Clinical Characteristics and Histopathological Findings in 120 IgA Nephropathy Patients in Thailand

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The authors reviewed the clinical and pathological findings in 120 IgA-nephropathy (IgAN) patients diagnosed at King Chulalongkorn University Hospital from 1994 to 2005. The average age of the patients was 36 years. Male and female ratio was 1:1.2. Thirty percent of the patients had hypertension. Thirty-four percent of the patients had serum creatinine greater than 1.5 mg/dl and had urine protein greater than 3 g/day. The most common presentation was asymptomatic urinary abnormalities (43%) followed by nephrotic syndrome (36%). Of note, many of the presented patients had advanced pathological classification and high tubulointerstitial (TI) fibrotic score. The clinico–pathological correlation was found significantly between serum creatinine and degree of TI fibrotic score by univariate analyses. Compared to other reports from Asian countries, the presented population had many worse prognostic markers including a decline in renal function, advanced pathologic findings, and high TI fibrotic scores. Further study on prognosis in Thai patients should be performed to help decision making in management of IgAN patients.

Keywords: *IgA nephropathy, Clinical, Pathology, Thailand*

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IgA nephropathy (IgAN), was firstly described by Berger and Hinglais in 1968[1]. It is now generally known to be the most common form of primary glomerulonephritis throughout the world[2] particularly in Asian and European countries, The diagnosis of IgAN exclusively relies on the demonstration by immunofluorescense (IF) of glomerular staining that is IgA-dominant or IgA co-dominant, involving the mesangium in a patient without evidence of systemic lupus erythematosus (SLE) or Henoch-Sch nlein Purpura (HSP)[6-7]. Although, light microscopic (LM) finding is unnecessary for making the final conclusion, it remains ultimately useful for indicating the chronicity and severity of the disease. In this regard, IgAN has a high diversity on LM features ranging widely from minimal histologic lesions to severe diffuse proliferative lesions with crescent formation or to advanced glomerulosclerosis at the other end, much as is the case with lupus nephritis. The most common histologic lesions are focal proliferative glomerulonephritis, accounting for between 40 and 50% of cases in both adults and children. In addition to the glomerular alterations, a variety of tubulointerstitial (TI) and vascular changes may be identified in patients with IgAN, including interstitial fibrosis, tubular atrophy, interstitial inflammation, vascular sclerosis, or red-cell casts and proteinaceous casts within the tubules. Assessment of these features may provide important prognostic information for patients with IgAN[6,8].

The typical renal manifestations are hematuria, which is usually microscopic, painless, and incidentally detected, or is gross hematuria associated with an upper respiratory tract infection (synpharyngitic hematuria)[3,9]. Other symptoms may be unexplained hypertension, nephrotic-range proteinuria, impairment of renal function, and occasionally end stage renal failure (ESRF)[3,9,10]. Rapidly progressive glomerulonephritis or acute renal failure occur rarely[10-11].

In Thailand, no one has ever reported the clini-

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cal manifestation and histopathologic finding of IgAN. Therefore, the objective of the present study was to do a detailed analysis of clinical, laboratory and pathological findings of renal biopsy. It is also to investigate the association among these factors.

Material and Method

1. Patient selection

Patients with a diagnosis of IgAN were selected from the renal biopsy registry that was done at the King Chulalongkorn University hospital from 1994 to 2005. The diagnosis of IgAN was reconfirmed by a compatible pathological finding on IF staining and by a clinicopathologic correlation. Patients were excluded if there were clinical, laboratory or serologic evidences of other systemic diseases, such as SLE, HSP, or chronic liver diseases.

2. Clinical Information

Baseline clinical and laboratory data of the renal biopsy were collected retrospectively from the primary case records of the time of the diagnostic. Patient characteristics including age, gender, mean arterial pressure calculated from systolic and diastolic blood pressure, concurrent anti-hypertensive medications, serum creatinine and creatinine clearance (measuring by 24-hr urine collection or estimation by Gault-Cockroft equation), and degree of proteinuria (measuring by UPCI or 24-hr urine protein were recorded. Indication for renal biopsy [asymptomatic urinary abnormalities (AUA), acute glomerulonephritis (AGN), rapidly progressive glomerulo nephritis (RPGN), nephrotic syndrome (NS), and chronic renal failure (CRF)], were also recorded.

3. Definitions of clinical finding

3.1 AUA defined as urine RBC > 5/HPF or proteinuria < 2 g/day or both

3.2 Nephrotic range proteinuria defined as 24-hr urine protein > 3 g with or without other clinical characters of NS.

3.3 CRF defined as persistence of creatinine clearance < 60 ml/min for > 3 months without other obvious cause.

4. Renal biopsy and pathological assessment

The pathologic features were classified into 5 histologic grades according to Hass' classification[18], which have been independently verified to be clinically relevant by many experts. The classification combined various glomerular and TI features together. In brief, subclass I defined as minimal LM histologic lesion, subclass II histologically resembled focal-segmental glomerulosclerosis, subclass III were focal proliferative glomerulonephritis, subclass IV were diffuse proliferative glomerulonephritis, and subclass V were advanced chronic glomerulonephritis. Besides the classification system, three other specific pathologic changes, such as percentage of crescentic glomeruli, TI fibrotic score and availability of arteriolar change were individually scored

5. Statistical analysis

Statistical analysis was performed by using the SPSS statistical package (SPSS version 13.0). Results were presented as means ($\pm$ SD) for normally distributed data, or median with percentiles for non-normally distributed data. Generally, more than two distributed continuous variables were compared using univariate analyses. A p-value of less than 0.05 was taken to indicate statistical significance.

Results

1. Clinical Characteristics

From the biopsy registry, 120 IgAN patients who had complete clinical information for reviewing were identified. There was a slight female preponderance at the ratio of 1: 1.2. The average age at biopsy was 36 (13-69 yrs) and 70% of all cases ranged between 25 to 50 years old. One third of the patients had hypertension and renal insufficiency with a mean serum creatinine of 1.88 mg/dl (0.4 to 11 mg/dl) and mean creatinine clearance of 67 ml/min (1.1 to 186 ml/min). The mean daily proteinuria level was 3 g (0 to 18.1). More detailed general conditions are displayed in Table 1

2. Pathological classification

Class V were the most common pathologic features of the patients and, comprised of 35%, followed by class II (28%), class I (19%), and class III (13%), and class IV (5%). In accord with class V, forty-two percent of the patients had moderate to severe TI fibrotic score and 24% had some degrees of arteriolar change.

3. Clinico-pathological correlation

Univariate analysis found significant correlation of serum creatinine and TI fibrosis. None of the remaining clinical markers showed the same correlation with the pathological features found in the renal biopsy. (data not shown)

Table 1. Indications for biopsy and pathological findings in patients with IgAN (N = 120)

Indications for biopsy	No. of patients (%)
Asymptomatic urinary abnormalities (N = 117)	53 (45.3%)
Acute glomerulonephritis	1 (0.9%)
Rapidly progressive glomerulonephritis	11 (9.4%)
Nephrotic range proteinuria	42 (36%)
Chronic kidney disease	10 (8.5%)
Pathologic classifications (N =106)	
Class I	20 (18.9%)
Class II	30 (28.3%)
Class III	14 (13.2%)
Class IV	5 (4.7%)
Class V	37 (34.9%)
Tubulointerstitial fibrotic score (N = 120)	
No	54 (45%)
Focal (< 10%)	13 (10.8%)
Mild (10-25%)	22 (18.3%)
Moderate (25-50%)	12 (10%)
Severe (> 50%)	19 (16%)
Presence of crescentic glomeruli	21 (17.5%)
Presence of arteriolar change	29 (24.2%)

Discussion

IgAN is the most common cause of primary glomerulonephritis worldwide. Studies from many countries throughout Asia, including China, Japan, and Korea found the prevalence of IgAN among primary glomerular diseases ranged from 22% to 47%[20-22]. In Thailand, the prevalence of IgAN has not been well established and was roughly estimated to be about 20%. From the authors' previous report, IgAN was the second most common primary glomerular diseases accounting for 22%[27].

Currently, this is the largest report of IgAN from Thailand consisting of 120 patients. The predominant mode of presentation was asymptomatic urinary abnormalities (45%), closely followed by NS (36%). One third of the patients had hypertension and a decline in renal function. Although, the majority of the patients presented with asymptomatic urinary finding, many of the patients had advanced pathological classification and high TI fibrotic score. The constellation of worse clinical and pathologic findings contradicts the results from many different Asian countries, for instance, Japan, Korea, and Hong Kong[19,22-25]. The discrepancy could be partly explained by the differences in accessibility to medical service and availability to perform a kidney biopsy, in medical screening systems, in kidney biopsy policy, and in decision to refer patients to nephrologists. In addition, the role of race and geographic difference should be considered[3-5]. However, a recent report with 478 IgAN patients from India had some similarities to the presented result. One third of the Indian patients presented with NS, hypertension and renal failure.

As mentioned above, one third of the presented patients had many poor prognostic factors; for example, high serum creatinine and daily proteinuria higher than 1 g, Haas's class V, and moderate–severe TI fibrotic score. Could these prognosis factors could apply to Thai patients? How can they be managed? Further study on prognostic factors and outcome of IgAN in Thailand should be performing to answer these questions.

Conclusion

The present study provides an insight into clinical and pathological findings of IgAN in Thailand, which is different from previous studies in Asia in some aspects. Further studies need to be done to evaluate the prognosis factors and outcome of IgAN in Thailand.

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รายงานการศึกษาลักษณะทางคลินิกผลตรวจทางห้องปฏิบัติการและลักษณะทางพยาธิวิทยาของผู้ป่วยโรคไตอักเสบไอจีเอ ในโรงพยาบาลจุฬาลงกรณ์สภากาชาดไทย

ตรี เหรียญสุวรรณ, เถลิงศักดิ์ กาญจนบุษย์, ทรงเกียรติ หลิวสุวรรณ, สมชาย เอียมอ่อง

รายงานการศึกษาย้อนหลังอาการแสดงทางคลินิก ผลตรวจทางห้องปฏิบัติการ และลักษณะทางพยาธิวิทยาของผู้ป่วยโรคไตอักเสบชนิดไอจีเอ (IgA nephropathy: IgAN) จำนวน 120 ราย โดยการคัดเลือกผู้ป่วยจากฐานข้อมูลผู้ป่วยไตอักเสบทั้งหมดของโรงพยาบาลจุฬาลงกรณ์ ตั้งแต่ปี พ.ศ. 2537 ถึง พ.ศ. 2548 พบว่าผู้ป่วย IgAN มีอายุเฉลี่ย 36 ปี มีสัดส่วนของเพศหญิงมากกว่าเพศชายในอัตรา 1.2:1, มีความดันโลหิตสูงเฉลี่ยร้อยละ 30, มีการเสื่อมหน้าที่ของไต แสดงโดยค่าพลาสมาครีอะตินินสูงกว่า 1.5 มก./ดล. ร้อยละ 34 โดยผู้ป่วยส่วนใหญ่ (ร้อยละ 43) จะไม่มีอาการผิดปกติใด ๆ ทางคลินิกขณะที่แพทย์ทำการวิเคราะห์ชิ้นเนื้อไตเว้นแต่บังเอิญตรวจพบความผิดปกติของปัสสาวะเท่านั้น รองลงมาคือมีอาการเข้าได้กับกลุ่มอาการทางคลินิกของภาวะเนฟโฟรติก (36%) เมื่อทำการตรวจวิเคราะห์ชิ้นเนื้อไตของผู้ป่วยพบว่าชิ้นเนื้อส่วนใหญ่จะมีการเสื่อมสภาพของเนื้อไตอย่างต่อเนื่องและเรื้อรัง ดังจะเห็นได้จาก ร้อยละ 35 มีการเปลี่ยนแปลงของชิ้นเนื้อเป็นแบบ advanced chronic glomerulosclerosis, ร้อยละ 55 มีพังผืดจำนวนมากกระจายอยู่ในเนื้อไตรอบ ๆ ท่อไต (tubulointerstitial fibrosis) และร้อยละ 24 มีการหนาตัวขึ้นของผนังหลอดเลือด จากที่ได้กล่าวมาทั้งหมดพบว่าผู้ป่วยคนไทยมีรอยโรคที่เรื้อรังมากกว่ารายงานที่ได้จากต่างประเทศ ทั้งประเทศในแถบภูมิภาคเอเชียเอง หรือ ต่างภูมิภาค ทั้งนี้อาจสืบเนื่องมาจากความแตกต่างในระยะเวลาที่แพทย์ส่งตัวผู้ป่วยมารับการเจาะเนื้อไตพิสูจน์ หรือเกิดจากรอยโรค IgA nephropathy ของคนไทยมีความจำเพาะเป็นเอกลักษณ์ต่างจากผู้ป่วยจากประเทศอื่น ๆ