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Clinical Pathological Analysis and Treatment of Iga Nephropathy with a Few Quantity of Renal Crescent Formation

Zhonghui Jia*, Lin shan, Jiang, Jianqing and Wei li

The nephrological department of Tianjin general hospital, Tianjin, China

Abstract

Background: IgA nephropathy was a syndrome of uniform morphology, diverse clinical features and uncertain prognosis, presence of crescents around blood vessels indices the unfavorable long-term prognosis, if the proportion of crescent in glomeruli exceeding ratio of 50%, we give the active treatment of prednisone pulse therapy, but in most condition, IgA nephropathy was diagnosed with a few of the proportion of crescent, these patient are the precondition of crescent IgA nephropathy or a special group of disease? Steroid therapy are suitable for these patient, especially for the patient with bulk fibrous crescent in renal tissue? How about the prognosis of IgA nephropathy with a few quatity of crescent formation, so we extended our original study to aim directly at above assumption. In this study, we report the results of an extended 2-year follow-up of our original randomized cohort of IgAN subjects who had crescentic formation using either steroid therapy alone or steroid pulse one kind of immunodepressant. **Objective:** To observe the clinical and pathological characteristics of IgA nephropathy (IgAN) with a few quality crescent formation in 63 patients.

Methods: Clinic pathological data of 63 patients with IgAN accompanied by crescents were analyzed. These patients were accepted in the group and were renal biopsied according to the percentage of glomeruli affected by crescents less than 50 % during 2007-2008, and their clinical and laboratory data were collected. **Results:** (1) Clinical features: all the patients aged 28.3±5.6 years had hematuria and proteinuria and gross hematuria (28.6 %) and large mounts of proteinuria were also common, protein excreted in urine was more than 3.5g per day in 14.2 % of the patients. The patient's accompied by hypertension was 60.3% and five patients present with malignant hypertension, and acute renal insufficiency were found by 7.9%. 38 patient present with increased serum level of IgA immuglobin.

(2) Renal pathology: the glomeruli were affected by crescents from 5 % to 47 %.Most crescents were cellular. All the cases had a diffuse mesangial proliferation and all the patients presented deposition of IgA, IgM and C3 in mesangial area. There were 9 specimens combined with the deposition of IgA around capillary. 18 patients were given steroid therapy with renal function ameliorated, serum creatinine of 3 patients with fibrous crescent formation were obviously decreased after large amount of steroid invention.

Conclusion: The main clinical features of IgAN with crescent formation were hematuria combined with proteinuria , especially persistent gross hematuria and severe proteinuria and some patients with AKI. However, the severity of clinical features and number of crescent was not positively relative. The hematuria, elevated plasma IgA and tonsils edema were independent risk factors of crescent formation in renal tissue. The steroid therapy for the patient with fibrous crescent in renal tissue showed a promising clinical effect, especially for the patients with fibrous crescent formation, so the clinical manifestation combined with pathological injury of renal tissue may contribute to the decision of therapy protocol.

Keywords: IgA nephropathy; Crescent formation; Plasma IgA ; Tonsil edema

Introduction

Clinical observations of patients who have undergone renal transplantation have provided strong support for the notion that IgA nephropathy is a systemic disease. IgA nephropathy was a syndrome of uniform morphology, diverse clinical features and uncertain prognosis, especially for the pathological type of crescent formation in the renal tissue, some patient of this type manifest with only mild microscopic hematuria, but with rather quatity of crescent in glomerular, except for renal biopsy, the clinical and experimental index establishment of judgement for the pathological changes degree are in demand. The energetic treatment for patient with crescent formation not more than 50% are invariably ignored by therapy decision maker, What is more, the clinical effect of steroid therapy for the patient with fibrous crescent in renal tissue especially for the patients with fibrous crescent formation is disputed, whether the long-term therapy of small dose of steroid is needed for the patient with mild laboratory change but with crescent formation are due to be identified.

Patients and methods

63 Patients of either gender accepted in hospital from 2007.3 to 2008.12 were eligible if they had histologically confirmed IgAN with a few quantity of crescent formation (<50%) and clinically excluded the systemic disease of SLE, Henoch-Schönlein Purpura Nephritis, the related clinical and experimental date were collected.

Histological assessment the histological diagnosis of IgAN was based upon the demonstration of mesangio proliferative changes on

***Corresponding author:** Zhonghui Jia, Anshan road 154, Tianjin, china 300052, Tel: 86-022-60362340; Fax: 86-02260362591; E-mail: jzhtff@yahoo.com.cn

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light microscopy and the concomitant presence of predominant or codominant mesangial deposition of IgA. Histological grading of all renal biopsy samples were determined by a central pathologist

Treatment of patient

Total of 48 patient accepted different dose of steroid therapy, five of which were given a pulse dose therapy of methyl prednisone for three days

Immune depressant treatment

mycophenolate for patients, cyclophosphamide for one patient, Tripterygium wilfordii for12 patient, Leflunomide Tablets for patients, angiotensin-converting enzyme inhibitor and receptor antagonist were used to control the blood pressure.

Patient follow-up

On study entry in 2007, full medical histories and physical findings were documented. Baseline investigations included full blood count, liver and renal biochemistries, 24-h urine protein excretion urinary albumin-to-creatinine ratio, creatinine clearance rate, serum IgA level, and plasma lipid profile. At each clinic visit, blood pressure, body weight, blood count, renal function, 24-h urine protein, urinary albumin-to-creatinine ratio, and creatinine clearance were monitored. To reduce variability, all assays were performed at a single central laboratory using standard methods.

Study end points

The primary composite outcome for between-group comparison was renal survival. ESRD was defined as the need to start dialysis or undergo kidney transplantation. Secondary outcomes included changes in urinary protein excretion rate and albumin-to-creatinine ratio, and the composite end point of doubling of baseline serum creatinine, end-stage renal failure, or death.

Statistical analysis

Data are presented as means ± s.e. The main efficacy analysis was performed on an intention-to-treat basis and included all patients who underwent randomization, multiple factor logistic regression analysis. All the date was analyzed applying soft ware of SPSS 15, discrepancy was defined as statistical significance for $P<0.05$.

Results

Clinical features

Just as showed in the (Table1), all the patients aged 28.3±5.6 years had hematuria and proteinuria, and gross hematuria (28.6 %) and large amount of proteinuria were also common , protein excreted in urine was more than 3.5g per day in 14.2 % of the patients. The patients accompied by hypertension was 60.3% and five patient present with malignant hypertension, and acute renal insufficiency were found by 7.9%. 38 patient present with increased serum level of IgA immuglobin.

The hematuria, elevated plasma IgA and tonsil edema were independent risk factors (Table 2).

Abnormal urine analysis is mostly seen in the onset symptom in IgA nephropathy with a few quatity of crescentic formation (Figure 1)

Circumstance of treatment

All the patient with renal dysfunction accept the therapy of different dose of steroid, After the therapy of steroid, the renal function of all the patient including 3 case of fibrous crescent in renal tissue improved for different degree, case in which reform the normal renal function (Figure 2).

After the follow-up for one year, 10 patients present the stabilizing normal renal function At the end point of follow-up for two years, five patient present with renal function injury, one of which got a doubled serum creatinine. one patient died from lung infection. eight patients

Clinical features	**results**
Gender	Male28/ Female35
age	28.3±5.6
Duration (days)	21.5±7.6
hypertesion (%)	60.3
tonsil edema (%)	65.1
Urine protein (g/24h)	1.21±0.62
Addision of urine redblood cell (ul)	821±235
Acute kidney injury(%)	7.9
Increased level of IgA (%)	60.3

Table1: Baseline clinical and histological characteristics of study.

Clinical feathers	partial regression coefficient	standard error	P value	OR Value
gross hematuria	1.086	0.057	0.043	2.257
tonsoli edema	0.058	0.025	0.026	1.568
Increased level of IgA	1.112	0.087	0.037	3.156

Table 2: Clinical multiple factor regression analysis of degree of crescent formationin in IgA nephropathy.

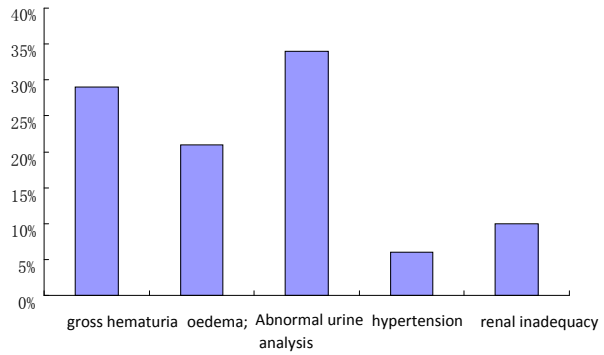

Figure 1: The different onset symptom of IgA nephropathy with a few quatity of crescentic formation.

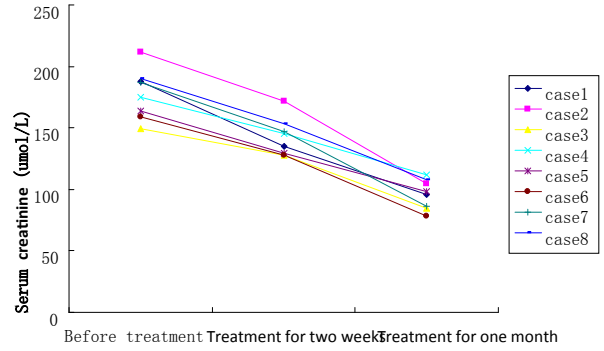

Figure 2: Short-term follow-Up and Outcome of the patient with renal dysfunction after treatment of steroid.

keep a stable renal function. Five of the fifteen patients not received the steroid treatment manifested with obvious increased urine protein at the 2 years follow up point, two of which present with gross hematuria.

Discussion

The clinical situation of IgA nephropathy can be in diversity just like showed in our study, which manifest with nephritic syndrome, acute kidney injury and mild abnormal urine test or only hypertension. Histologic evidence of recurrent IgA nephropathy is observed in over 35 percent of patients who receive renal allografts as treatment for end-stage renal disease due to IgA nephropathy. When a kidney obtained from a donor with asymptomatic IgA nephropathy is transplanted into a recipient with end-stage renal disease due to a disease other than IgA nephropathy, the deposits in the donor kidney rapidly disappear. Some but not all patients with IgA nephropathy have elevated serum IgA levels or elevated levels of IgA in a complex with fibronectin. However, no antigen has been consistently detected in circulating immune complexes containing IgA or in biopsy specimens from the kidneys of patients with IgA nephropathy. [1-4], our study showed that elevated plasma IgA and tonsoli edema were independent risk factors of crescent formation in renal tissue

Age of IgA patient varies separately and in our study present a mean age for 28years old and with youngest 15years old . One study by Daniel for 233 case of IgA N showed crescent formation got to 17.15%. One investigation reveals an incidence of 21.3% for crescent formation in IgAN of age between 4 and 14 years old, 1.9 % a study for 75 primary IgAN, 29 patients of which present with renal crescent formation [5-10], our study showed that the patient with renal crescent formation were companied with the elevated plasma IgA and tonsil edema, in our study, notwithstanding some patient showed the clinical manifestation of mild abnormal urine test, but in the renal tissue of which was found overtopping 20% crescent formation even fibrous nature, so the renal biopsy and rigorous follow-up is very important for these group of patients. Tangzheng proved that steroid adding the CTX are beneficial for the protein uria and renal function in the patient with large mount of renal crescent formation in kidney after a follow up of 29.18month. In our study steroid combined with immunodepressant treatment can sustain the recovered renal function for one year for the patient with acute kidney injury at the onset.

Potential mechanisms whereby this mucosal T-cell defect, which produces no clinically apparent symptoms, promotes glomerular deposition of IgA in patients with IgA nephropathy await definition. In some patients with IgA nephropathy, production of IgA1 in the bone marrow is increased and may be responsible for the observed increase in serum IgA1 levels [11-13]. Our study showed that elevated plasma IgA and tonsils edema were independent risk factors of crescent formation in renal tissue, the renal biopsy seemed to be very important for the patient with mild abnormal urin test but with elevated plasma IgA.

Since the features of IgA nephropathy identified by light microscopy are nonspecific, immune fluorescence in our study demonstrating a predominant deposition of IgA are essential to establish a definitive diagnosis of IgA nephropathy. There were 9 specimens combined with the deposition of IgA around capillary The immune-complex deposits are found predominantly within mesangial regions of glomeruli, with focal paramesangial or subendothelial extension. A variety of other immunoglobulins and complement are frequently co-distributed with IgA, including IgM, IgG, C3, but the position of IgA immunoglobulins in glomeruli contribute to the pathological type of IgA nephropathy, Since for large parts of IgA patients with pathological change of mesangial proliferation without crescent, so the deposition of IgA around capillary may be the cause of crescent formation just showed in our study.

IN our study, many patient only manifest with mild Abnormal urine analysis but with fibrous crescent formation in renal tissue [14-17]. In the early stages of the disease, many patients have no obvious symptoms and are unaware of any problems. In these patients, IgA nephropathy may be suspected only during routine screening or investigation of another condition. However, some patients may present with aggressive disease.

Crescents found on biopsy in this clinical setting imply a significantly more ominous outlook. Our Studies have suggested that the prognosis in IgA with crescents is worse than in other crescent disorders, with reported renal survival rates as low as 50% at 1 year and 20% at 5years. This is not the same as finding capsular adhesions or small non circumferential crescents in the glomeruli of patients but without the clinical scenario of rapid deterioration in renal function. This can be more common and in 1 series this type of crescent was present in 28% of biopsy specimens. In the setting of acute kidney injury, IgAN, unlike antiglomerular basement membrane disease, does not have exuberant or extensive extra capillary proliferation, so the exact number of crescents that should trigger alarm and more aggressive treatment is not well defined. However, even if only 10% to 20% of glomeruli show significant active crescents, in association with a decreasing GFR and/or increased proteinuria, this should be considered as indicative of an active disease process in our opinion and deserves aggressive treatment. If the crescents are fibrous or even fibro cellular, as opposed to cellular, they are less likely to reflect active disease and their response to intense immunosuppression is less likely. If either type of crescents is seen in the setting of severe glomerulosclerosis and extensive tubulointerstitial injury, a poor prognosis is almost inevitable. Serologic testing may be useful to rule out additional factors and to help identify patients with a better outlook.

However, In our report of fibrous crescent IgAN, for instance, a subgroup of patients with responded well to steroid and immunosuppression. In general, there are few characteristic clinical signs, however, microscopic hematuria and proteinuria may be persistently or intermittently detected for many years.

Just as showed in our study, patients with IgA nephropathy usually present with one of the following: episodes of macroscopic hematuria that may coincide with an infection of the upper respiratory tract (this presentation usually occurs in patients under 40 years of age, and loin pain often accompanies hematuria, or abnormal sediment in the urine and proteinuria in patients without symptoms (this presentation is usually more common in older patients but is observed in patients of all ages [18-20]. As previously discussed, the decision by a nephrologist to recommend renal biopsy in a patient without symptoms who has microscopic hematuria and mild proteinuria varies from region to region and remains a matter of debate even when IgA nephropathy is highly suspected. This relates in part to the lack of effective treatment in the early stages of the disease and the realization that none may be necessary. Moreover, although some mild cases progress to renal failure, there are no consistent genetic, immunologic, clinical, or morphologic markers that predict progressive disease in a patient without symptoms who has minor urinary abnormalities [20-22].

For patients with only minor urinary abnormalities who do not have hypertension, the general consensus is not to offer specific treatment but to follow such patients prospectively over many years. Up to 23 percent of patients will have a complete remission [23-25]. Our study showed that a small dose of steroid may be beneficial in patients of IgA nephropathy with crescent formation in aspect of avoidance from protein uria and hypertension. For the patient with fibrous crescent formation in glomeruli, we have proved that the renal function of patient with fibfous crescent in renal tissue can also be ameliorated by treatment of steroid combined with immunodepressant.

Finally, in our study, the tonsoli edema was proved as the independent risk factors of crescent formation in renal tissue, so the tonsillectomy, a popular practice in France and Japan, might be beneficial in patients with IgA nephropathy who have recurrent tonsillitis with crescent formation in renal tissue. A group of patients in France who underwent tonsillectomy had subsequent reductions in episodic hematuria and proteinuria. A prospective controlled study of the effect of tonsillectomy is needed because of the high degree of variability of IgA nephropathy; no study to date has shown long-term preservation of renal function in patients who undergo onsillectomy. variant of IgAN and which patients also may be amenable to therapy thus requires integration of both the clinical data (acute kidney injury) and histologic findings (pattern of acute crescentic glomerulonephritis with potentially reversible damage). As always, the potential benefits of an immunosuppression regimen should be balanced carefully against the risk such therapy carries for the patient.

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