The Unusual Case

Crescentic glomerulonephritis with normal renal function after 28 years of follow-up

Margarita Villa, Giovanni Battista Fogazzi and Gian Carlo Ambroso

Divisione di Nefrologia e Dialisi, Ospedale Maggiore, IRCCS, Milano, Italy and Centro de Nefrologia, Hospital de Clinicas, Avenida Italia, Montevideo, Uruguay

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Introduction

Crescentic glomerulonephritis is a condition which usually leads to chronic renal failure over short periods of time [1,2]. In this paper we describe a patient who in her childhood presented with a severe crescentic glomerulonephritis and who had an unexpected course at a 28-year follow-up.

Case

In December 1969 a 7-year-old girl was admitted to our division for a severe oliguric renal failure. There was a 2-week history of vomiting associated with a progressive decrease of urine output without apparent triggering or precipitating factors. Specifically, there was no episode of infection, and signs or symptoms pointing to systemic disease were completely absent.

On admission the patient was afebrile, normotensive, and without oedema. Plasma creatinine was 9.0 mg/dl and blood urea 390 mg/dl. C3 was normal. Urine output was about 100 ml/24 h, proteinuria was 570 mg/24 h. Urine sediment contained erythrocytes (+ + +), leukocytes (+), hyaline and granular casts (+ +). Urine culture was negative. Peritoneal dialysis was immediately started, but was discontinued after 5 days due to a spontaneous improvement of renal function.

Twenty-two days after admission, when plasma creatinine was 1.6 mg/dl and urine output was 1150 ml/24 h, the patient had a percutaneous renal biopsy.

The tissue core contained 50 glomeruli, 50% of which were sclerotic with large fibro-cellular crescents occupying the Bowman’s spaces (Figure 1). Cellular crescents were present in about 80% of the patent glomeruli, which showed mild mesangial matrix expansion and mesangial cell proliferation without polymorphonuclear infiltration or fibrinoid necrosis. Fucsinophilic deposits by trichrome stain were not found. Mononuclear cell infiltrates were present in several interstitial areas, and there was focal tubulitis. Interstitial fibrosis was focal and mild. Some tubules contained tubular cell casts, and showed focal epithelial flattening. Arteries were mildly thickened, but without arteritis. Immunofluorescence and electron microscopy were not available at that time in our unit.

After these findings, the patient was given azathioprine (3 mg/kg/day) and prednisone (0.6 mg/kg/day), and was discharged with the diagnosis of extracapillary glomerulonephritis. Plasma creatinine was 0.8 mg/dl, creatinine clearance was 61 ml/min, proteinuria was 1.4 g/24 h. The urine sediment still contained erythrocytes (+ +), leukocytes (+), and casts (+ +).

A young doctor, Claudio Ponticelli, who at that time was in his early thirties and was in charge of the patient, wrote to her general practitioner:

‘... the renal biopsy of this child has shown a glomerulonephritis with prevailing extracapillary proliferation. This is one of the most severe types of glomerulonephritis, which usually leads to uraemia and death in a few months. However, we have had a similar patient who is still living with normal renal function more than 2 years after the onset of the disease. This patient had been treated with immunosuppressive drugs ... In consideration of this remarkable result and of the likely immunologic pathogenesis of the disease we think a treatment with azathioprine and prednisone is appropriate also in this case ...’.

Thirteen months later, in February 1971, the child was re-admitted to our unit. Immunosuppressive treatment had been stopped by the patient’s parents in August 1970. Plasma creatinine had increased to 1.2 mg/dl and creatinine clearance had decreased to
44 ml/min. Urinalysis was normal. Therefore, a further evaluation was considered necessary. Physical examination showed nothing irregular, and the patient still had normal blood pressure. Blood tests and urinalysis were also normal.

A second renal biopsy was performed. The renal tissue contained 12 glomeruli, seven of which (58%) were globally sclerotic. The patent glomeruli showed mild mesangial matrix expansion and mild intracapillary proliferation. Interstitial fibrosis was focal. There was mild arteriosclerosis. At immunofluorescence no immunoglobulins, C3, or fibrinogen were found.

After these findings, the patient was discharged without therapy. Shortly after, she was lost to follow-up. However, in November 1997 the patient was seen again by one of us (A.G.C.) in a consultation for her fifth pregnancy. The first two pregnancies as well as the fourth had been uneventful, while the third pregnancy had been complicated by eclampsia with acute renal failure (serum creatinine up to 3.4 mg/dl), followed by spontaneous remission. The fifth pregnancy and the delivery were both normal. At the time of writing (April 1998) the patient is well. Her plasma creatinine is 0.9 mg/dl, urinalysis is normal, and blood pressure is 130/80 mmHg without therapy.

Discussion

The patient we have described suffered in her childhood from a severe crescentic glomerulonephritis. Due to the lack of more clinical information and also the lack of the sophisticated techniques available today it is not possible to establish the exact nature of the disease. The patient’s history and histology (absence of humps) do not provide arguments for the presence of post-infectious glomerulonephritis, and the absence of systemic manifestations does not favour, but does not definitely exclude, the possibility of ‘paucimmune’ extracapillary glomerulonephritis. Obviously, serological diagnosis was not available in those days.

Independently of the nature of the renal disease, this case is unusual because of a benign long-term course in spite of severe renal disease at the onset and extensive glomerular sclerosis in the second renal biopsy, as well as for the 28-year follow-up. To the best of our knowledge this is the longest follow-up described for an extracapillary glomerulonephritis.

How can such a benign evolution be possible? We know that the outcome of extracapillary glomerulonephritis is usually poor: 66% to 75% of adults develop renal failure at 2 years [3,4], and up to 40% of children are in end-stage renal failure at 1 year [5,6]. However, the value of some parameters usually seen as indicators of a bad prognosis has recently been reduced. Oligoanuria at presentation is now considered to correlate with early course but not with the long-term outcome [7–10]. The percentage of glomeruli with crescents correlates more with the initial renal function impairment rather than with renal function at follow-
up [5–8,11]. In addition, especially in children with post-streptococcal nephritis, crescents may resolve [1,5,12]. On the other hand, in recent years, an important role in the progression of glomerular diseases has been attributed to the co-existence of tubular atrophy and interstitial fibrosis [13], either of which was mild in this particular case. Immunosuppressive therapy is another important factor which can influence the outcome of extracapillary glomerulonephritis [1]. Prednisone and azathioprine had been administered for several months to our patient, which may have played a role in preventing the progression of the renal damage. In retrospect, the clairvoyance of the physician in charge of the patient must be applauded, who selected immunosuppressive therapy on the basis of a priori reasoning and anecdotal observations despite absence of definite proof of its efficacy. An additional explanation for the lack of progression in our case may have been the absence of proteinuria and hypertension, which are now considered as important factors of progression of renal disease [14,15]. However, even after these considerations, it is still difficult to explain the positive outcome for our patient. All this seems to challenge the accepted view that nephron mass loss is an important factor in the progression of renal disease [16,17].

In our opinion this case clearly demonstrates how difficult the prediction of the long-term outcome of a renal disease in a single patient can be. It also shows how imperfect our knowledge about the progression of renal disease still is.

References