Etiopathological Study of Crescentic Glomerulonephritis and its Outcome: A Retrospective Analysis

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Abstract

Introduction: Crescentic Glomerulonephritis (CGN) is most aggressive structural phenotype and accounts for 2%-7% of renal biopsy in most series. The aim of study was to assess the clinical feature and outcome of CGN at our centre.

Material and Methods: The renal biopsy performed during the period of January 2015 to January 2018 was studied and patients showing crescentic glomerulonephritis on histology were selected for this study. The clinical presentation, immunological assay, biochemical and haematological investigations, treatment protocol and final outcome at three month of these patients were analysed in the present study.

Results: Of 380 biopsy, 26 (male=17, female=9) patients had histological evidence of CGN (6.8%). The age of patients ranged between 13-75 (mean=43) years. Fibro cellular and cellular crescent was noted in 84.61% and 15.38% of patients respectively. Small vessels vasculitis and granuloma was observed in 5 (19.23%) cases. Based on immunohistopathology, we observed type I (n=3), type II (n=8), type III (n=5), type IV (n=3), and type V (n=7) crescentic GN in 11.53%, 30.76%, 19.23%, 11.53% and 26.92% of patients respectively. Haemodialysis was given to 22(84.61%) and 4(15.38%) patients were treated with immunosuppressive therapy. Plasma pheresis was used in two double positive (ANCA + Anti GBM Ab) patients. Remaining 21(80.76%) has progressed to ESRD over a period of 2-3 months.

Conclusion: Type II (immune complex) CGN was most common type followed by type V (immune negative) and type III (pauci-immune) CGN. The crescentic GN had worse prognosis with >80% of patients progressed to ESRD within 3 month of time from onset of illness. Early diagnosis and treatment is associated with favourable outcome.

Introduction

The WHO definition for glomerular crescents is “two or more layers of proliferating cells between the visceral and parietal epithelial epithelial cells that are partially or completely filling the Bowman’s space”. While occasional crescents may be seen in various renal diseases, the presence of crescents in more than 50% of the glomeruli defines “Crescentic glomerulonephritis” as per WHO recommendations.2,3 Active crescents tend to be cellular and consist of a mixture of inflammatory cells (leukocyte), intrinsic epithelial epithelial cells of the Bowman’s capsule, extracellular matrix, and few fibroblasts. Over time, the cellular crescents develop into fibro cellular and fibrous crescent. The initiating event is the development of physical gaps (also called rents or holes) in the glomerular basement membrane and Bowman’s capsule. Clinical hallmark of CGN is rapidly progressive glomerulonephritis (RPGN). RPGN refer to clinical syndrome characterised by rapid and progressive loss of renal function over hours and days, often accompanied by oliguria or anuria and features of acute glomerulonephritis including dysmorphic erythrocyturia, and glomerular proteinuria.1 Crescentic Glomerulonephritis (CGN) is most aggressive structural phenotype and accounts for 2%-7% of renal biopsy in most series and a smaller proportion of all patients with end stage renal disease.3-5 There is significant heterogeneity in the aetiology and outcome of CGN with limited data from India.7-10 The clinical feature and histopathological spectrum of CGN was reported in paediatric patient from India.9,10 However, data in adult patients are scarce. This study aims to identify aetiology and assess the clinical feature, histomorphology and outcome of CGN at our centre.

Material and Methods

This retrospective observational study was conducted in the department of nephrology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India from January 2015 to January 2018. Twenty six biopsy proven crescentic glomerulonephritis patients with variable presentation were included in this study. Crescentic glomerulonephritis was defined by crescent formation over 50% sampled glomeruli in biopsy specimen.

The patient’s detail clinical history and physical examination record were retrieved and analysed. The laboratory investigations including Complete Haemogram, ESR, Renal function test, Liver function test, Lipid profile and immunological assay (RA factor, C3, C4, ANA, Anti ds DNA antibody, PR3 ANCA, MPO ANCA and Anti GBM Ab). The result of urinalysis was noted if available. Renal biopsy sample was preserved in 10% buffered aqueous formaldehyde solution for light microscopy. Sample were studied under light microscopy using Haematoxylin and eosin stain, Periodic acid-Schiff stain, Acid fuchsin Orange G and Periodic acid Silver Methanamine stain. Electron microscopy and Immunofluorescence study were not done due to lack facility at this centre. Renal biopsy were examined in detail for total number of glomeruli,
number of completely sclerosed glomeruli, percentage of glomeruli with crescent formation, features of vasculitis, and extent of interstitial fibrosis and tubular atrophy. Crescentic glomerulonephritis are classified based on immunohistological features into following five groups type I, II, III, IV, and type V. Records of treatment and immunosuppressant used were collected. Total numbers of patients requiring haemodialysis at the time of hospitalisation were noted. Renal function test, Urine microscopy, Complete Blood Count and requirement of haemodialysis assessment were done monthly, till their last follow up. Outcome assessments at three month were carried using improvement in renal function and progression to End Stage Renal Disease (ESRD).

**Observation and Results**

Of 380 biopsy, twenty six (Male=17, Female=9) patients with age range of 13 to 75 (Mean=43) years had histological evidence of crescentic glomerulonephritis (6.8%) and these patients were included in the study. Physical examination revealed Pallor (92.3%), Oedema (76.9%) and hypertension (69.2%). Anuria was noted in 18 (69.2%) of patients. Headache, convulsion and joints pain was present in one patient each (Table 2). Macroscopic hematuria was seen in 8(30.7%) cases and remaining 18(69.2%) cases had microscopic hematuria. Haemoglobin concentration was less than 10 gm% in all cases. RPGN was the mode of clinical presentation in all (100%) patients with uremic manifestation in 22 (84.6%). HIV, hepatitis B and C infection were negative in all cases. Immunological assay revealed low C3 in six (n=6), low C3andC4 in two (n=2) case. MPO and PR3 ANCA were positive in 3 female and 2 male patients respectively. Anti GBM Ab was noted in 3 cases (36.0-101.0 u/ml). Three patients had double positive (ANCA + Anti GBM Ab) (Table 3). Nine (34.6%) cases had crescent involving >75% glomeruli and remaining seventeen (65.3%) cases showed crescents in 50-75% of sampled glomeruli. Fibro cellular and cellular crescent was noted in 84.61% and 15.38% of patients respectively. Twenty cases (76.9%) had <50% and six cases (23.0%) had >50% completely sclerosed glomeruli. Diffuse and patchy chronic tubulointerstitial nephritis was noted in (n=17; 65.3%) and (n=9; 34.6%) of cases respectively. Features of vasculitis and granuloma formation were observed in 5 (19.23%) cases (Table 4). Based on histological finding and immunology, we observed type I (n=3), type II (n=8), type III (n=5), type IV (n=3), and type V (n=7) crescentic GN in 11.53%, 30.76%, 19.23%, 11.53% and 26.92% of patients respectively. Type II (Immune complex) crescentic GN was the commonest pattern on histology, followed by type V (Immune negative) and type III (Pauci immune) (Table 5). Haemodialysis was given to 22(84.61%) and 4(15.38) patients were treated with immunosuppressive therapy without Haemodialysis. Standard immunosuppressive (Cyclophosphamide + Corticosteroid) therapy was used depending upon the immunological category of RPGN. Plasmapheresis was given to 2 double positive (ANCA + Anti GBM Ab) patients. After 3 month follow up, only five patients had improvement in renal function and become dialysis independent. These five patients were in Type II (n=1), Type III (n=1), Type IV (n=1) and Type V (n=2) RPGN category (Table 1). Remaining 21(80.76%) patients showed no improvement in renal function. They were dialysis dependent and had progressed to ESRD over a period of 2-3 months.

### Discussion

Crescentic glomerulonephritis (CGN) is an important pathologic correlate of rapidly progressive renal failure and it is most aggressive structural phenotype and accounts for 2%-7% of renal biopsy in various reported series and accounts for a smaller proportion of all patients with end stage renal disease (ESRD). In our study, it accounted for 6.8% of cases. The incidence of CGN varies with geographic location and policies of kidney biopsies. Incidence of CGN was 1.75% in a study from China. Gupta et al reported incidence of CGN in 2.65%. In an earlier study from our institute Choudhury TA et al found incidence of 5.5%. However, studies from South Africa (3.8%) and Western Europe and North America (2-10%) showed a near-similar incidence. Thus, over observation was similar to other published studies.

The mean age of our study population was 43 years with Male: Female ratio 1.8:1. Nagaraju et al. reported almost similar mean age (42.5±17.27 years). CGN occurs at all ages. In our study commonest age group affected was between 19-59 years (65.3%) followed by 60 years (26.9%). Two patients (7.6%) were of paediatrics age (<19 years). Overall, CGN is uncommon in children. In a study from University of North Carolina Nephropathy Laboratory, patients less than 20 years constituted 11.5% of all cases of CGN. Gupta et al, reported patients less than 14 years constituted 26% of all cases of CGN. Our result on incidence of CGN
probably to the high prevalence of infection with nephritogenic strains and regional and epidemiological variations. In present study, we found type III CGN (pauci-immune) as a second most common aetiology of CGN and it was predominantly present in adult patients (19-59 years). Type I, Type IV, and Type V CGN also were common in adult patients.

The prognosis in CGN is dependent on the age, aetiology, extent of the renal failure and the histological subtype. A strong predictor of outcome for all types of CGN is the severity of renal insufficiency at the time of presentation. The overall prognosis in our study remained poor with >75% circumferential crescents, and fibrous crescents. The overall prognosis in our study remained poor with >80% reaching ESRD over 3 months. In subtype, Type I CGN had poorest outcome and all (100%) patients of this category progressed into ESRD. We observed 70-90% of patients with CGN (Type II to V) progressed to ESRD. Rampelli SK et al. reported 48.6% ESRD due to CGN in their study. Few other Indian studies have reported low rates of ESRD and mortality in contrast to our study. In those studies, patients had a much lower serum creatinine levels at presentation and included children. The poor outcome of our study cohort may be attributed by late presentation, severe renal failure (s. creatinine >6 mg/dl), requirement of haemodialysis (84.61%), anuria and features of chronicity on histological examination (Table 4) in majority of patients at the time of presentation. In present study only five (19.23%) patients have recovery in renal function and becomes dialysis independent.

CGN needs aggressive management with high-dose corticosteroids and cytotoxic drugs. Plasmapheresis is indicated for anti-GBM disease and ANCA-associated GN with pulmonary haemorrhage. Studies have shown that the severity of renal insufficiency before initiation of treatment is a strong predictor of renal outcome. Pathologic severity in terms of activity of crescents and chronicity of glomerular and tubulo-interstitial disease also correlates with prognosis.

### Conclusion

We observed, Type II (immune complex) CGN was most common type followed by type V (immune negative) and type III (pauci-immune) CGN. The crescentic GN had worse prognosis with >80% of patients progressed to ESRD within 3 month of time from onset of illness. The presence of oligaemia, high serum creatinine and requirement of haemodialysis at admission are associated with poor outcome. Early diagnosis and standard immunosuppressive treatment may be associated with favourable outcome. Crescentic GN should be kept in mind in differential diagnosis of unexplained Acute Kidney Injury.

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### References