therefore, investigated the incidence and clinical significance of anti-moesin autoantibodies in patients with small-vessel vasculitis.

Methods: Serum samples were obtained from patients undergoing initial kidney biopsy for the diagnosis and treatment of vasculitis. Serum anti-moesin autoantibodies were semi-quantitatively analyzed by western blotting using an antigen purified recombinant human moesin protein generated in Escherichia coli BL21.

Results: Anti-moesin autoantibodies were present in the sera of 44% (15/34) of patients with microscopic polyangiitis (MPA), 63% (5/8) of patients with anti-glomerular basement membrane (GBM) disease, 15% (2/13) of patients with IgA vasculitis, and 43% (3/7) of patients with lupus nephritis, but were not detected in any of the 4 patients with granulomatosis with polyangiitis. The incident rate was significantly higher in patients with MPA (P < 0.02) and anti-GBM disease (P < 0.008) than in healthy volunteers. Assessment of all 34 patients with MPA showed that the Birmingham Vasculitis Activity Score (BVAS) was significantly higher (P < 0.02) in patients with than in those without the anti-moesin autoantibodies. The BVAS was also significantly higher in MPA patients with both anti-moesin autoantibodies and myeloperoxidase (MPO)-antineutrophil cytoplasmic antibodies (ANCAs) than in those with MPO-ANCAs alone (P < 0.01). The estimated glomerular filtration rate was significantly lower in MPA patients with both anti-moesin autoantibodies and MPO-ANCAs than in patients with MPO-ANCAs only (P < 0.02).

Conclusions: Anti-moesin autoantibodies showed a high incidence in MPA and anti-GBM disease. The presence of both anti-moesin antibodies and MPO-ANCAs was associated with increased vasculitis activity and a deteriorated kidney function in MPA patients.

Key words: anti-moesin autoantibody, ANCA-associated vasculitis, microscopic polyangiitis, anti-GBM disease, small vessel vasculitis

Introduction

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is characterized by necrotizing vasculitis affecting small vessels and by crescentic glomerulonephritis with myeloperoxidase (MPO)-ANCA or proteinase-3 (PR3)-ANCA. Anti-moesin autoantibody was initially discovered in an experimental model of spontaneous crescentic glomerulonephritis-forming mice/Kinjoh (SCG/Kj), regarded as an animal model of human AAV. Anti-moesin autoantibodies have also been detected in the sera of patients with MPO-AAV and may be a novel biomarker for AAV.

The cell cortex containing the ERM family proteins (ezrin, radixin, and moesin), plays an essential role in a signaling pathway between transmembrane receptors and intracellular signaling components and in interactions between the plasma membrane and the actin cytoskeleton. Moesin proteins have been detected on the surface of human T cells, B cells, NK cells, and monocytes, as well as on human neutrophils in areas of...
inflammation. Anti-moesin antibodies derived from the sera of patients with aplastic anemia stimulated human peripheral blood mononuclear cells to secrete tumor necrosis factor-alpha (TNF-α) and interferon-gamma (IFN-γ). Increased plasma TNF-α stimulates neutrophils to produce inflammatory cytokines, including interleukins (IL)-1 and -6 and interferons, and to express cell adhesion molecules, including P-selectin glycoprotein ligand-1 (PSGL-1) and L-selectin, on the cell surface. Activated neutrophils adhere to vascular endothelial cells through the binding of PSGL-1 with P-selectin. Human umbilical vein endothelial cells (HUVEC) also express intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1), as well as moesin and ezrin, on the apical surfaces of cells under inflammatory conditions, resulting in activated neutrophils firmly adhering to and showing transendothelial migration on vascular walls. Although activated monocytes, IL-2-activated lymphocytes, IL-1β, IFN-γ, and TNF-α directly injure HUVECs, TNF-α-induced neutrophil-mediated cytotoxicity of human vascular endothelial cells is considered a major inducer of anti-moesin autoantibody-mediated vascular endothelial cell damage and of the development of vasculitis. Alternatively, anti-MPO autoantibodies have also been shown to stimulate human neutrophils to damage HUVECs, and a transfer of maternal MPO-ANCA results in microscopic polyangiitis (MPA) with pulmonary hemorrhage and renal involvement in human neonates. These findings indicate that both human MPO-ANCA and anti-moesin autoantibody may be significant in the onset and development of MPA and AAV. This study, therefore, investigated the incidence and clinical significance of anti-moesin autoantibodies in patients with small vessel vasculitides.

**Subjects and Methods**

**Patients**

This study enrolled patients aged ≥18 years who underwent initial kidney biopsy for the diagnosis and treatment of kidney disease at the Department of Nephrology, Kitasato University Hospital, from 2002 to 2013. Non-selective, consecutive cases were included in this study. Their medical records were reviewed retrospectively. Factors analyzed included patient age, gender, serum creatinine level, estimated glomerular filtration ratio (eGFR), urinary protein excretion, serum albumin level, MPO-ANCA level by enzyme-linked immunosorbent assay (ELISA) (normal value <10 EU) and Birmingham vasculitis activity score (BVAS) at the time of kidney biopsy. Healthy volunteers aged ≥18 years with a normal body mass index, normal blood pressure, normal urinalysis, and an eGFR ≥90 ml/min were enrolled as control subjects. The study protocol was approved by the Ethical Review Committee for Clinical Study of Kitasato University School of Medicine (B14-39).

**Blood sample collection**

Sera were obtained at the time of the first kidney biopsy, just before the initial treatment, and stored at -80°C until assayed. All subjects provided written informed consent to donate blood for this clinical study.

**Glutathione-S-transferase (GST)-tagged human moesin protein expression and purification**

A cDNA (NM_002444.2) encoding full-length human moesin protein was synthesized and purified by TaKaRa Custom Services (Otsu) and inserted into a modified pGEX-6P-1 vector (GE Healthcare, Little Chalfont, Buckinghamshire, UK). This expression vector, encoding glutathione-S-transferase (GST)-tagged human moesin cDNA, was transfected into *Escherichia coli* (E. coli) BL21(D3)pLysS competent cells (Promega, Madison, WI, USA) using a heat-shock method. The cells were cultured overnight in 20 ml of Lysogeny broth (LB) medium at 37°C with vigorous shaking. Liquid cultures were added to 180 ml of LB medium and grown at 37°C with vigorous shaking to an optical density at 600 nm of 0.6. Fusion protein expression was induced by the addition of 1 μl of 100 mM isopropyl-β-d-thiogalactopyranoside per ml culture volume (final concentration =1.0 mM), followed by an additional incubation for 3 hours at 37°C. The cells were pelleted at 1,500 × g for 20 minutes at 4°C and resuspended in 10 ml sonication buffer, consisting of phosphate buffered saline (PBS) containing 1% Triton X-100. After washing 3 times, the samples were sonicated on ice and centrifuged at 20,000 × g for 30 minutes at 4°C. Most of the GST fusion proteins were contained in the cell pellets. These proteins were purified under denaturing conditions with phosphate buffer containing 8 M urea and allowed to refold by removing the urea by dialysis. The proteins were batch purified using prepacked Glutathione-Sepharose 4B (GE Healthcare Bio-Sciences AB, Uppsala, Sweden). Briefly, proteins were added to 100 μl of a 50% slurry of Glutathione-Sepharose 4B equilibrated with PBS and incubated with gentle agitation at 4°C for 90 minutes. The mixture was centrifuged, and the beads were washed 3 times with 1 ml ice-cold PBS containing 0.5% Triton X-100 and once with 1 ml sonication buffer.
containing 50 mM Tris-HCl (pH 8.0), 50 mM NaCl, 1 mM EDTA (ethylenediaminetetraacetic acid), and 1 mM dithiothreitol. The proteins bound to the beads were eluted by incubation in 100 μl of 16 mM glutathione elution buffer at 4°C for 10 minutes, followed by centrifugation at 1,500 × g for 20 seconds at 4°C. This GST-tagged recombinant human moesin protein without N-glycosylation was used as the antigen-detecting anti-moesin autoantibody in western blot analyses.

Sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and western blot analyses
Eight nanograms of GST-tagged recombinant human moesin protein were applied to each lane of a 5% SDS-gradient gel under reducing conditions. After electrophoresis, the proteins were transferred to polyvinylidene difluoride membranes. The membranes were blocked by incubation in 20 mM Tris-buffered saline containing 0.1% Tween 20 (TBS-T) and 2% Amersham ECL Prime Blocking Agent (GE Healthcare), followed by incubation with 1 ml of 1.25 μg polyclonal goat anti-GST IgG (GE Healthcare), diluted 1:2,000, for 1 hour at room temperature. After washing, the membrane was incubated with 1 ml of 0.375 μg horseradish peroxidase (HRP)-conjugated rabbit anti-human IgG (H+L) (Zymed, South San Francisco, CA, USA), diluted 1:4,000, overnight at 4°C. Proteins were visualized with Amersham-enhanced-chemiluminescent reagent (ECL, GE Healthcare, Buckinghamshire, UK).

Semi-quantitative analysis for anti-moesin antibodies
The staining levels of this band were semi-quantitatively evaluated as negative (-), weakly positive (1+), moderately positive (2+), and strongly positive (3+), with 1+, 2+, and 3+ defined as positive for anti-moesin antibodies. Serum titers of the anti-moesin antibodies were evaluated by visual assessment with staining standards of (-), (1+), (2+), and (3+).

Statistical analysis
Statistical comparisons were made using Mann-Whitney U tests, chi-square tests, and G-tests. Data were expressed as mean ± 1 SD. P values of <0.05 were considered statistically significant.

Results
Patients enrolled in this study
This study enrolled 12 normal volunteers and 66 patients, including 34 with MPA, 4 with granulomatosis with polyangiitis (GPA, formerly Wegener's granulomatosis), 7 with lupus nephritis and diffuse proliferative glomerulonephritis (class IV), 13 with IgA vasculitis and 7 with lupus nephritis and diffuse proliferative glomerulonephritis (class IV), 13 with IgA vasculitis.

Table 1. Data were expressed as mean ± SD.

<table>
<thead>
<tr>
<th>Diagnosed disease</th>
<th>Number of patients</th>
<th>Age (Years)</th>
<th>Gender (M : F)</th>
<th>Urinary protein excretion (g/day)</th>
<th>Serum albumin (g/dl)</th>
<th>Serum creatinine (mg/dl)</th>
<th>eGFR (ml/min./1.73m²)</th>
<th>MPO-ANCA (EU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microscopic polyangiitis (MPA)</td>
<td>34</td>
<td>66 ± 14</td>
<td>13 : 21</td>
<td>1.0 ± 1.3</td>
<td>3.2 ± 0.7</td>
<td>3.6 ± 4.3</td>
<td>28 ± 29</td>
<td>240 ± 376</td>
</tr>
<tr>
<td>MPA with MPO-ANCA</td>
<td>28</td>
<td>65 ± 15</td>
<td>10 : 18</td>
<td>1.1 ± 1.3</td>
<td>3.2 ± 0.7</td>
<td>2.7 ± 1.7</td>
<td>29 ± 29</td>
<td>292 ± 397</td>
</tr>
<tr>
<td>MPA without MPO-ANCA</td>
<td>6</td>
<td>69 ± 9.3</td>
<td>3 : 3</td>
<td>1.9 ± 1.4</td>
<td>3.0 ± 0.5</td>
<td>7.8 ± 8.9</td>
<td>19 ± 26</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>Granulomatosis with polyangiitis (Wegener's')</td>
<td>4</td>
<td>51 ± 25</td>
<td>2 : 2</td>
<td>0.9 ± 0.6</td>
<td>3.5 ± 1.1</td>
<td>1.2 ± 1.4</td>
<td>88 ± 48</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>IgA vasculitis (Henoch-Schönlein purpura nephritis)</td>
<td>13</td>
<td>48 ± 21</td>
<td>7 : 6</td>
<td>4.3 ± 6.5</td>
<td>3.8 ± 0.7</td>
<td>0.9 ± 0.3</td>
<td>74 ± 33</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>Lupus nephritis</td>
<td>7</td>
<td>39 ± 16</td>
<td>2 : 5</td>
<td>2.4 ± 3.1</td>
<td>2.5 ± 0.5</td>
<td>0.9 ± 0.3</td>
<td>66 ± 22</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>Anti-GBM disease</td>
<td>8</td>
<td>58 ± 20</td>
<td>4 : 4</td>
<td>0.6 ± 0.8</td>
<td>3.4 ± 0.6</td>
<td>6.0 ± 4.7</td>
<td>20 ± 20</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>Total</td>
<td>66</td>
<td>58 ± 19</td>
<td>28 : 38</td>
<td>1.8 ± 3.4</td>
<td>3.3 ± 0.7</td>
<td>2.9 ± 3.8</td>
<td>44 ± 37</td>
<td>124 ± 294</td>
</tr>
</tbody>
</table>

Serum creatinine levels in anti-GBM disease ranged from 0.91 to 12.5 mg/dl, and eGFR levels from 3.7 to 51.7 ml/min/1.73m². Mean creatinine concentration and mean eGFR in anti-GBM disease were calculated as shown in the Table.
(formerly Henoch-Schönlein purpura nephritis), and 8 with anti-glomerular basement membrane (GBM) disease. Their clinical characteristics are shown in Table 1. MPA patients were of mean age 66 ± 14 years, with a mean eGFR of <30 ml/minutes, proteinuria range of 1.1 – 1.9 g/day, and mean serum albumin level >3.0 g/dl. Patients with GPA had a mean eGFR of 88 ± 48 ml/minutes and moderate proteinuria of 0.9 ± 0.6 g/day. Patients with IgA vasculitis had a high level of proteinuria, 4.3 ± 6.5 g/day, and a mean eGFR of 74 ± 33 ml/minutes. Patients with lupus nephritis had a moderate level of proteinuria, 2.4 ± 3.1 g/day, and a nephrotic range of serum albumin, 2.5 ± 0.5 g/dl. Patients with anti-GBM disease showed the lowest kidney function, with an eGFR of 20 ± 20 ml/minutes, and the lowest level of proteinuria, of 0.6 ± 0.8 g/day. The 12 normal volunteers consisted of 9 males and 3 females, of mean age 36 ± 13 years.

**Incidence of MPO-ANCAs in patients with small vessel vasculitis**

MPO-ANCAs were tested in all patients enrolled in this study. Although 28 (82%) of the 34 patients with MPA were positive for MPO-ANCAs, none of the patients with GPA, IgA vasculitis, lupus nephritis, or anti-GBM disease was positive for MPO-ANCAs. Mean levels of MPO-ANCAs in all MPA patients and those with MPO-ANCAs were 240 ± 376 and 292 ± 397 EU, respectively. Of 19 MPA patients without anti-moesin autoantibodies, 15 (79%) were positive and 4 (21%) were negative for MPO-ANCAs. Of the 15 patients with anti-moesin autoantibodies, 13 (87%) were positive and 2 (13%) were negative for MPO-ANCAs (Table 1, Figure 3A, C).

**Detection and evaluation of serum anti-moesin autoantibodies**

The GST-tagged moesin protein yield was 2 μg per 200 ml of *E. coli* BL21 (D3) pLysS competent cell culture. Eight nanograms of *E. coli*-produced recombinant human moesin protein with a GST tag were applied to lanes 1 – 6 in Figure 1. Proteins reacting with the anti-GST antibodies are shown in lane 1, and proteins reacting with anti-human moesin antibodies are shown in lane 2; the 92-kD band in the latter was considered recombinant human moesin. The observed molecular weight difference of 2.5-kD between the observed and the expected sizes was deemed acceptable and is likely to reflect small differences in the shape of the synthetic moesin protein and standard marker proteins. This band was negative (-) in lane 3, weakly positive (1+) in lane 4, moderately positive (2+) in lane 5, and strongly positive (3+) in lane 6. Serum titers of the anti-moesin antibodies were based on the degree of staining in lanes 3 – 6. The sera from all 12 normal volunteers aged 24 – 64 years were negative for anti-moesin autoantibodies.

**Incidence of anti-moesin autoantibodies in patients with small-vessel vasculitides**

Anti-moesin autoantibodies were present in the sera of 44% (15/34) of patients with MPA, 46% (13/28) of patients with MPA and MPO-ANCAs, and 33% (2/6) of patients with MPA without MPO-ANCAs (Figure 2), with no significant differences among these 3 groups by the G-test. Anti-moesin autoantibodies were present in 63% (5/8) of the patients with anti-GBM disease, 15% (2/13) of the patients with IgA vasculitis, and 43% (3/7) of the patients with lupus nephritis.
of the patients with lupus nephritis but was not detected in any of the 4 patients with GPA (Figure 2).

The incidence of anti-moesin autoantibodies was significantly higher in patients with MPA (P < 0.02) and anti-GBM disease (P < 0.008) than in normal volunteers but did not differ in normal volunteers and patients with IgA vasculitis (P = 0.50), lupus nephritis (P = 0.07), or GPA.

Of the 15 MPA patients positive for anti-moesin antibodies, 9 (60%) were weakly positive, 4 (27%) were moderately positive, and 2 (13%) were strongly positive (Table 2). These antibodies were moderate to strongly positive in 3 of 7 patients with lupus nephritis and in 2 of 13 with IgA vasculitis but were present at various levels in 5 of 8 patients with anti-GBM disease (Table 2).

Figure 2. Incident rates of anti-moesin autoantibody in patients with small-vessel vasculitis MPA, microscopic polyangiitis; ANCA, myeloperoxidase (MPO)-anti-neutrophil cytoplasmic antibody; GPA, granulomatosis with polyangiitis. Parentheses show the number of patients investigated. Incident rates of anti-moesin autoantibody in all 34 MPA patients (P < 0.02) and anti-GBM disease (P < 0.008) were significantly higher than in normal volunteers.

Table 2. Numbers of patients in each diagnostic subgroup with and without anti-moesin autoantibody

<table>
<thead>
<tr>
<th>Diagnosed disease</th>
<th>Numbers of patients</th>
<th>Patients with and without anti-moesin autoantibody</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(-) (++) (+) (+++)</td>
</tr>
<tr>
<td>Microscopic polyangiitis (MPA)</td>
<td>34</td>
<td>19 9 4 2</td>
</tr>
<tr>
<td>MPA with MPO-ANCA</td>
<td>28</td>
<td>15 7 4 2</td>
</tr>
<tr>
<td>MPA without MPO-ANCA</td>
<td>6</td>
<td>4 2 0 0</td>
</tr>
<tr>
<td>Granulomatosis with polyangiitis</td>
<td>4</td>
<td>4 0 0 0</td>
</tr>
<tr>
<td>(Wegener’s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgA vasculitis (Henoch-Schönlein purpura nephritis)</td>
<td>13</td>
<td>11 0 1 1</td>
</tr>
<tr>
<td>Lupus nephritis</td>
<td>7</td>
<td>4 0 1 2</td>
</tr>
<tr>
<td>Anti-GBM disease</td>
<td>8</td>
<td>3 2 2 1</td>
</tr>
</tbody>
</table>
Figure 3. Birmingham vasculitis activity score (BVAS) and estimated glomerular filtration rate (eGFR) in patients with microscopic polyangiitis (MPA). Assessment of all 34 MPA patients showed that (A) BVAS was significantly higher ($P < 0.02$) in patients with than in those without the anti-moesin antibody. Evaluation of the 28 MPA patients with MPO-ANCA showed that (B) BVAS was significantly higher ($P < 0.01$) in patients with than in those without the anti-moesin antibody. In all 34 MPA patients, (C) eGFR did not differ ($P < 0.20$) between the patients with and those without the anti-moesin antibody. In 28 MPA patients with MPO-ANCA, (D) eGFR was significantly lower ($P < 0.02$) in patients with than in those without the anti-moesin antibody.
**Effect of anti-moesin autoantibodies on the Birmingham Vasculitis Activity Score (BVAS) in MPA patients at diagnosis**

The mean Birmingham Vasculitis Activity Score (BVAS) in all 34 MPA patients with and in those without MPO-ANCAs was 16.1 ± 4.9 but was significantly higher in patients with than in those without anti-moesin autoantibodies (18.3 ± 5.8 vs. 14.4 ± 3.2, P < 0.02). There was no significant difference in rates of MPO-ANCAs between 15 MPA patients with anti-moesin antibodies and 19 without (Figure 3A). Assessment of the 28 MPA patients with MPO-ANCAs showed that mean BVAS was also significantly higher in the 13 patients with than in the 15 patients without anti-moesin autoantibodies (18.5 ± 4.1 vs. 14.3 ± 2.6, P < 0.01) (Figure 3B).

**Effect of anti-moesin autoantibodies on eGFR in MPA patients at diagnosis**

Evaluation of all 34 MPA patients with and those without MPO-ANCAs showed that mean eGFR was similar in patients with and in those without anti-moesin autoantibodies (23.8 ± 26.7 vs. 30.5 ± 30.3 ml/minutes, P < 0.20), with similar rates of MPO-ANCAs observed in the 15 MPA patients with anti-moesin antibodies and the 19 patients without anti-moesin antibodies (Figure 3C). Analysis of the 28 MPA patients with MPO-ANCAs showed that eGFR was significantly lower in the 13 MPA patients with than in the 15 patients without anti-moesin autoantibodies (21.6 ± 24.7 vs. 35.9 ± 31.9 ml/minutes, P < 0.02) (Figure 3D).

**eGFR and serum anti-moesin autoantibodies in other small vessel vasculitides**

Mean eGFR was similar in the 3 lupus nephritis patients with and the 4 without anti-moesin autoantibodies (68 ± 30 vs. 65 ± 18 ml/minutes). Mean eGFR also did not differ significantly in the 5 anti-GBM disease patients with and the 3 patients without anti-moesin autoantibodies (27.3 ± 22.6 vs. 7.4 ± 3.3 ml/minutes, P = 0.39), or in the 2 IgA vasculitis patients with and the 11 patients without anti-moesin autoantibodies (61 ± 15.3 vs. 76.3 ± 35.1 ml/minutes, P > 0.2).

**Discussion**

This study revealed that the incidence of anti-moesin autoantibodies in patients with small-vessel vasculitis was 44% in patients with MPA, 63% in those with anti-GBM disease, 43% in patients with lupus nephritis, and 15% in patients with IgA vasculitis, but was absent from patients with GPA. Compared with normal volunteers, the incidences of the anti-moesin antibodies were significantly higher only in patients with MPA (P < 0.02) and anti-GBM disease P < 0.008). In patients with lupus nephritis, the 43% incidence was close to that seen in MPA patients, yet no significant difference was observed in comparison with normal volunteers. This result was most likely because of the small sample size. This is also the most likely reason for the 15% incidence in patients with IgA vasculitis showing no significant difference compared with controls. Therefore, a comparison of the significance in incidence of anti-moesin antibodies in patients with lupus nephritis and IgA vasculitis should be evaluated in a larger number of individuals.

Anti-moesin autoantibodies were first identified in the sera of 32 (53%) of 60 MPO-AAV patients during treatment (n = 16), the quiescent phase (n = 41), and the relapsed phase (n = 3). In comparison, the present study found that anti-moesin autoantibodies were present in 44% of the patients with MPA at the initial diagnosis and just before treatment. Taken together, these findings suggest that anti-moesin autoantibodies may also arise after treatment. ELISAs showed that 31 of 32 (97%) patients with both MPO-AAV and anti-moesin autoantibodies had anti-moesin autoantibody titers <170 units/ml. Since the normal concentration of anti-moesin autoantibodies in healthy controls was found to be ≤51.4 units/ml, the anti-moesin autoantibody titers in 97% of patients with MPO-AAV were less than 3.3-fold higher than the upper limit of the normal range. The present study revealed that 9 (60%) of 15 patients had weakly positive titers of anti-moesin autoantibodies, suggesting that most patients with MPA or MPO-AAV have low titers of anti-moesin autoantibodies.

Patients with MPA have acute progressive systemic vasculitis and rapidly progressive glomerulonephritis syndrome at the onset of disease. We found that the BVAS was significantly higher in MPA patients with than in those without anti-moesin autoantibodies (P < 0.02), as well as being significantly higher in patients with MPA and MPO-ANCA than in those patients without anti-moesin autoantibodies (P < 0.01). These results suggest that the anti-moesin autoantibodies accompanied by MPO-ANCAs may increase vasculitis activity in MPA. Patients with MPA also had low kidney function, with eGFR <30 ml/minutes at the time of diagnosis. In MPA patients with MPO-ANCAs, eGFR was significantly lower in patients with than in those without anti-moesin autoantibodies. However, eGFR did not differ significantly in total MPA patients with or those without the anti-moesin autoantibodies, most likely because of
the high positive rate of MPO-ANCA in each subgroup. These results suggest that anti-moesin antibodies accompanied by MPO-ANCAs may also contribute to further deterioration of kidney function.

The presence of serum anti-MPO antibodies has been found to severely aggravate anti-GBM disease in a rat experimental model. In this study, 63% of the patients with anti-GBM disease had anti-moesin autoantibodies instead of MPO-ANCAs, with the highest serum creatinine level of 6.0 mg/dl. Anti-moesin autoantibodies could stimulate mononuclear cells to secrete TNF-α, resulting in neutrophil activation. These neutrophils may secrete inflammatory cytokines and express cell adhesion molecules on their surfaces, which may damage vascular endothelial cells. Therefore, the anti-moesin autoantibody may have a role in clinical presentation or disease progression of anti-GBM disease. Further investigation is required to evaluate the clinical significance of the anti-moesin autoantibody in anti-GBM disease.

In conclusion, we have shown a high incidence of anti-moesin autoantibodies in patients with MPA and in anti-GBM disease. The anti-moesin autoantibodies accompanied by MPO-ANCAs increased vasculitis activity and deteriorated kidney function in MPA patients.

Acknowledgments

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References


