Case Report

Idiopathic Membranous Glomerulonephritis in Patients with Type 2 Diabetes Mellitus

Faissal Tarrass, Abhelkabir Anabi, Mohamed Zamd, Beyounes Ramdani, Mohamed Gharbi Benghanem, Driss Zaid, Saida Sqalli

The occurrence of membranous glomerulonephritis (MGN) in patients with type 2 diabetes mellitus (DM) is a rare event and of pathogenetic interest. We report two males (52 and 64 years old) with type 2 DM and nephrotic syndrome of recent onset. Renal biopsy was performed because of the unusual clinical pictures: microscopic hematuria; heavy proteinuria without evidence of diabetic retinopathy; and, in one case, a sudden onset of renal failure. Renal biopsy disclosed pure MGN without glomerulosclerosis. In both cases, clinical history, physical examination and biologic assessment failed to reveal the cause; MGN was thus considered idiopathic. Treatment, including glycemic control and angiotensin-II receptor blockers, led to resolution of proteinuria in one case. We suggest that renal biopsies should be performed in diabetic patients with a sudden onset of renal failure, proteinuria without retinopathy, or other evidence of microvascular disease. [Hong Kong J Nephrol 2005;7(1):34–7]

Key words: membranous glomerulonephritis, renal biopsy, type 2 diabetes mellitus

INTRODUCTION

Diabetic nephropathy (DN) is the most frequent cause of renal disease in patients with diabetes mellitus (DM). The most common histologic lesions are either diffuse or nodular glomerulosclerosis and hyalinosis of small arterioles [1]. Although less frequent, other types of primary glomerular diseases may affect the kidney and cause proteinuria or renal insufficiency in these patients [1]. Precise diagnosis of these various diseases has obvious prognostic and therapeutic implications [1,2].

We report two patients with type 2 DM who had clinical and laboratory features of nephrotic syndrome. In both cases, histologic examination of renal biopsies disclosed idiopathic membranous glomerulonephritis (MGN).

CASE REPORTS

Case 1
A 52-year-old male was admitted for evaluation of rapidly deteriorating renal function. Five years pre-
viously, he had been diagnosed with type 2 DM and hypertension. There was no known history of diabetic ketoacidosis, retinopathy, or polyneuropathy. On physical examination, the patient’s blood pressure was 160/85 mmHg, heart rate was 76 beats/min, and temperature was 36.8°C. Peripheral edema was present. The lung fields were clear, and the heart and abdomen were normal. Urinalysis showed 4+ protein and 3+ blood; microscopic analysis disclosed 8–10 red blood cells and 3–5 granular casts per high-power field. Laboratory assessments showed normal hematology, electrolytes, and liver function tests. The serum creatinine level was 221.2 μmol/L, creatinine clearance was 30 mL/min, albumin was 27 g/L, fasting blood glucose was 8.85 mmol/L and proteinuria was 8 g/day. Ultrasound examination showed normal renal size without abnormal features. A percutaneous renal biopsy was performed because of the magnitude of proteinuria and the rapidity with which renal function had deteriorated. Microscopic examination of sections from the biopsy material showed diffuse thickening of the glomerular capillary wall with the presence of spikes along the capillary basement membrane (Figure 1). There was no cellular proliferation, mesangial matrix expansion, or arteriolar hyalinosis. Tubules and interstitium were unremarkable.

Immunofluorescence microscopy revealed finely granular deposits positive for immunoglobulin G (IgG) and the complement factors C3 and C1q along the glomerular basement membrane (GBM) of all glomeruli. All laboratory screening for secondary causes was negative or normal, including tests for complement profile, antinuclear antibodies, antineutrophilic cytoplasmic antibodies, hepatitis B virus (HBV) and hepatitis C virus (HCV) serology, human immunodeficiency virus (HIV) serology, and serum immunoglobulins. A chest X-ray and abdominal echography were normal. There was no evidence of occult gastrointestinal bleeding. It was concluded that the patient had idiopathic MGN, and he was given angiotensin-II (AT)-receptor blockers. After a follow-up duration of 4 months, the AT-receptor blockers continued to provide good blood pressure control, and, at his most recent visit 1 month ago, the patient had a serum creatinine level of 265.5 μmol/L, creatinine clearance of 24.5 mL/min, and urinary protein excretion of 2.70 g/day.

Case 2
A 64-year-old male presented for evaluation of microscopic hematuria and proteinuria. There was no known history of type 2 DM, diabetic ketoacidosis or hypertension. Funduscopy was normal. On admission, the patient’s blood pressure was 130/70 mmHg, heart rate was 74 beats/min, and temperature was 37°C. The patient appeared “puffy” and had pretibial edema. Urinalysis showed 3+ protein, and microscopic hematuria with occasional granular and hyaline casts. Laboratory investigations revealed proteinuria (6.5 g/day), with a serum albumin level of 22 g/L, and fasting blood glucose level of 11.8 mmol/L. Serum creatinine was 70.8 μmol/L, and creatinine clearance was 78 mL/min. Hematologic parameters and liver function tests were normal. Renal ultrasound showed normal kidney size without abnormal features. Immunology showed no changes in immunoglobulin levels, and there was no monoclonal band in serum. Complement factors (C3, C4), anti-DNA antibodies and antinuclear antibodies were normal.

As there was an absence of retinopathy and other evidence of microvascular disease, and in light of heavy proteinuria, a needle biopsy of the kidney was performed to delineate the histologic lesion. Eighteen glomeruli and two glomerular scars were examined. All glomeruli showed uniform changes. The GBMs were slightly thickened and, on silver stain, showed discrete spike formation on their outer aspects. There was no mesangial matrix increase or mesangial hypercellularity. Extraglomerular blood vessels showed no pathologic changes. The interstitium was, focally, slightly fibrotic with a few atrophic tubular cross sections in areas of fibrosis. Immunofluorescence microscopy revealed diffuse staining for both IgG and C3 in a granular pattern along the GBM (Figure 2). Serologic tests for HBV, HCV and HIV were negative. Chest X-ray and abdominal echography were unremarkable. There was no evidence of occult gastrointestinal bleeding. No possible causative agents (drugs or toxins) could be identified. The patient received furosemide and AT-receptor blockers. With this regimen, proteinuria decreased continuously, achieving levels of less than 1 g/day after 2 months. At 3 years

Figure 1. Case 1: a glomerulus showing distinct spikes on the outer aspect of the capillary basement membrane (periodic acid-Schiff stain; original magnification × 100).
after admission, the patient’s serum creatinine level was 101.7 μmol/L, creatinine clearance was 56 mL/min, and urinary protein excretion was 0.35 g/day.

**DISCUSSION**

About 10–35% of patients with type 2 DM eventually develop DN over the course of several years; DN then progresses towards end-stage renal disease [1]. Recently, there have been several reports of non-diabetes-related, sometimes treatable, renal diseases in patients with type 2 DM [1–3]. Biopsy studies suggest that up to one-third of patients with type 2 DM have glomerular lesions unrelated to or in addition to DN [1]. Reported types of superimposed glomerular diseases include IgA nephropathy, endocapillary proliferative glomerulonephritis, minimal change disease, membranoproliferative glomerulonephritis, rapidly progressive glomerulonephritis, and cryoglobulinemic glomerulonephritis [1–3]. To our knowledge, MGN has been reported in patients with DM.

We suggest that renal biopsy should be performed in diabetic patients with unusual features, such as proteinuria without retinopathy and sudden deterioration of renal function. Renal histology under these circumstances may help clinicians to uncover some of the superimposed and treatable disorders, and may thus favorably influence the course of renal disease.

In summary, the appearance of urinary changes or a rapid deterioration of renal function against a natural history of DN increases the possibility of non-diabetic renal disease [1]. The use of renal biopsy to confirm such a diagnosis may be of fundamental importance to both treatment and prognosis.

**REFERENCES**

3. Costero O, Diaz C, de Alvaro F, Torre A, Gil F, Picazo ML,

---

**Table.** Reports in the medical literature of membranous glomerulonephritis and diabetes mellitus

<table>
<thead>
<tr>
<th>Authors [Ref]</th>
<th>Year</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yoshikawa et al [8]</td>
<td>1990</td>
<td>15</td>
</tr>
<tr>
<td>Furuta et al [10]</td>
<td>1992</td>
<td>3</td>
</tr>
<tr>
<td>Gambara et al [12]</td>
<td>1993</td>
<td>2</td>
</tr>
<tr>
<td>Lee et al [1]</td>
<td>1999</td>
<td>3</td>
</tr>
<tr>
<td>Costero et al [3]</td>
<td>2001</td>
<td>1</td>
</tr>
<tr>
<td>All authors</td>
<td>–</td>
<td>68</td>
</tr>
</tbody>
</table>


