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Original Article

The study of the constitution, mucosal inflammation, chinese medicine syndrome types and clinical pathology in IgA nephropathy

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Abstract: Objective: This study aims to investigate the constitution, mucosal inflammation, Chinese medicine syndrome types, and the clinical pathological characteristics of patients with IgA nephropathy (IgAN). Methods: Through a cross-sectional and retrospective study, we investigated 262 patients with IgAN in Guangdong provincial TCM hospital and the Third Hospital of Peking University between January 2011 and January 2014. Chinese medicine syndrome types, clinical and pathological data, constitution questionnaires, and the mucosal inflammation were obtained. Results: The constitution of the Yin-Yang harmony was the most common (40.5%), followed by Qi-deficiency (31.3%). Upper respiratory infection, chronic periodontitis and cystitis were common in patients with IgAN. Qi-deficiency of the spleen and kidney was the common type: 69.1%. Asymptomatic abnormal urinalysis (50.4% of patients) and CKD 1 (48.5%) were the most common clinical presentations. Haas was the most common pathological presentation (47.3%). In patients with Qi-deficiency of the spleen and kidney, the constitution of the Yin-Yang harmony presented with more non-mucosal inflammation, more CKD3-4, higher serum creatinine, urea nitrogen, and serum CH50 lever, and lower GFR, when clinically compared to patients with the constitution of Qi-deficiency. Conclusions: Asymptomatic abnormal urinalysis is the most common clinical type. Frequent upper respiratory infection, chronic periodontitis and recurrent cystitis were common in patients with IgAN. For IgAN patients with Qi-deficiency of spleen and kidney, the constitution of the Yin-Yang harmony had higher serum CH50 levels, lower incidence of mucosal inflammation, increased risk of declined renal function and more severe renal pathological changes.

Keywords: IgA nephropathy, constitution, mucosal inflammation, chinese medicine syndrometype, clinical pathological relationship

Introduction

IgA nephropathy (IgAN) is the most common primary glomerulonephritis worldwide, and the important cause of end-stage renal failure [1]. Genetic factors play an important role in the process of the occurrence and development of IgAN [2]. The characteristics and constitution of traditional Chinese medicine theory has certain similarities. The constitution often determines the bias of the Chinese Medicine Syndrome types [3]. Hence, the study of the constitution features of patients with IgAN has good guidance value to explore the prevention of IgAN. Abnormal mucosal immune response is one of the pathogeneses widely recognized for IgAN [4, 5]. This study aims to investigate the constitution, mucosal inflammation, Chinese medicine syndrome types, and the clinical and pathological characteristics of patients with IgAN, and to analyze their relationships, in order to provide scientific basis and new ideas for the management of IgAN.

Materials and methods

Patients, study design and oversight

Through this cross sectional and retrospective study, 262 patients with IgAN in Guangdong provincial TCM hospital and the Third Hospital of Peking University between January 2011 and January 2014 were investigated. Chinese medicine syndrome types, clinical and pathological data, the constitution questionnaire and muco-

Table 1. Distribution of constitution

Name	N	Percent (%)
Yin-Yang harmony constitution	106	40.5
Qi-deficiency constitution	82	31.3
Yang deficiency constitution	27	10.3
Yin-deficiency constitution	29	11.5
Phlegm dampness constitution	17	6.5
Damp heat constitution	16	6.1
Blood stasis constitution	4	1.5
Qi stagnation constitution	5	1.9
Allergic constitution	20	7.7

Table 2. Distribution of mucosal inflammation

Name	N	Percent (%)
Repeated upper respiratory infection	173	66
Chronic tonsillitis	61	23.3
Chronic periodontitis	115	43.9
Chronic gastritis	55	21
Repeated defecate deformed	53	20.2
Repeated dermatitis	100	38.2
Repeated ulcers of oral mucosal	46	17.6
Recurrent urinary tract infections	13	5
No Repeated mucosal inflammation	25	9.5

Table 3. Distribution of TCM syndrome type

Name	N	Percent (%)
Wind-heat invading lung	5	1.9
Lower energizer dampness-heat	7	2.7
Qi-deficiency of spleen and kidney	33	12.6
Yin-deficiency of liver and kidney	8	3.1
Qi and Yin-deficiency	181	69.1
Yang deficiency of spleen and kidney	28	10.7
Total	262	100

sal inflammation and their possible triggers were collected, in order to explore the possible relationships.

Diagnostic, inclusion and exclusion criteria

IgAN diagnostic criteria: With reference to the Kidney Disease Branch of the China association of Chinese medicine in 2007 of [The diagnosis, Syndrome differentiation type of IgA nephropathy, and curative effect evaluation (trial scheme)] standards [6].

Constitution criteria: With reference to the China Association of Chinese medicine in 2009 of the [Traditional Chinese medicine constitution classification and decision] standards [7].

Clinical classification of IgAN: With reference to the [Chinese kidney disease] Editor-in-chief Lei-Shi Li, Zhi-Hong Liu [8].

Mucosal inflammation criteria: With reference to the literature [9-11].

Renal pathology classification standard of IgAN: With reference to the Haas classification standard [12].

Inclusion criteria: (i) patients who were consistent with the diagnosis of primary IgAN standards, (ii) patients who provided an informed consent and good cooperation with the investigation team. and (iii) no limitations on gender and age.

Exclusion criteria: Patients under these conditions were excluded: (i) patients with secondary IgAN, (ii) patients combined with other renal diseases, and (iii) patients with other serious diseases such as heart failure, system, liver cirrhosis, cerebral infarction, cerebral hemorrhage, and blood disease.

Data collection

TCM syndrome diagnostic methods: First, the diagnosis was made by an trained attending doctor or vice director doctor, and was consistent with the unified standard of TCM syndromes in IgAN patients; then, the director doctor made the definitive diagnosis and determined the TCM syndrome type.

Laboratory examination: Patients in the hospital were given routine blood examinations, including renal function and urine analysis; and including all conventional methods for detection.

Diagnostics of the constitution: Patients were required to fill in the blanks of the constitution scale, which was calculated and saved by a trained attending doctor or vice director doctor; then, the director doctor made the definitive diagnosis and determined the constitution type.

Statistic analysis

SPSS 18.0 software was used for data processing, using the two-side test ($P<0.05$ was considered statistically significant). Measure-

Table 4. Distribution of clinical classification

Name	N	Percent (%)
Mass proteinuria type	32	12.2
Hypertention type	59	22.5
Asymptomatic abnorrmal urinalysis type	132	50.4
Gross hematuria type	31	11.8
End stage renal disease type	8	3.1
Simple microscopic hematuria type	0	0
Vasculitis type	0	0
Total	262	100

Table 5. Distribution of CKD staging

Name	N	Percent (%)
CKD1	127	48.5
CKD2	56	21.4
CKD3	57	21.8
CKD4	14	5.3
CKD5	8	3.1
Total	262	100

Table 6. Distribution of renal pathology classification

Name	N	Percent (%)
Haas I	37	14.1
Haas II	21	8.0
Haas III	124	47.3
Haas IV	44	16.8
Haas V	36	13.7
Total	262	100

ment data was expressed as Mean ± standard deviation (SD), and count data was expressed as rate and percentage. Paired *t*-test was used for the comparison of data in the normal distribution. Nonparametric test was used for data in non-normal distributions. The comparison between these two groups was examined by the independent two-sample *t*-test, if the data was normally distributed. Non-parametric test was used for non-normal distribution data. Chi-square test was used for count data examination. Logistic regression analysis was used for the multivariate analysis.

Results

Baseline characteristics

The male-to-female ratio of patients was 1.03:1, average age was 34.53±12.75 years old, and 38.5% of patients presented their disease within the age of 14-29 years old. The time between initial presentation and renal biopsy was 18.43±29.03 months.

Distribution of constitution, mucosal inflammation TCM syndrome type, clinical classification, renal pathology classification

Since some patients have two or three constitution characters and mucosal inflammation, The computation was repeated according to occurrence frequency. The constitution of the Yin-Yang harmony was the most common (40.5%), followed by the Qi-deficiency (31.3%) (**Table 1**). Upper respiratory infection, chronic periodontitis, and cystitis were very common in patients with IgAN (**Table 2**). Qi-deficiency of the spleen and kidney were the common type: 69.1% (**Table 3**). Asymptomatic abnormal urinalysis (50.4% of patients) and CKD 1 (48.5%) were the most common clinical presentations (**Tables 4** and **5**). Haas III was the most common pathological presentation (47.3%, **Table 6**).

Comparisons between Qi-deficiency of the spleen and kidney, and the constitution of the yin-yang harmony in IgAN patients and the constitution of Qi-deficiency in IgAN patients in renal function and immunity

In the investigation, the main constitution types in the 262 cases of IgAN patients were the constitution of the Yin-Yang harmony and Qi-deficiency. The main Chinese medicine syndrome type was Qi-deficiency of the spleen and kidney. Therefore, the clinical data of patients with Qi-deficiency of the spleen and kidney type were compared between the constitution of Yin-Yang harmony patients (92 cases) and Qi-deficiency patients (49 cases). Patients with Qi-deficiency of the spleen and kidney and the constitution of Yin-Yang harmony presented with more non-mucosal inflammation, more CKD3-4, higher than the latter in terms of the level of serum creatinine, urea nitrogen, serum CH50, and lower in GFR, when clinically compared to patients with the constitution of Qi-deficiency (**Table 7**).

Discussion

This study indicated that asymptomatic abnormal urinalysis (50.4% of patients) was the most common clinical presentation of IgAN in

Table 7. Comparisons between qi deficiency of spleen and kidney which the constitution of yin-yang harmony IgAN patients and the constitution of qi deficiency IgAN patients in renal function and immunity m (ql, qu) or Mean ± SD

Type	Qi deficiency of spleen and kidney patients which the constitution of Yin-Yang harmony (n=92)	Qi deficiency of spleen and kidney patients which the constitution of qi deficiency (n=49)	Z/t	P
No repeated mucosal inflammation	13 (9.2%)	3 (2.1%)	-6.573	0.014
CH50	43.68±1.19	36.32±9.86	3.504	0.001
BUN	7.07±4.07	5.25±2.47	-2.735	0.005
SCR	126.45±103.32	107.78±143.12	-0.574	0.375
eGFR	76.84±37.79	95.07±36.30	-2.867	0.006

patients. Hence, these can be easily overlooked. Regular health examinations are significantly important for the early discovery, prevention and intervention of this disease.

The constitution of the Yin-Yang harmony (40.8% of the patients) is more common. Furthermore, in the constitution characteristics of the 262 cases with IgAN, 50.4% of asymptomatic urinary abnormalities were consistent. This further indicates the occult of IgAN, which is easy to be misdiagnosed or untreated; quietly aggravating the condition.

It is known that genetic risk factors and mucosal immunity play very important roles in the pathogenesis of IgAN [13]. Upper respiratory infection, chronic periodontitis, and cystitis are very common in patients with IgAN [14-16]. Hence, we believe that in addition to the attention given by clinicians to respiratory infections, more attention should be given to chronic periodontitis, repeated inflammation of the skin and chronic gastrointestinal inflammation in IgAN; which can be easily overlooked.

Constitution has an important influence in the onset of the disease, which often determines the tendency of the disease and the change in syndrome types. Currently, there are more studies on IgA nephrotic syndrome [17-19], but the model can reflect a certain stage of the disease and not reflect the tendency of the patient. Our study suggests that the Qi-deficiency of the spleen and kidney was the common type: 69.1%. Hence, we have to analyze clinical indicators of the same syndrome type of different constitution of IgAN, in order to determine the clinical effect of the constitution for the spleen and kidney deficiency type IgAN.

Furthermore, our study suggest that IgAN patients with Qi-deficiency of the spleen and kidney and the constitution of the Yin-Yang harmony had higher serum CH50 levels, low incidence of mucosal inflammation, increased risk of declined renal function, and more severe renal pathological changes than that in patients with Qi-deficiency of the spleen and kidney and the constitution of Qi-deficiency. Hence, we believe that this difference may be worthy of further investigation. In addition, syndrome differentiation combination constitution may be more conducive to the clinical diagnosis and treatment of disease [20]. Even with the same syndrome type of IgAN, if the constitution was different, the prevention and treatment should be different. Therefore, we consider the combination of syndrome differentiation with constitution differentiation has a certain reference value for the forecast of the diagnosis and treatment of IgAN.

Through this research on the constitution, mucosal inflammation and unhealthy life style, Chinese medicine syndrome type and clinical pathology are related. We consider that starting from the constitution, changes in patients with bad life style, timely elimination and prevention of mucosal inflammation, and syndrome differentiation of traditional Chinese medicine combined with comprehensive measures of immune suppression of modern medicine should be a feasible idea and method of the prevention, cure and management of IgAN.

Therefore, we consider the combination of syndrome differentiation with constitution differentiation has a certain reference value for the forecast of the diagnosis and treatment of IgAN.

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Disclosure of conflict of interest

None.

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