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Original Investigation

Etiology and Outcome of Crescentic Glomerulonephritis From a Single Center in China: A 10-Year Review

Shasha Chen, PhD, Zheng Tang, PhD, Haiyan Xiang, PhD, Xiaowei Li, PhD, Hao Chen, PhD, Haitao Zhang, PhD, Weixin Hu, PhD, Caihong Zeng, PhD, and Zhihong Liu, MD

Background: The disease spectrum of crescentic glomerulonephritis (GN) has been described in only a few previous studies, and detailed epidemiologic data from China are unavailable to date.

Study Design: Case series.

Setting & Participants: 528 patients with biopsy-proven crescentic GN in 2003 to 2013 from a single center.

Predictor: Crescentic GN was classified into 3 types according to immunofluorescence findings: type I was defined as linear deposition of immunoglobulins along the glomerular basement membrane; type II, as glomerular deposition of immune complex; and type III, as pauci-immune deposition.

Outcomes: Demographic, clinical, and serologic characteristics.

Results: Of 528 cases identified, 208 (39.4%) were men, with a mean age of 37.6 ± 16.4 (SD) years at kidney biopsy. 61 (11.6%) patients had type I crescentic GN, 331 (62.7%) had type II (lupus nephritis, 34.3%; immunoglobulin A [IgA] nephropathy, 17.4%), and 136 (25.8%) had type III. Proportions of patients with acute kidney injury (AKI), acute kidney diseases and disorders without AKI, and chronic kidney disease were 86.9%, 0%, and 13.1% for type I; 42.0%, 19.6%, and 38.4% for type II; and 84.6%, 2.9%, and 12.5% for type III crescentic GN, respectively. Serum antineutrophil cytoplasmic antibodies were detected in 11 (18.0%) patients with type I, 15 (4.5%) with type II, and 117 (86.0%) with type III. Anti–glomerular basement membrane antibodies were found in 60 (98.4%) patients with type I, 3 (0.9%) with type II, and 5 (3.7%) with type III. 5-year cumulative renal survival rates for patients with types I, II, and III were 17.6%, 70.1%, and 44.3%, respectively.

Limitations: Retrospective study, single-center experience.

Conclusions: Lupus nephritis may be the most common type of crescentic GN in China, followed by pauci-immune crescentic GN and IgA nephropathy. Almost half the patients presented with AKI, whereas 28.8% of cases showed chronic kidney disease. Clinical manifestations and outcomes varied according to crescentic GN type. The distinction between subtypes based on immunofluorescence and serologic findings has important implications for therapy and outcome.

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INDEX WORDS: Crescentic glomerulonephritis; crescents; type; etiology; antineutrophil cytoplasmic antibody (ANCA); anti-glomerular basement membrane (anti-GBM) antibody; linear deposits; immune complex; granular deposits; pauci-immune; kidney biopsy; renal pathology; renal histology; clinical follow-up; kidney survival; rapidly progressive; kidney disease; China.

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A serious condition with rapidly progressive deterioration in kidney function,[1] crescentic glomerulonephritis (GN) is present in approximately 4% to 10% of total kidney biopsies.[2,3] Up-to-date epidemiologic data regarding kidney disease in adults are available from large national kidney biopsy registries, including those from Saudi Arabia,[4] the United States,[5] India,[6] Japan,[1] and Spain.[7] In 2003, we described the clinical features and renal histology of 172 consecutive patients with crescentic GN identified from 9,828 kidney biopsies performed at our institution from 1989 to 2001.[8] We reported that immune-complex crescentic GN was the most common type of crescentic GN in China. Since this study, we have noticed an increasing incidence of crescentic GN associated with cases of kidney biopsy. The distinction between subtypes based on immunofluorescence and serologic findings has important implications for therapy and outcome. However, to our knowledge detailed epidemiologic and clinicopathologic data from China during the past decade have not yet been published. The aim of this study was to investigate the etiology, clinicopathologic features, and outcome of histologically diagnosed crescentic GN in a large representative center from China during a 10-year period.

From the National Clinical Center of Kidney Disease, Jinling Hospital, Nanjing University School of Medicine, Nanjing, China.

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Address correspondence to Zheng Tang, PhD, 305 East Zhong Shan Road, Research Institute of Nephrology, Nanjing Jinling Hospital, 210002 Nanjing, China. E-mail: tang_dr@163.com

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METHODS

Study Population

A total of 528 patients with biopsy-proven crescentic GN diagnosed in January 2003 to January 2013 in the renal division of Nanjing Jinling Hospital (the largest referral renal center in China) were included in this retrospective study. Patients with fewer than 10 nonsclerotic glomeruli in sampled renal tissue were excluded. Clinicopathologic and follow-up data were obtained from the electronic medical record system. This work was approved by the Ethics Committee of Jinling Hospital, and we received informed consent from all patients.

Pathologic Studies

All biopsy specimens were examined by light microscopy, and immunofluorescence was reviewed by 2 nephropathologists (CZ and HC) blinded to patient outcome. Lupus nephritis was diagnosed and classified based on the International Society of Nephrology/Renal Pathology Society classification.[9] Tubulointerstitial lesions, including tubular atrophy and interstitial fibrosis, were semiquantitatively graded as none (0), mild (1), moderate (2), or severe (3).[10] The extent of interstitial inflammation by each method was semiquantitatively scored (without prior knowledge of clinical outcomes) from 0 to 3, which corresponded to 0%, <20%, 20% to 50%, or >50% involvement of the tubulointerstitium, respectively.[11]

Definitions

Crescentic GN was defined as more than half the total glomeruli affected by large crescents, as assessed by light microscopy.[12,13] Immunofluorescence microscopy was used to determine the type of crescentic GN. Type I included cases of anti–glomerular basement membrane (anti-GBM) disease characterized by linear deposits of antibodies along the GBM. Type II was a heterogeneous group of primary or secondary glomerular diseases with granular deposits of immunoglobulins and complement fractions on the glomerular tuft. Type III was defined as the absence of immune deposits in kidney tissue.[5,14,15]

Clinical presentations included acute kidney injury (AKI), acute kidney diseases and disorders (AKD) without AKI, and chronic kidney disease (CKD). AKI was defined as an increase in creatinine level by 0.3 mg/dL (26.5 mmol/L) within 48 hours or a percentage increase in serum creatinine ≥ 50% (1.5-fold from baseline) within 7 days or urine volume ≤ 0.5 mL/kg/h for 6 hours. CKD was defined as estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 or markers of kidney damage for more than 3 months (including nephrotic syndrome, asymptomatic urinary abnormalities, or nephritic syndrome). AKD without AKI was defined as eGFR < 60 mL/min/1.73 m^2 for less than 3 months or a decrease in eGFR ≥ 35% or an increase in creatinine level > 50% or markers of kidney damage for less than 3 months.[16]

Decreased eGFR was defined as eGFR < 60 mL/min/1.73 m^2. Nephrotic syndrome was defined as proteinuria with protein excretion > 3.5 g/d and serum albumin level < 35 g/dL, with eGFR ≥ 60 mL/min/1.73 m^2. Asymptomatic urinary abnormalities were defined as proteinuria with protein excretion < 3.5 g/d and/or hematuria with more than 3 red blood cells per high-power field, without edema, hypertension, or decreased eGFR. Nephritic syndrome was defined as hematuria, proteinuria (protein excretion < 3.5 g/d), hypertension, and edema, with eGFR ≥ 60 mL/min/1.73 m^2. The life-table end point was defined as chronic kidney failure (ie, eGFR < 15 mL/min/1.73 m^2, initiation of dialysis therapy that continued for >3 months, or transplantation).[17] Serum creatinine was measured by an enzymatic method and recalibrated to standardized creatinine measurements. eGFR was calculated with the CKD-EPI (CKD Epidemiology Collaboration) creatinine equation.[18] eGFR categories included ≥90, 60 to 89, 30 to 59, 15 to 29, and <15 mL/min/1.73 m^2.[19]

Statistical Analysis

All data were analyzed using the statistical software SPSS, version 19.0 (IBM). Quantitative data were expressed as mean ± standard deviation or median with interquartile range. All parameters were compared by χ^2 test or Fisher test for categorical data and *t* test, 1-way analysis of variance, or Kruskal-Wallis test for continuous data. Kaplan-Meier curves and log-rank test were used to analyze and compare time from entry to chronic kidney failure (renal survival). $P < 0.05$ was considered significant.

RESULTS

Etiology, Demographics, and Kidney Manifestations

A total of 528 patients with biopsy-proven crescentic GN diagnosed January 2003 to January 2013 were recruited for this retrospective study, accounting for 1.56% (528 of 33,747) of the total nontransplant kidney biopsies in this period. The disease composition of crescentic GN was as follows: 181 (34.3%) had lupus nephritis, 136 (25.8%) had pauci-immune nephritis, 92 (17.4%) had immunoglobulin A (IgA) nephropathy, 61 (11.6%) had anti-GBM kidney disease, 39 (7.4%) had Henoch-Schönlein purpura nephritis, 11 (2.1%) had membranoproliferative glomerulonephritis, 5 (0.9%) had idiopathic crescentic glomerulonephritis, 2 (0.4%) had hepatitis B virus–associated nephritis, and 1 (0.2%) had focal segmental glomerulosclerosis (Table S1, available as online supplementary material).

Of 528 patients with crescentic GN, 208 (39.4%) were men and 320 (60.6%) were women, with an average age of 37.6 ± 16.4 (standard deviation) years at biopsy (Table 1). The median interval between onset of the disease and kidney biopsy was 2 (range, 1-6) months. Female predominance was observed in type II crescentic GN, whereas types I and III were almost equally distributed between sexes. There were clear incidence peaks for crescentic GN: in those aged 14 to 24 and 45 to 54 years in the type I group, 14 to 44 years in the type II group, and 45 years or older in the type III group. Among all 528 cases, clinical presentations of crescentic GN included AKI in 58.1%, AKD without AKI in 13.1%, and CKD in 28.8%; 35.4% needed dialysis at the time of kidney biopsy; and 71.0% had decreased eGFRs at presentation (mean baseline eGFR, 40.6 ± 38.6 mL/min/1.73 m^2). In patients with type III, and especially type I with acute onset, crescentic GN mostly presented with AKI. Those with type I had higher rates of gross hematuria and oliguria and higher serum creatinine levels. Those with type II had a younger age, longer disease duration, greater female predominance, lower serum creatinine levels, higher amount of proteinuria, and more severe hypoproteinemia; they also had highly variable clinical presentations ranging from