Clinical features in two patients with IgA glomerulonephritis and thin-basement-membrane disease

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Abstract

Background. Both IgA glomerulonephritis (IgA gn) and thin basement membrane disease (TBMD) are common forms of glomerulonephritis. Patients with these conditions may present with identical clinical features, but higher urinary RBC counts, heavier proteinuria, and impaired renal function are more common in patients with IgA gn. Because IgA gn and TBMD are common, some patients will have both diseases.

Subjects. We describe the clinical features of two individuals with both IgA gn and TBMD, and compare them with the clinical and laboratory characteristics in patients with TBMD (n = 15) or IgA gn (n = 32) alone.

Results. IgA gn was found in two individuals of the 110 with TBMD who were studied. They both had haematuria with >100,000 RBC/ml and proteinuria >0.2/day (one had more than 1 g/day). These features were more consistent with IgA gn than TBMD alone. However, both individuals had normal serum creatinine and creatinine clearance at presentation. Additional clinical features were macroscopic haematuria in one and hypertension in both.

Conclusions. IgA deposits are not uncommon in patients with TBMD, and these patients have clinical features that resemble those seen in IgA gn rather than TBMD. Patients with both IgA gn and TBMD do not necessarily have the worse prognosis noted in some patients with IgA gn.

Key words: IgA glomerulonephritis; thin-basement-membrane disease

Introduction

Thin-basement-membrane disease (TBMD) is a common form of glomerulonephritis occurring in up to 10% of the population [1]. Other family members are affected in about 30% of cases [2], and the inheritance then follows an autosomal dominant pattern [3,4]. TBMD is characterized by diffuse thinning of the glomerular basement membrane (GBM) on ultrastructural examination of renal biopsies [2,5,6]. Localized areas of thinning of the GBM are found in some conditions other than TBMD. There can be areas of localized or generalized thinning in IgA gn [7], early Alport syndrome [8], minimal-change and focal sclerosing glomerulonephritis, as well as in some forms of SLE [9]. These conditions can be excluded by the light-microscope and immunofluorescence findings. In patients with TBMD, persistent microscopic haematuria is the most common clinical feature, but macroscopic haematuria, proteinuria, and hypertension may occur; patients rarely, however, progress to renal failure [2,5,10,11].

IgA glomerulonephritis (IgA gn) is another common form of kidney disease [12,13], with an incidence approximating that of TBMD in patients presenting with persistent haematuria. We have shown recently that patients with IgA gn are more likely to have higher urinary RBC/ml, heavier proteinuria, and impaired renal function at presentation than patients with TBMD alone. We did not find that a family history of renal disease, macroscopic haematuria, or hypertension discriminated between patients with IgA gn and TBMD [unpublished findings]. However, macroscopic haematuria associated with infections, urinary RBC casts, and the presence of glomerular crescents on renal biopsy are probably more suggestive of IgA gn than TBMD.

Double glomerulopaties are not uncommon [14,15], and some individuals can have both TBMD and IgA gn [16–18]. The aim of this study was to determine how often TBMD and IgA gn occurred together, and whether these patients had any distinctive clinical or prognostic features.

Patients

Biopsy results from the years 1985 to 1993 were reviewed. The diagnosis of TBMD was made on the basis of consistent...
thinning of the GBM on grid analysis measurement of renal biopsy specimens examined ultrastructurally. All patients with TBMD had a GBM width less than 250 nm. The diagnosis of IgA gn was made when there was mesangial cell proliferation and matrix expansion on light microscopy, together with mesangial deposits of IgA on immunofluorescent examination of renal biopsy material. In the patients with IgA gn there was no history suggesting Henoch–Schönlein purpura, alcoholic liver disease, or coeliac disease.

The diagnosis of TBMD was made in 110 biopsies, and in two of these there were features of IgA gn as well (2%). We have compared the clinical and histological features of these two patients, with the clinical and histological features seen in 15 patients with TBMD or 32 patients with IgA gn alone.

In the 17 patients with TBMD, there was no family history of Alport syndrome or inherited deafness and the light-microscopy was normal or with only a slight increase in the number of mesangial cells or matrix.

**Patient 1**

A 50-year-old male was referred for investigation of macroscopic haematuria and loin pain, which had occurred intermittently for 10 years. On examination he was hypertensive with a BP of 160/90, with arteriovenous nipping only on fundoscopy. He had mild psoriasis. ESR was 60 mm/h. He had more than 100 000 RBC/ml in his urine and 500 mg/24 h of proteinuria. Creatinine clearance was 1.89 ml/s. Urine cytology was unremarkable. Serum protein electrophoresis revealed a raised IgA at 4.49 g/l. IVP, cystoscopy, and renal angiography were all normal.

The renal biopsy showed essentially a normal appearance on light microscopy, but mesangial IgA deposits and small amounts of IgM and C1q were demonstrated by immunofluorescence. On ultrastructural examination the GBM was uniformly and diffusely thinned and the presence of the mesangial deposits was confirmed.

The macroscopic haematuria resolved and the patient’s BP was controlled with enalapril. At review over the next 3 years, there was persistence of the haematuria at low levels. A repeat creatinine clearance at the most recent visit 1 year after presentation was 2.3 ml/min with an ESR of 17.

**Patient 2**

A 47-year-old Greek Australian female was found to be hypertensive on routine physical examination (BP 160/90 mmHg), but the rest of the physical examination was normal. She had a family history of hypertension.

Her urinary sediment contained more than 100 000 RBC/ml and occasional red cell casts, but the patient had never had an episode of macroscopic haematuria. She had 1.57 g of protein/24 h and a creatinine clearance of 1.6 ml/s. Her ESR was 60; ANA and anti-dsDNA antibody tests were negative. Renal ultrasound and IVP were normal.

The light-microscope appearance of the renal biopsy was again essentially normal, but there were IgA deposits on immunofluorescence examination and a uniformly thinned GBM on ultrastructural examination.

Over the following weeks the patient’s BP was readily controlled with atenolol 50 mg daily, but she subsequently failed to return for review.

A comparison of the clinical details of these two patients and clinical features seen in individuals with TBMD or IgA gn alone are shown in Table 1. Neither patient with both TBMD and IgA gn had a family history of TBMD or IgA gn. Both patients were distinguished from the patients with TBMD alone by their degree of haematuria and the presence of proteinuria. These features were more in common with the patients with IgA gn. However hypertension was present in both patients but serum creatinine and creatinine clearance were normal in both.

**Discussion**

We found two patients with both IgA gn and TBMD when the renal biopsies of 110 (2%) individuals with

<table>
<thead>
<tr>
<th>Presentation</th>
<th>IgA plus TBMD (n=2)</th>
<th>TBMD (n=15)</th>
<th>IgA gn (n=32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>1M, 1F</td>
<td>15F</td>
<td>10M, 22F</td>
</tr>
<tr>
<td>Age (years)</td>
<td>47, 50</td>
<td>44 (30–63)</td>
<td>31 (25–61)</td>
</tr>
<tr>
<td>Width of GBM (nm)</td>
<td>240, 230</td>
<td>&lt;250</td>
<td>&gt;250</td>
</tr>
<tr>
<td>Family history</td>
<td>0/2</td>
<td>2/15 (13%)</td>
<td>3/32 (9.4%)</td>
</tr>
<tr>
<td>Macrohaematuria</td>
<td>1/2</td>
<td>2/15 (13%)</td>
<td>10/32 (31%)</td>
</tr>
<tr>
<td>Haematuria (&gt;100 000 RBC/ml)</td>
<td>2/2 (100%)</td>
<td>5/15 (30%)</td>
<td>22/32 (69%)</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>&gt;0.2 g/day</td>
<td>2/2 (100%)</td>
<td>9/15 (60%)</td>
</tr>
<tr>
<td></td>
<td>&gt;1 g/day</td>
<td>1/2 (50%)</td>
<td>2/15 (13%)</td>
</tr>
<tr>
<td>Hypertension (BP &gt;140/90 mmHg)</td>
<td>2/2 (100%)</td>
<td>3/15 (20%)</td>
<td>10/32 (31%)</td>
</tr>
<tr>
<td>S creatinine ≥0.11 mmol/l</td>
<td>0.2 (10%)</td>
<td>0.15 (0%)</td>
<td>7.32 (22%)</td>
</tr>
<tr>
<td>Cr clearance ≤1.2 ml/min</td>
<td>0/2 (0%)</td>
<td>2/15 (13%)</td>
<td>4/14 (29%)</td>
</tr>
</tbody>
</table>
TBMD were reviewed. This incidence is lower than the 13/67 (19%) patients with IgA gn and TBMD reported elsewhere [18]. A diffusely thinned GBM should be demonstrated before the diagnosis of TBMD is made.

Focally thinned GBM may be found incidentally in IgA gn as well as in a number of other conditions. In the other report, ‘focal or diffuse’ thinning of the GBM was present in 14% of 90 patients with IgA gn [17,18], and the number of patients with diffusely thinned membranes consistent with TBMD was not indicated. We did not include in our series patients with focal thinning of the GBM.

While our initial search showed more than two patients with mesangial deposits, these were not confirmed when the corresponding electron-micrographs were examined. It is not clear if the presence of mesangial IgA deposits were confirmed ultrastructurally in other series, and this precludes an accurate estimate of IgA gn and TBMD occurring together from being determined from these reports. If IgA gn and TBMD were found together as often as suggested elsewhere [18], it is remarkable that there have not been more case reports of patients with both conditions.

We have shown in our study that patients with both IgA gn and TBMD may have higher counts of urinary RBC/ml, more marked proteinuria, and a higher BP than those with TBMD alone. The higher urinary RBC excretion and heavier proteinuria in patients with both diseases are more consistent with IgA gn. However the serum creatinine and creatinine clearance in each patient were normal suggesting that renal function is not necessarily worse in individuals with both TBMD and IgA gn. This conclusion is borne out by the description elsewhere [16] of a woman with both TBMD and IgA gn who had persistent microscopic haematuria, infection-associated macroscopic haematuria, proteinuria of 0.4 g/day and hypertension, but a normal serum creatinine. However, another series with a high incidence of IgA gn and TBMD occurring together [18] has suggested that such individuals often have severe disease. Thus patients with both IgA gn and TBMD were more likely to have nephrotic-range proteinuria (58%, compared with 11% in patients with TBMD alone), hypertension (55% vs 33%), renal insufficiency (54% vs 9%), and progressive renal impairment on follow-up (36% vs 11%).

Other forms of glomerulonephritis may occur more often in patients with TBMD than in normal individuals because of a damaged or more permeable basement membrane, or simply because these two forms of glomerulonephritis are common conditions. Our patients with both IgA gn and TBMD had clinical features more suggestive of IgA gn than TBMD, but did not have the impaired renal function found in a subset of patients with IgA gn. It is likely that when IgA gn and TBMD occur together, a spectrum of severity of IgA gn can be found. The outcome in individual patients may be related more to the severity of the histological lesion than to just the presence of mesangial IgA deposits. However the presence of superimposed IgA gn may be responsible for the clinical presentation of these patients.

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References
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