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Membranous nephropathy occurred in a patient with Turner's syndrome during rhGH treatment

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An 11-year-old girl with membranous nephropathy with Turner's syndrome is reported. Hematuria and proteinuria were noted after started the recombinant human growth hormone (rhGH) treatment. The renal biopsy showed membranous nephropathy. She went into complete remission after 6 months of treatment with predonisolone, dipyridamole, and angiotensin-II receptor blocker, rhGH treatment was continued during the treatment of membranous nephropathy without problems.

We must carefully follow up for any renal complication in those who have Turner's syndrome and who have received rhGH treatment.

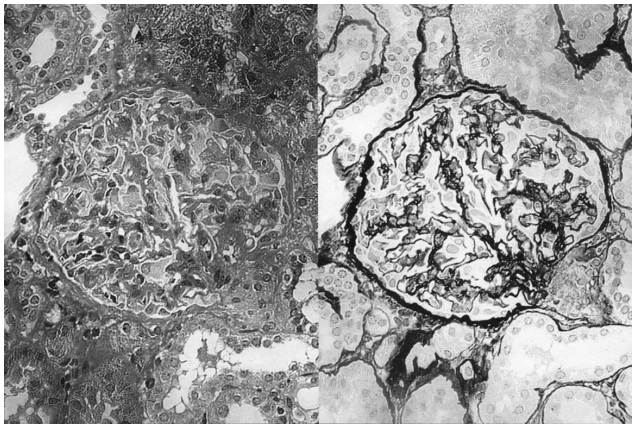
Key words: membranous nephropathy, Turner's syndrome, rhGH

Introduction

Turner's syndrome is a disease caused by complete deletion of X chromosome or mosaicism of the short arm of the X chromosome. It occurs in 1 of 10,000 girls. Short stature, sterility, and webbed neck are characteristic findings, and congenital heart and urinary tract abnormalities are often associated with this syndrome. Urinary tract abnormalities like horseshoe kidney and duplication of pelvis or urinary tract appears in 33% to 43% of these patients with Turner's syndrome.[1,2] There are a few reports of Turner's syndrome associated with chronic nephritis.[3,4] We report a case of Turner's syndrome with membranous nephropathy raised during recombinant human growth hormone (rhGH) treatment.

Case

An eleven-year-old girl with short stature was diagnosed to have Turner's syndrome (45XO). She also had webbed neck and horseshoe kidney. When she was 10 years old, rhGH treatment (0.35 mg/kg/week) was started. Nine months after starting rhGH, she developed severe proteinuria with hematuria. Her serum protein was 5.0 g/dl and serum cholesterol was 315 mg/dl. Urinary protein was 3+ and urinary occult blood was 3+ with 94 RBC/ HPF (red blood cell/ high-power field) in the sediments. Serum creatinine and complement levels were normal, antinuclear antibody titer was normal. Renal biopsy performed at the age of 11 years showed diffuse and segmental mesangial cell proliferation with slight matrix increase by light microscopy (Figure 1) and subepithelial deposits were found by electron microscopy (Figure 2). There were no crescents or subendothelial deposits. She was diagnosed as having membranous nephropathy. She was treated with predonisolone (1 mg/kg/day) and



A **B**

Figure 1. Diffuse and segmental mesangial cell prolifration with slight mesangial matrix increase is noted. Masson trichrome stain (**A**) and PAM stain (**B**) (×200).

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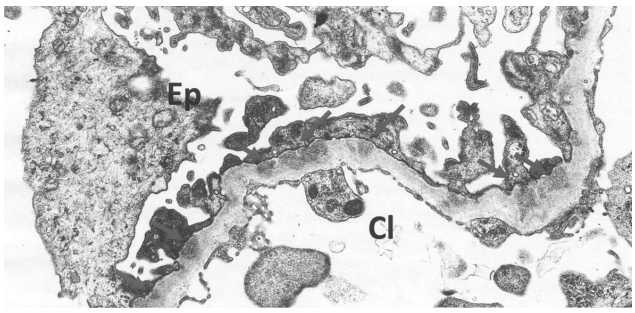

Figure 2. Subepithelial deposits along GBM are seen. Electron microscopy (×3,000)

dipyridamole (3 mg/kg/day), angiotensin-II receptor blocker (ARB) (valsartan 0.5 mg/kg/day). She went into complete remission 5 months later. Nephrotic syndrome did not relapse during the 3 years of rhGH treatment.

Discussion

There are some reports shows about the relationship between Turner's syndrome and the autoimmune disorders of Hashimoto's disease,[5,6] Juvenile rheumatoid arthritis,[7] Crohn's disease[8,9] and systemic lupus erythematodes (SLE).[10]

There are also several case reports of renal disease such as IgA nephropathy and focal glomerulosclerosis (FSG) associated with Turner's syndrome.[4,11] The etiology of these renal diseases in Turner's syndrome is not known.

Goodyer et al. reported a patient with Turner's syndrome and membranous proliferative glomerulonephritis.[3] Pathological findings of our patient suggest idiopathic membranous nephropathy. She did not have clinical findings or laboratory data suggesting SLE.

Treatment with rhGH is useful for growth failure in short stature children. But there are some reports of renal disease occurring during rhGH treatment. Renal function was exacerbated by rhGH therapy in those patients or caused glomerulonephritis.[12] Idiopathic membranous nephropathy is rarely occures in childhood. To our knowledge, there is only one report that shows membranous nephropathy occurring during rhGH treatment without anti-GH antibody.[13]

Natural-killer activity was depressive in patients with low GH.[14] Rapaport et al.[15] showed that the percentage of B cells transiently decreased to subnormal levels after rhGH treatment suggesting that the patients' immune responses were changed by rhGH. GH increased serum concentrations of mannan-binding lectin (MBL).[16] Glomerular deposition of MBL is present in 24% of deposition of IgA nephropathy.[17] The immunorogical effect of MBL may participate in membranous nephropathy of Turner's syndrome.

The blood hormone levels are normal in patients with Turner's syndrome, but in those cases, the immune abnormalities are known. As the GH has an effect on glomerular podocytes in GH transgenic mice it may develop MN during rhGH administration in patients with Turner's syndrome.[18] The present case also developed proteinuria during rhGH treatment. We used steroids then the proteinuria and hematuria improved and the renal function did not deteriorate during rhGH treatment in this patient.

Formerly, rhGH was a standard treatment for short stature in patients with Turner's syndrome. We must carefully follow up the effects of GH on nephritis in patients with Turner's syndrome who are receiving rhGH treatment.

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