Reversible renal failure in focal glomerular sclerosis

SOHJI NAGASE, TARO TERASAKI, MOTOAKI SANO, HIROMI INAGE, AKIO KOYAMA, MITSUHARU NARITA and SHIZUO TOJO

Department of Internal Medicine, Institute of Clinical Medicine, The University of Tsukuba, Ibaraki, Japan

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Abstract

A 51-year-old housewife complaining of edema was admitted to our hospital. Investigations revealed proteinuria of nephrotic level and slightly decreased renal function. Renal biopsy was performed and subtle changes which suggested early figures of focal glomerular sclerosis were observed. In spite of steroid therapy, severe proteinuria persisted and renal function gradually decreased. Finally, hemodialysis was performed because of congestive heart failure from the 70th hospital day. The urine output then decreased by degrees and she became anuric in 5 months. The anuric state continued for about 6 months, but she started to excrete urine again about 1 year after the beginning of hemodialysis. Subsequently, the urine volume and creatinine clearance increased gradually and no hemodialysis was required on the 700th day after onset of the disease. Renal biopsy was performed again about 3 years after onset of the disease. The specimen showed typical features of focal glomerular sclerosis. We would like to report this rare example of recovery from severe renal failure in spite of apparent progression of the renal histology. This case had taken a longer period than any other reported case to recover from severe renal failure.

Introduction

Focal glomerular sclerosis (FGS) is considered to be idiopathic and resistant to steroids. The prognosis of this disease is poor in general [1-3] and the patients frequently progress to end-stage renal failure.

In the present case, we caught early figures of FGS by serial section of a biopsy specimen. This case progressed to end-stage renal failure and required hemodialysis about 3 months after onset of the disease. In spite of progression of the renal histology, the patient recovered from severe renal failure 2 years after onset of the disease.

This paper describes the clinical course and histopathological findings of the case and discusses the factors which affect the improvement of renal function.

Case report

A 51-year-old housewife was admitted to hospital on **day**, complaining of facial and pretibial edema. She had no history of prior renal disease or systemic illness. Physical examination revealed periorbital and pretibial pitting edema but was otherwise noncontributory. The blood pressure was 140/80 mmHg. The heart beat was regular and its rate was 70/min.

The results of laboratory investigations on her admission to hospital were as follows. Urinalysis revealed a specific gravity of 1.023, 525 mg/dl of protein, 1 to 5 red blood cells/hpf, and multiple granulated or hyaline casts. The complete blood cell count and coagulation study were within the normal range. The erythrocyte sedimentation rate was 125 mm/h. The serum total protein was 5.1 g/dl and serum albumin, 2.1 g/dl. The blood urea nitrogen was 32.8 mg/dl and serum creatinine, 1.7 mg/dl. The serum total cholesterol was 513 mg/dl. Serum electrolytes
and liver function were normal. The antistreptolysin O (ASO) titer was within normal limits. Rheumatoid factor and C-reactive protein (CRP) were negative. Antinuclear factor and anti DNA-antibody were also negative. The C3 and C4 concentration, and CH50 were normal. A chest X-ray film showed that the cardiac size was at the upper limit of the normal and there were no pleural effusion. An electrocardiogram revealed no prominent abnormality. Intravenous pyelogram showed no abnormality. Ultrasonic examination of the bilateral kidneys yielded normal results. Open renal biopsy was performed on the 8th hospital day. The findings are described in detail below.

The clinical course of this patient over 4 years is summarized in Fig. 1. Oral and intravenous administration of furosemide was initiated on admission. Although the urine output increased gradually, urinary protein excretion also increased according to the urine volume, and massive proteinuria of over 8 g/day continued. Meanwhile, the creatinine clearance decreased from 30 ml/min to 10 ml/min, and the concentration of blood urea nitrogen and serum creatinine increased. On the 14th hospital day, oral prednisolone therapy was initiated at a dose of 30 mg/day combined with dipyridamole at a dose of 300 mg/day. In addition, semi-pulse therapy was initiated on the 50th hospital day, i.e. methylprednisolone was administered to the patient intravenously at doses of 300, 300 and 400 mg on the 1st, 2nd and 3rd day, respectively. Despite such therapy, massive proteinuria persisted and renal function and urine volume decreased gradually. On the 70th hospital day, hemodialysis was initiated because of congestive heart failure resistant to diuretics. The hemodialysis was continued three times weekly. The urine flow then decreased by degrees, and the patient became anuric in 5 months. The anuric state continued for about 6 months, but the patient started to excrete urine about 1 year after the beginning of hemodialysis. The urine output then increased by degrees. On the 700th day after onset of the disease, the urine volume remained over 1500 ml/day, and no more hemodialysis was required. The results of laboratory
examinations at this point were as follows: serum creatinine level, 3.1 mg/dl; creatinine clearance, 10 ml/min; urinary protein excretion, 2.5 g/day; and serum total protein and albumin were within the normal range. Computed tomography of the bilateral kidneys and angiography of the bilateral renal arteries using radioisotope revealed no evidence of renal infarction or renal vein thrombosis. Furthermore, the laboratory findings at about 1 year after discontinuation of the hemodialysis were as follows: serum creatinine level, 2 mg/dl; creatinine clearance, 21 ml/min; sodium thiosulfate clearance, 14.5 ml/min; and paraaminohypuric acid clearance, 127 ml/min. The urine volume was over 2000 ml/day, and urinary protein excretion had already normalized. At this point, i.e. about 3 years after onset of the disease, a 2nd renal biopsy was performed. The histopathological findings are described in the next section.

About 2 years have passed since discontinuation of the hemodialysis. The patient maintains a favorable condition and is free from hemodialysis or nephrotic syndrome.

**Histopathological Findings**

**1st Renal Biopsy**

A renal specimen including 116 glomeruli was obtained by open biopsy. Light microscopy revealed no extra- and endocapillary cell proliferation in the glomeruli or thickening of the glomerular basement membrane (Fig. 2). A few insudative lesions in the arterioles of the vascular pole and slight intimal thickening in the arterioles were seen. Slight interstitial fibrosis and tubular degeneration were present. Furthermore, detailed examinations were performed by making serial sections of the same specimen. It was clarified by light microscopy that adhesion between the capillary wall and Bowman’s capsule, and slight hyalinosis in the same portion were present (Fig. 3). In addition, cell proliferation in Bowman’s space was also observed in the serial sections (Fig. 4). Fluorescent microscopy for immunoglobulins, complements and fibrinogen yielded negative results. Electron microscopy revealed detachment of epithelial cells from the glomerular basement membrane in the capillary loop of glomerulus (Fig. 5).

The 2nd Renal Biopsy

A renal specimen including 58 glomeruli was obtained by needle biopsy. Light microscopy showed that the majority of the glomeruli (about 90%) had fallen into global or segmental sclerosis and one third of the glomeruli demonstrated...
segmental hyalinosis (Fig. 6). Adhesion between the capillary wall and Bowman's capsule was present in 3 glomeruli. Mesangial proliferation or abnormality of the capillary wall was not present in any glomeruli. In the interstitium, marked tubular atrophy and hyaline deposition in the wall of arterioles and small arteries were present. Immunofluorescent microscopy revealed
the deposition of immunoglobulins, only in the sclerotic glomeruli.

Discussion

This case raises two problems. One is why the patient was able to break away from hemodialysis after a long anuric period, and the other is what histopathological diagnosis should be assigned to this patient. The latter problem will be examined first, in order to establish a diagnosis, and the former problem will be discussed.
subsequently.

Renal biopsy was performed twice at an interval of about 3 years. The histopathological findings of the specimen obtained at the 2nd renal biopsy were compatible with FGS based on the details described above. On the other hand, the findings of the 1st renal biopsy appeared to represent minor glomerular abnormality at first sight. However, the detailed examinations by serial sectioning of the specimen revealed that some subtle glomerular changes had already occurred. There have been few reports on the early figures of FGS in humans and experimental animal models [4-6]. These reports suggested that the glomerular injury of FGS might be initiated through the detachment of podocytes, demudation of the glomerular basement membrane and adhesion between the capillary and Bowman's capsule. In addition, a possible relationship between FGS and hyaline arteriosclerosis was reported [7]. The findings of the present serial sections of the specimen obtained at the 1st renal biopsy were compatible with these proposals. The changes in the 1st renal biopsy materials were considered to represent early figures of FGS, since a histopathological diagnosis of FGS was confirmed in the subsequent renal biopsy.

There have been many cases going on hemodialysis due to renal failure via the nephrotic state [8-14]. Usually, the renal failure is irreversible and is attributed to anatomic obliteration of the glomerular filtering bed by endocapillary and/or extracapillary cell proliferation, by thickening of the capillary walls, by sclerosis or by some combination of these morphological changes. However, some cases of reversible renal failure in nephrotic syndrome have been reported [9, 11]. The histopathological findings in almost all of these cases comprised minimal changes. The main factor which worsened the renal function was not morphological alterations but functional mechanisms in these reported cases. In the present case, the histopathological changes did not indicate just minor glomerular abnormality, and progression of the glomerular damage was confirmed by the 2nd renal biopsy. Since the findings of the 1st renal biopsy could not explain the severe renal failure, it is possible that the main factor which affects the deterioration and the improvement of renal function is functional mechanisms. Several factors have been proposed as causes of deterioration of renal function in nephrotic syndrome with minor glomerular lesions. Chamberlain et al. [8] mentioned renal vein thrombosis, reduction of renal blood flow due to hypovolemia, and tubular occlusion by protein casts as factors which may worsen the renal function in nephrotic syndrome. On the other hand, Esparza et al. [13] noted the importance of preexisting arteriosclerosis besides hypovolemia. Further, Lo'venstein et al. [14] suggested the importance of intrarenal edema. The specimen of the 1st renal biopsy did not showed either prominent interstitial edema, tubular occlusion by protein casts or arteriolar sclerosis. In addition, no evidence suggestive of cortical necrosis or renal vein thrombosis was obtained in the examinations at the onset of the disease. Based on these findings, it is possible that the main factors which worsen renal function could be hypovolemia and/or reversible alteration of the permeability of the glomerular basement membrane.

There is no previous report of a patient recovering from severe renal failure after receiving treatment by hemodialysis for 2 years. Furthermore, the present patient was anuric for about half of the period. The question remains as to why recovery from renal failure occurred at 2 years after the beginning of hemodialysis. In this case, it is possible that both correction of functional alteration and progression of the morphological changes occurred simultaneously, since the specimen obtained at the 2nd renal biopsy was severer than the 1st one. Due to such progression of the renal histology, this case apparently took a longer period than other cases to recover from severe renal failure.

We have reported a rare case of FGS recovering from severe renal failure after treatment by hemodialysis for 2 years. At present, this patient still remains in a favorable condition. Further studies are needed to clarify the pathogenesis of reversible renal failure in nephrotic syndrome.
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References