Parent and Child Cases of IgA Nephropathy Associated with von Recklinghausen's Disease

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Table 1. Serological typing for HLA-A, -B, -C, -DR, and -DQ antigens

Dear Sir,

We present parent and child cases of IgA nephropathy associated with von Recklinghausen's disease.

Case 1: In April 1987, a 41-year-old woman was referred to our department because of episodes of proteinuria and occult hematuria concomitant with febrile upper respiratory tract infections. A renal biopsy done at this time revealed IgA nephropathy, moderate degree. In 1988, she was diagnosed as having von Recklinghausen's disease at the Dermatology Department of our hospital. In 1995, her renal function deteriorated gradually, so she was admitted for a second renal biopsy. Physical examination revealed multiple soft, small tumoral masses, which were pathologically diagnosed as being fibromas, along with café-au-lait spots and diffuse freckles. Her extremities were also slightly edematous. Abnormal laboratory findings were: urinary protein 2+, occult hematuria 3+, urinary protein excretion 0.8 g/day, BUN 19 mg/dl, serum creatinine 0.89 mg/dl, uric acid 6.0 mg/dl, creatinine clearance 58.5 ml/min, and serum β 2-microglobulin 2.79 μ g/ml. Her serum IgA level was normal. Microscopic examination of her renal biopsy tissues revealed sclerotic lesions such as global sclerosis or adhesions of Bowman's capsule, and marked tubulointerstitial lesions were found. Immunofluorescent findings revealed IgA and C3 mesangial deposits. Electron microscopic examination showed slight dense deposits in the mesangial areas.

Case 2: A 24-year-old man, the son of case 1, was referred to our hospital in January 1989 because of episodes of proteinuria and occult hematuria concomitant with upper respiratory tract infections. He was also diagnosed as having von Recklinghausen's disease at the Dermatology Department of our hospital in 1989. He was admitted to our hospital in September

1994 due to gradual increasing of proteinuria. Physical examination revealed multiple soft, small tumoral masses which were pathologically diagnosed as being fibromas, and he had café-au-lait spots and diffuse freckles as well. Abnormal laboratory findings were: urinary protein 2+, occult hematuria 2+, urinary protein excretion 3.3 g/day, serum total protein levels 5.7 g/dl, BUN 20 mg/dl, serum creatinine 1.25 mg/dl, uric acid 6.5 mg/dl, creatinine clearance 59.8 ml/min, and serum β_2 -micro-globulin 3.71 $\mu\text{g/ml}$, but the serum IgA level was within the normal range. Microscopic examination of his renal biopsy tissues revealed that 3 of 13 glomeruli were sclerotic,

and fibrocellular crescents or adhesions were also noted. In addition, slight tubulointerstitial lesions were found. Immunofluorescent findings revealed IgA and C3 mesangial deposits. Electron microscopic examination revealed that dense deposits were scattered in the mesangial areas. None of these patients lost constitutional heterozygosity for any of the markers on chromosome 17p or 17q. Moreover, none of these patients were found to contain germline mutations of p53 gene at exon 3-9. On the other hand, HLA typing revealed B35, DR4 and DQ4 in both patients (table 1).

Cases such as these, in which IgA nephropathy is associated with von Recklinghausen's disease, are very rare. Von Recklinghausen's disease is a common autosomal dominant disorder characterized by abnormalities in multiple tissues derived from the neural crest, particularly benign neurofibromas whose malignant transformation to neu-

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rofibrosarcomas can be fatal [1,2]. Recently, the NF1 gene was mapped to a region of chromosome 17q, and the formation of malignant neurofibrosarcomas may result from several independent genetic events including mutation of the NF1 gene, the tumorigenic mechanism of which is unknown, and subsequent loss of a tumor suppressor gene on 17p, most likely p53 [3]. Although no genetic relationship between IgA nephropathy and von Recklinghausen's disease was apparent in these 2 cases, some investigators have reported that the prevalence of DQ4/8/9 and DR4 is high among Japanese patients with IgA nephropathy [4, 5]. The present cases provide further evidence of an association between DR4-DQ4 and Japanese with IgA nephropathy.

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