Progression of Renal Failure Delayed by Use of Losartan in a Case of IgA Nephropathy

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Abstract

We report a case of IgA nephropathy with renal failure in which the deterioration of renal function was inhibited by the addition of angiotensin II receptor blocker (ARB) losartan. Before administration of losartan, the mean decline in the patient’s glomerular filtration rate (GFR) was 0.64 ml/min/1.73 m²/month. Losartan treatment was started when serum creatinine rose above 4.0 mg/dl. With this treatment the serum creatinine level has remained stable for 3.5 years, and the mean decline in GFR was 0.06 ml/min/1.73 m²/month. We document successful retardation of renal failure with the use of losartan. Our experience suggests that dialysis therapy can be delayed significantly in patients using this drug.

Key words: dialysis, angiotensin II receptor blocker, renal failure, hypertension, proteinuria

Introduction

The incidence of end-stage renal disease requiring chronic dialysis therapy is increasing worldwide (1–3). The progression of renal failure is relentless in most cases of renal disease once the glomerular filtration rate (GFR) has begun to decline. Angiotensin converting enzyme inhibitor (ACEI) and angiotensin II receptor blocker (ARB) are effective not only to reduce proteinuria but also to retard the progression of renal failure in both diabetic (4, 5) and non diabetic patients (6, 7). However, physicians often hesitate to prescribe ACEI or ARB for patients with renal failure when serum creatinine is 3.0 mg/dl or more (8, 9).

We report a case in which the progression of renal failure was halted by the long-term use of ARB that was started when the serum creatinine was increased to more than 4.0 mg/dl. The reciprocal of serum creatinine, which has been used to monitor the progression of chronic renal disease (10), was determined before and after the start of losartan, and the values were compared.

Case Report

A 26-year-old woman was admitted to our department for evaluation of proteinuria and hematuria. When she was 8 years old, a doctor treating for cold-like symptoms also identified proteinuria. However, she had no other episode of proteinuria during her childhood or adolescence. In 1990, at the age of 22, she had one episode of macrohematuria. In December 1994, she was referred to our hospital for the surgical treatment of a right mandibular tumor (fibrous dysplasia). During preoperative testing, proteinuria and hematuria were identified, and she consulted us on April 12, 1995. She was admitted to our hospital on May 18.

Upon admission, vital statistics and test results were as follows: height 146.8 cm, weight 54.9 kg, BMI 25.4, temperature 36.7°C, heart rate 72 beats/min, blood pressure 136/84 mmHg, proteinuria (2+), urinary protein excretion 1.8 g/day, occult blood (+), WBC 10,400/µl, hematocrit 36.9%, platelet 254,000/µl, total protein 5.4 g/dl, albumin 3.2 g/dl, BUN 17 mg/dl, creatinine 1.43 mg/dl, uric acid 6.9 mg/dl, sodium 140 mEq/l, potassium 4.5 mEq/l, total cholesterol 252 mg/dl, triglyceride 181 mg/dl, C3 56 mg/dl (60-120), C4 23 mg/dl (20-50), CH₅₀ 33 IU/ml (22-44), IgG 797 mg/dl, IgA 299 mg/dl, IgM 219 mg/dl, 24h-CCr 51.0 ml/min. Light microscopy of a percutaneous renal biopsy specimen showed mesangial proliferative glomerulonephritis. Six out of 15 glomeruli showed global hyalinosis, and remaining 9 glomeruli showed mild to moderate mesangium matrix expansion. Significant interstitial fibrosis and cell infiltration were also noted. Immunofluorescent staining showed granular deposits of IgA and C3 in the mesangium. Blood pressure was controlled with a combination of calcium channel blocker and beta-blocker.

The last 7 years of the patient’s clinical history are shown in Fig. 1. She delivered a baby girl without incident in January 1997. Thereafter, she participated in the TCV-116 clinical trial for 4 months, taking a drug later identified as candesartan cilexetil (4 mg/day). During the trial period, her creatinine level remained fairly stable.

In August 1998, losartan was made available for the first
Figure 1. Patient's clinical course. Reciprocal serum creatinine and the start of losartan treatment.

Figure 2. Patient's clinical course. Blood pressure and serum potassium.
Losartan and Prevention of Renal Failure

Table 1. Glomerular Filtration Rate (GFR) before and after Losartan Administration

<table>
<thead>
<tr>
<th></th>
<th>GFR</th>
<th>ΔGFR, per month</th>
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<tr>
<td>Before losartan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>March 1998</td>
<td>16.4</td>
<td></td>
</tr>
<tr>
<td>September 1998</td>
<td>11.3</td>
<td>-0.64</td>
</tr>
<tr>
<td>After losartan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>March 1999</td>
<td>10.8</td>
<td></td>
</tr>
<tr>
<td>August 2000</td>
<td>10.7</td>
<td></td>
</tr>
<tr>
<td>February 2000</td>
<td>10.7</td>
<td></td>
</tr>
<tr>
<td>September 2001</td>
<td>10.5</td>
<td></td>
</tr>
<tr>
<td>March 2001</td>
<td>10.1</td>
<td></td>
</tr>
<tr>
<td>October 2001</td>
<td>8.9</td>
<td></td>
</tr>
<tr>
<td>March 2002</td>
<td>8.9</td>
<td>-0.06</td>
</tr>
</tbody>
</table>

GFR was calculated by the method described by Couchoud et al (11). ΔGFR was calculated between March 1997 and September 1998 (before losartan) and between September 1998 and March 2002 (after losartan).

The present case is noteworthy because renal failure was successfully inhibited with losartan in this patient even though her serum creatinine had reached 4.44 mg/dl. The JNC-VI (8) and the Japanese Society of Hypertension (9) advise judicious use of ACEI and ARB in patients whose serum creatinine is over 3.0 mg/dl. Therefore, we explained the advantages and adverse effects of losartan to the patient before starting the drug. She was fully informed and was fully committed to the treatment.

ACEI and ARB effectively decrease proteinuria and control blood pressure. Our patient’s initial urine protein was 2–3 g/day, and her blood pressure was 152/92 to 140/84 mmHg. Both the hypertension and proteinuria were controlled well with these drugs. Analysis of the treatment of hypertension in renal dysfunction has shown that more than 2.5 antihypertensives are needed to control blood pressure in most cases (12). In the present case, losartan was added to a calcium channel blocker and beta-blocker. Zucchelli et al have reported positive results with ACEI and a calcium channel blocker (13).

Hyperkalemia can be a life-threatening side effect of ACEI and ARB when they are used for patients with renal failure. However, Taguma et al used captopril for 10 uremic diabetic patients with a mean serum creatinine level of 4.7 mg/dl (range, 1.9 to 8.0 mg/dl) (14). They observed no significant change in serum potassium with administration of captopril. Because the 10 participants were hospitalized patients; the study did not ensure that ACEI and ARB could be used safely with renal failure. The present patient had one episode of hyperkalemia of 6.1 mEq/l, during which she complained of anorexia and constipation. After that episode, her serum potassium was controlled with potassium binder.

Since the initiation of losartan treatment in September 1998, when our patient’s serum creatinine rose above 4.0 mg/dl, her health status has remained stable for 3.5 years without dialysis. This successful delay in the initiation of dialysis therapy is significant. On average, dialysis becomes necessary within 2 years after serum creatinine reaches 4.0 mg/dl (15). It is not uncommon to see patients introduced to dialysis therapy within 1 month of their first visit to a nephrologist (16, 17), and such patients would not be expected to benefit from ACEI and ARB treatment. We recently reported evidence of a high incidence of end-stage renal disease following stroke and acute myocardial infarction (18). Use of ACEI and ARB may prolong life in patients with hypertension or a history of cardiovascular events (19); therefore, the mean age at the start of dialysis may continue to increase with widespread use of this treatment.

In summary, we observed preservation of renal function with administration of an ARB (losartan) in a case of IgA nephropathy. This case suggests that ARB may be useful even when the serum creatinine level is over 3.0 mg/dl, if the patient is competent to understand medical advice and drug therapy.

References


