Membranous Nephropathy Associated with Chronic Thyroiditis

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Dear Sir,

In membranous nephropathy, the deposits of immune complexes in the glomerular basement membrane are shown in immunofluorescence. Recently, several cases of immune complex-type nephritis in which components of the thyroid gland are considered to be antigens have been reported [1-7]. We discuss a possible association between membranous nephropathy and chronic thyroiditis in such a case.

A 43-year-old Japanese female was referred to our hospital for the evaluation of proteinuria. There were a diffusely enlarged, slightly hard struma and moderate edema of the lower extremities. The laboratory findings were as follows: urinary protein, 3.7 g/day; C₃, 0.56 g/l; C₄, 0.11 g/l; antinuclear antibody, 1:640; anti-DNA antibody, undetectable; antimicrosome antibody, 1:6,400; antithyro-globulin antibody, undetectable; TSH, 6.0 mU/l; free T₃, 0.026 nmol/l; free T₄, 12.5 pmol/l; total protein, 45 g/l; creatinine, 33.3 μmol/l; and total cholesterol, 6.53 mmol/l. A renal biopsy with immunofluorescent study using antihuman IgG, IgM, and C₃ antibodies revealed diffuse granular deposits along the glomerular capillary walls. However, such deposits were not demonstrated when using antithyroglobulin and antimicrosome antibodies. An electron-microscopic study revealed exclusive subepithelial electron-dense deposits. From these findings, the diagnosis of membranous nephropathy associated with chronic thyroiditis was made. In addition, natural killer (NK) activity was 1.4% (normal: 9-30%), while the percentage of CD3⁺, CD4⁺ and CD8⁺ lymphocytes, lymphocyte blast formation reactive to PHA, ConA, and PWM; and antibody-dependent cell-

ated cytotoxic activity were all within the normal range. A month later, the administration of triiodothyronine 25 µg/day for hypothyroidism and of prednisolone 50 mg/day for membranous nephropathy were started. Urinary protein gradually decreased, serum level of total protein increased, and the struma decreased in size within 2 months. Prednisolone was tapered off and she is quite well presently.

Several cases of chronic glomerulonephritis complicating chronic thyroiditis have been reported. However, details are not known about the relationships between the two diseases. Several cases in which hypo- or hyper-thyroidism and glomerulonephritis coexist including 3 cases of membranous nephropathy were reported previously [1,4,6]. However, the histopathological findings were heterogeneous among them.

Antithyroglobulin and/or antimicrosome antibodies were detected in 9 such cases [1-7] suggesting that thyroid antigen-antibody complexes could be involved in the onset of glomerular lesions. In our case, glomerular deposition of thyroglobulin or microsome was not demonstrated; unfortunately, unknown antigen-antibody complexes associated with thyroid components might have existed. Of course, a chance association could not be excluded.

It is known that various abnormalities in the lymphocyte functions exist in autoimmune diseases such as systemic lupus erythematosus (SLE). While antinuclear antibody was positive in our case, SLE was clinically unlikely. Among immunological tests performed, only NK activity was reduced. Decreased NK activity was rarely reported in both chronic thyroiditis and membranous nephropathy. Although the relationship between autoimmune diseases and NK activity was not clarified, the decrease in NK activity might be responsible for the occurrence of the two diseases.

References

- O'Regan S, Fong JSC, Kaplan BS, Chadarevian JP, Lapointe N, Drummond KN: Thyroid antigen-antibody nephritis. *Clin Immunol Immunopathol* 1976;6:341-346.
- Plotz DW, Fitz A, Schnetzler D, Seidenfeld J, Wilson CB: Thyroglobulin-antithyroglobulin immune complex glomerulonephritis complicating radioiodine therapy. *Clin Immunol Immunopathol* 1978;9:327-334.
- Jordan SC, Johnston WH, Bergstein JM: Immune complex glomerulonephritis mediated by thyroid antigens. *Arch Pathol Lab Med* 1978;102:530-533.
- Horvath F Jr, Teague P, Gaffney E, Mars DR, Fuller TJ: Thyroid antigen associated immune complex glomerulonephritis in Graves's disease. *Am J Med* 1979;67:901-904.
- Jordan SC, Buckingham B, Sakai R, Olson D: Studies of immune-complex glomerulonephritis mediated by human thyroglobulin. *N Engl J Med* 1981;304:1212-1215.
- Wever HP Jr, Cawley LP: Membranous glomerulonephritis: Thyroid antigen-antibody immune complex MGN. *J Kans Med* 1981;82: 397-399.
- Mizuno M, Hasegawa H, Fujishiro T, Murai S, Yanai T, Kojima K, Funahashi N, Ogawa T, Kawashima S: Chronic thyroiditis complicated by nephrotic syndrome and mixed hydronephritis. *Jpn J Nephrol* 1987;29:561-569.