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Original Article

The Pattern of Histologically-Proven Acute Post-infectious Glomerulonephritis in Tunisian Adults Seen in 1976 - 2004

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Abstract

Introduction: Acute post-infectious glomerulonephritis (APIGN) is uncommon in adults. It is widely recognized that the prognosis of APIGN is good in children. There is however little information about its long-term prognosis in adults.

Methods: Between December 1976 and October 2004, 148 adult cases of APIGN were managed in our center. We retrospectively reviewed these patients' records and evaluated their clinical course and outcome.

Results: The mean age of studied patients was 36±15 years, and the male to female ratio was 2.3. The most common site of preceding infection was the respiratory tract (68.8%). At presentation, 89.2% had nephritic syndrome and 9.4% had rapidly progressive glomerulonephritis. Proteinuria was observed in 99.3%, hematuria in 95.3%, peripheral edema in 89.2% and hypertension in 81.8%. Most patients (60.7%) had acute kidney injury and four patients (2.7%) required dialysis. Renal biopsy showed diffuse endocapillary proliferative glomerulonephritis in 88.8% of patients, associated with extracapillary proliferation in 12%. After a median follow-up of 2.5 year, only two patients died and 16.12% of patients had persistent clinical and/or biological abnormality. Chronic kidney disease was noted in 10 patients (6.75%) including four patients (2.7%) who progressed to end-stage renal disease. Poor prognostic factors included nephrotic range proteinuria, extracapillary proliferation in renal biopsy, acute kidney injury and the need for dialysis.

Conclusion: In this cohort of patients, APIGN progressed to chronic kidney disease in less than 10% of patients.

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Introduction

Infection associated glomerulonephritis is rare in adults [1] and its incidence is progressively declining in developed countries [2]. The pattern of the disease has changed over recent decades. Not only streptococcal but also other bacterial, fungal, viral and parasitic infections can trigger the disease [3]. The more extensive use of renal biopsies highlighted atypical histological forms of the disease [4]. It has been widely recognized that the prognosis of acute post-infectious glomerulonephritis (APIGN) is good in children [5-9]. There is however little information about the long-term prognosis of APIGN in adults. In recent years only few studies with small numbers of patients [10] and relatively short period of follow-up [11, 12] have been reported. In this study, we retrospectively analyzed 148 cases of APIGN in adults diagnosed in our department during the period between 1974 and 2004, to evaluate the clinical and histological predictors of prognosis.

Methods

We retrospectively evaluated 184 patients diagnosed with APIGN on the basis of clinical parameters and renal biopsy in our department between December 1976 and October 2004. Inclusion criteria were age more than 18 years, clinical features of APIGN, evidence of preceding infection and renal biopsy showing glomerulonephritis (GN) with endocapillary proliferative and exudative features on light microscopy. We excluded patients with clinical or histological evidence of previous renal disease.

Chronic kidney disease (CKD) was defined by creatinine clearance (CrCl) less than 60 ml/min persisting for more than three months, estimated by the Cockroft-

Table 1: Main findings of renal biopsy by light microscopy in the studied cohort

Pathological finding	Number of patients (%)
Pure endocapillary proliferative GN	107 (72.3 %)
Pure endocapillary proliferative and exudative GN	24 (16.2 %)
Diffuse endo- and extracapillary proliferative GN	3 (2.0 %)
Diffuse necrotizing and crescentic GN*	14 (9.5 %)

* defined by crescents or necrosis involving ≥ 50% of glomeruli

Table 2: Renal status of the studied 148 patients at 2.5 years of follow up

Renal status	Number of patients (%)
Complete remission	114 (77.1 %)
Partial remission	24 (16.1 %)
Chronic kidney disease*	10 (6.8 %)

* This group includes four patients (2.7%) who progressed to end stage renal disease

Gault formula [13, 14]. Acute kidney injury (AKI) was defined by doubling of baseline serum creatinine and/or the initial need for dialysis. Complete remission was defined as return of renal function to normal (CrCl > 60 ml/min). In addition to clinical evaluation and blood pressure measurements, follow-up studies included: urinalysis, serum albumin, blood urea, electrolytes, creatinine and serum complement levels (C3 and CH50). Non-streptococcal infection was identified by positive cultures. Streptococcal infection was identified by positive cultures, elevated anti-streptolysin O antibody, or anti-DNase B antibody.

We used the SPSS statistical software 11.5 (Lead Technologies Inc., Chicago, USA) for statistical analysis. Data are expressed as mean ± SD or as median (interquartile range), as appropriate. Continuous variables were compared using the unpaired Student's t test and categorical variables were compared using the Chi-square test. Statistical significance was assumed at $P < 0.05$.

Results

The study included 148 patients; 103 males (69.6%) and 45 females (30.4%). Their mean age was 36 ± 15 years, 45.9 % were smokers, two had dyslipidemia (1.4%), four had hypertension (2.8%), six were diabetics (4.1%), and six (4.1%) had history of acute rheumatic fever. An upsurge of APIGN in fall and winter was noted, with a peak in November and December. Forty-nine percent of patients were of low socioeconomic status. The site of infection was identified in 85% of patients; the most common sites being the otolarynx (54.4%), upper respiratory tract (14.4%) and skin (16.8%). The infectious agent was identified in 42.6% of patients. Streptococcal infections were the most frequent and were identified in 34.5% of patients, followed by staphylococcus (2.7%), pseudomonas (2%), enterococcus (2%) and pneumococcus (1.4%). The latency period between the infection and the onset of the clinical syndrome ranged from 4–90 days, with a median of 10.4 days.

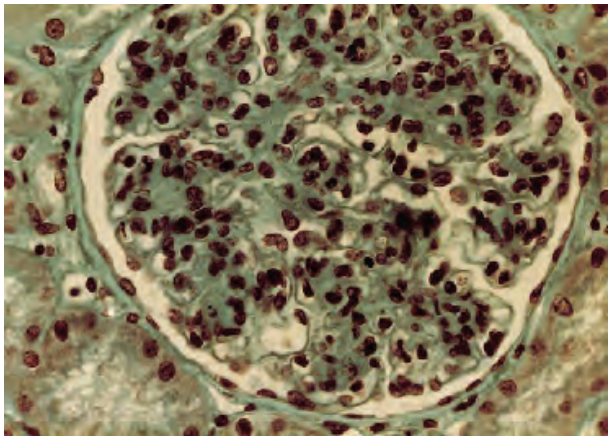
At presentation, 89.2% of patients had acute nephritic syndrome and 9.4% had clinical manifestation of rapidly progressive glomerulonephritis. Proteinuria was noted in 99.3% of patients, microscopic or macroscopic hematuria in 95.3%, peripheral edema in 89.2% and new-onset hypertension in 81.8%.

Most patients (60.7%) had acute kidney injury (AKI) but only 4 patients (2.7%) required dialysis during the disease course. The median serum creatinine at presentation was 1.3 mg/dl (range, 0.4-34.1 mg/dl). The mean creatinine clearance was 71 ± 30 ml/min and 96 patients (65.2%) had creatinine clearance more than 60 ml/min. The median 24 hour urine protein was 2.3 g, (range, 0-19 g/24 hours) and 38.4% patients had nephrotic range proteinuria. Testing for serum complement was performed for 93 patients, 52.9% of whom had depressed C3 level and 40.2 % had a depressed C4 level.

Renal biopsy findings are shown in Table-1. The most frequent histological pattern of glomerular injury was pure endocapillary proliferative GN (Figure-1). Steroids were used in 2.7 % of patients, all of whom presenting with crescentic GN.

In the short term, only two patients of our cohort died. The cause of death was probably related to uremia. Blood pressure was controlled in all patients within 20 ± 2.5

Figure 1: Pure endocapillary proliferative glomerulonephritis (Trichrom stain, original magnification x 400)



days. Hematuria disappeared within 6.8 ± 1 months and proteinuria disappeared within 3.3 ± 0.7 months from the onset of the disease. The outcome of studied patients after a median follow-up of 2.5 years is shown in Table-2.

Univariate analysis showed that among clinical parameters at presentation, the occurrence of nephrotic range proteinuria (P = 0.05), extracapillary proliferation in renal biopsy (P = 0.02), the development of AKI (P = 0.001) and the initial need for dialysis (P = 0.01) were significantly associated with developing CKD at follow up. Age was not a significant predictor of CKD.

Discussion

Post-infectious glomerulonephritis is an immunologic response of the kidney to infection, commonly triggered by streptococci, although many other organisms can cause the condition. In recent decades, the prevalence of APIGN has tended to decline in most industrialized countries [2, 12, 16], and some developing communities [15]. The incidence of APIGN in Tunisia between 1975-1985 and 1995-2005, fell from 15.9% and 21.6% to 6.9% and 7.7%, respectively (P < 0.0001) [15]. This paralleled a drop in the incidence of acute rheumatic fever in the Tunisian population, from 7.26/100.000 inhabitants in 1984 to 0.83/100.000 inhabitants in 2004, probably as a result of public health measures and the widespread use of antibiotics [15]. In the current study we analyzed the clinical, pathologic, and outcome data in a series of 148 adults with non-epidemic APIGN. In agreement with the study of Nasr *et al* [16], we found that the most common site of infection was the upper respiratory tract, the two most frequently identified infectious agents were Streptococcus and Staphylococcus and the most common histologic pattern was pure endocapillary proliferative GN.

Our cohort had better prognosis than Nasr *et al* cohort where only 56.1% of patients achieved complete remission, 26.8% had persistent renal dysfunction, and 17.1% progressed to ESRD [16]. The probability of complete remission in preceding series significantly declined from the early 1980s to the late 2000s, as observed in studies with adequate follow-up periods. In the 1970s, complete remission was reported in 70-80% of adults with APIGN [17, 18]. In the 1980s Vogl *et al* [19] reported complete remission in 69% of adults with post-streptococcal acute GN after a mean follow-up of 4.8 years, while Chugh *et al* [20] reported recovery in only 59% of adults followed for more than 2 years. Montseny *et al* [12] reported complete remission in only 26% of adults, half of them having an underlying disease. However, the short follow-up period of that study with a mean of nine months may have precluded the observation of late recoveries in other patients. Complete remission occurred after a median of 2.5 years in our series as well as in other older studies [5, 17]. Together with the reduced probability of complete recovery, in recent years there was an increasing incidence of progression to chronic kidney disease, from 3.3% in the 1970s [18], to 16–28% in the 1980s [19-21]. These data suggest that the long-term prognosis of APIGN is worsening in adults. This is probably due to the fact that the epidemiology of the infection has changed over the years in developed countries, with the typical post-streptococcal acute GN becoming rarer, while the number of cases with severe underlying diseases is progressively increasing. The better prognosis of our cohort is probably due to the younger age of our population and the absence of cardiovascular risk factors.

Few studies have investigated the prognostic indicators of progression to CKD. Some studies have reported that nephrotic range proteinuria [12, 19, 20] and AKI [20, 22] at onset were reliable predictors of poor prognosis. While in other studies [23, 24], neither the levels of plasma creatinine nor the amount of urinary protein excretion at presentation correlated with the long-term prognosis. In this study, extracapillary proliferation in renal biopsy and AKI were identified as poor prognostic factors. It is sometimes postulated that older patients have a higher risk for cardiovascular complications, incomplete recovery of renal function and mortality. In our series, older patients tended to have a worse prognosis than younger adults, but that did not reach statistical significance.

Conclusion

This study suggests that APIGN progresses to CKD in a small number of adult hospitalized patients in the current era. Risk factors for progression to CKD include the presence of the nephrotic range proteinuria, extracapillary proliferation, and severe AKI. This indicates the need for continued follow-up of this group of patients.

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