Clinicopathological Features in the Japanese Patients with IgA Nephropathy

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The actual state of IgA nephropathy in Japan was surveyed throughout the nation by a questionnaire. Five hundred patients were collected from 26 departments of pediatrics and 2,175 from 27 internal medicine. IgA nephropathy accounted for 19.2% of the children and 30.0% of the adults among primary glomerular diseases. Most of the patients, regardless children and adults, were detected by chance proteinuria and/or hematuria. No significant difference of renal glomerular findings were observed morphologically, between the children and the adults. IgA nephropathy was characterized by relatively benign clinical course, namely, 87.2% of the children and 74.6% of the adults had a favorable outcome. Nephrotic syndrome developed in 4.6% of the children and 3.7% of the adults, and hypertension in 4.6% and 10.6% of the children and the adults, respectively. While, the fact should not be neglected that 1.8% of the children and 8.0% of the adults developed renal failure or died.

Key Words: IgA nephropathy, Chance proteinuria and/or hematuria, Annual physical check-ups

INTRODUCTION

It is believed that patients with IgA nephropathy account for more than 30% of patients with primary glomerular diseases in Japan, and a number of investigations on IgA nephropathy is reported every year. The fact that annual physical check-ups at schools and offices are registered in Japan is the background of this high incidence of discovery of IgA nephropathy. Therefore, a good few patients with IgA nephropathy are detected because of these opportunities. This disease is widely observed in both children and adults, but the clinicopathological features almost always vary with the reports. In this sense, it is an important problem in Japan to investigate the etiology of this disease.

At the 24th Conference of the Japanese Society of Nephrology, the authors were in charge of a

symposium on "IgA nephropathy." Taking this opportunity, the actual state of IgA nephropathy in Japan was surveyed throughout the nation by a questionnaire.

MATERIALS AND METHODS

The subjects were 2,675 patients consisting of 500 patients from 26 departments of pediatrics and 2,175 from 27 departments of internal medicine. The 500 and 2,175 patients corresponded to 19.2% and 30.0%, respectively, of the patients with primary glomerular diseases examined by the fluorescent antibody technique.

As for the age distribution at renal biopsy, the number of patients aged 20 to 24 was the largest at 520 (19.4%), and there were 1,381 patients (51.6%) aged 15 to 29 (Figure 1).

There were 304 boys and 196 girls, showing a

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Fig. 1. Age distribution

ratio of 1.55:1, and there were 1,157 male adults and 1,018 female adults, for a ratio of 1.15:1.

Clinicopathological features were investigated by comparing the results from children and adults, respectively.

RESULTS AND DISCUSSION

Clinical features

Figure 2 shows the mode of onset and mode of detection (Figure 2). Chance proteinuria and/or hematuria, which is accidentally detected by

Fig. 2. Mode of onset

annual physical check-ups at schools and offices, was observed in 74.2% of the children and in 64.8% of the adults. Since the law obliges school-children and adults to undergo urinalysis in Japan, there are rather many cases of nephritis detected as chance proteinuria. This fact seems to be the greatest reason why IgA nephropathy is very frequently observed in Japan.^{1, 2)}

Table 1 shows the clinical symptoms and results of examinations before renal biopsy (Table 1). Approximately 20% of both the children and adults showed intermittent proteinuria, but, in most of the patients, mild proteinuria and hematuria persisted. Nephrotic syndrome was observed in 7.1% of the children and 4.6% of the adults, respectively.

CFR (Ccr) of more than 80 ml/min was observed in 87.5% of the children, 78.8% of the adults, while Ccr of less than 49 ml/min was particularly observed in 4.5% of the adults. It is believed that these findings resulted from the fact that more patients in whom the period from onset to renal biopsy was very long were included in the adult group as compared with the children.³⁾

It is believed that the serum level of IgA is generally high in IgA nephropathy, but this was the case in only 27.8% of the children and 46.4% of the adults.⁴⁾

Pathological features of the kidney

The renal biopsy findings of the subjects studied are as follows.

Table 1. Clinical features

	CHILDREN	ADULTS
● PROTEINURIA		
INTERMITTENT	20.4 (%)	18.8 (%)
PERSISTENT	72.5 "	76.6 "
NEPHROTIC SYNDROME	7.1 "	4.6 "
● HEMATURIA		
NEGATIVE	4.0 "	6.0 "
MICROSCOPIC	81.9 "	80.1 "
MACROSCOPIC	14.1 "	13.9 "
● GFR (Ccr)		
≥ 80 ml/min	87.5 "	78.8 "
79 ml/min ~ 50 ml/min	11.5 "	16.7 "
≤ 49 ml/min	1.0 "	4.5 "
● SERUM IgA		
NORMAL	72.2 "	53.6 "
HIGH	27.8 "	46.4 "

As a result of investigation of light microscopic finding on the basis of the classification of glomerular diseases by WHO, WHO-A, that is a minor lesion, was observed in 22.5% of the children and 19.4% of the adults, WHO-B, that is a focal glomerulonephritis, was observed in 28.2% of the children and 27.1% of the adults, WHO-C-1, that is diffuse mesangial proliferative glomerulonephritis, was observed in 49.7% of the children and 52.5% of the adults (Figure 3). Thus, there was no significant difference between children and adults in Japan in the light microscopic findings of IgA nephropathy.

Immunofluorescence features revealed IgA and IgG, IgM or C₃ in most of the children and most of the adults. On the other hand, IgA alone without complements was observed in 17.6% of the children in contrast to 6.9% of the adults (Figure 4).

Fig. 3. Histological classification

Fig. 4. Immunofluorescence

Fig. 5. Clinical course

Concerning the mode of glomerular deposits of IgA globulin, most of the patients showed a mesangial pattern, but IgA deposits were observed in the glomerular wall as well as the mesangium in 23.7% of the children and 31.9% of the adults. Some investigators in Japan consider such cases, in which immunoglobulin deposits are observed also in the glomerular wall, as a separate variant type, while others do not recognize this condition as IgA nephropathy.⁵⁾ Thus, no definite mode of treatment of such patients has yet been established.

Clinical course

The clinical course was studied in 481 children and 1,349 adults, and the mean follow-up period was 29 months and 39 months, respectively (Figure 5).

Clinical remission was observed in 20% of the children and 6.5% of the adults. The results of the present study revealed that most of the children and the adults showed a favorable course. On the other hand, however, the disease progressed in 12.8% of the children (1.8% of them had renal failure or died) and 26.2% of the adults (8.0% of them had renal failure or died).

During the period of observation of the course, 4.6% of the children and 3.7% of the adults, showed nephrotic syndrome. Hypertension occurred in 3.5% and 10.6% of the children and the adults, respectively.

The actual state of IgA nephropathy in Japan was revealed by a questionnaire as follows:

1. IgA nephropathy accounted for 19.2% and 30.0% of the children and the adults, respectively, among primary glomerular diseases.

2. It very often occurs in young adults, primarily aged 20–24 years, and particularly in men.

3. Most of children and adults had chance proteinuria and/or hematuria.

4. Mild persistent proteinuria and hematuria were observed in about 75.0% of both the children and the adults.

5. Although the renal function was in the normal range at renal biopsy in most of the patients, the number of adults who showed slight hypofunction was greater than that of children.

6. The ratio of A:B:C-1 of renal glomerular findings according to the WHO classification was approximately 1:1:2 in both children and adults.

7. Immunofluorescence features revealed IgA and IgG, IgM or complement in most of the children and the adults. On the other hand, IgA alone without complements was observed in 17.6% of the children in contrast to 6.9% of the adults.

8. Favourable results were obtained in 87.2% of the children and 74.6% of the adults, including those with clinical remission and in the "latent" stage. There was no significant difference in the incidence of nephrotic syndrome between the

children and the adults, at 4.6% and 3.7%, respectively, but hypertension was more often observed in the adults (10.6%) than in the children (4.6%).

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