Membranous Nephropathy Associated with Oxaprozin Treatment

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change was minimal, and arteriolosclerosis was mild. Silver methenamine stain disclosed 'spikes' over the outer part of the basement membrane of some loops. Immunofluorescent studies showed granular deposits of IgG and C3 along the glomerular capillary wall. Electron microscopy examination showed effacement of foot processes with subepithelial dense deposits (fig. 1). Pulmonary or gastrointestinal diseases were not found by routine radiological examinations. Conservative treatment with diet and salt restriction was started instead of cortico-steroid. In addition, enalapril 5 mg daily was added to nifedipine. The urine protein grad-

Dear Sir,

Nephrotic syndrome (NS) sometimes develops during treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) [1, 2]. Minimal change nephrotic syndrome (MCNS) is most frequent [1-3], but membranous nephropathy (MN) has also been reported in association with NSAIDs [4-8]. Herewith we describe a case of MN developing after treatment with oxaprozin.

A 36-year-old man with hypertension had been admitted to the Chiba University Hospital because of leg edema. The patient had no past history of renal disease, alcohol abuse, or recent infection. He had been given nifedipine for more than 2 years, but no side effect was noted. Two months before the admission, oxaprozin at a dose of 200 mg daily had been added because of persistent low back pain. Six weeks after oxaprozin was started, he noticed peripheral edema. He stopped taking oxaprozin, but the edema was progressive. On admission, he had massive edema of the legs and mild hypertension (165/92). Serum creatinine was 106 $\mu\text{mol/l}$, serum albumin concentration was 26 g/l, and urinary protein excretion was 4.5 g/day. Urinalysis showed a few red and white cells, but urine sugar was negative. Negative or normal values included complete blood count, fasting blood glucose, transaminases, HBs antigen, α -fetoprotein, carcinoembryonic antigen, rheumatoid factor, antinuclear and anti-DNA antibodies, complement, and cryoglobulinemia. The renal biopsy

was performed on the third hospital day. On light microscopy, the capillary walls were diffusely thickened. Tubulointerstitial

Fig. 1. Electron micrograph showing effacement of foot processes and subepithelial dense deposits. $\times 6,900$.

usually fell to 3 g/day over 1 month, and he was discharged. One year later he became well with no edema, and the urine protein decreased below 0.1 g/day.

MN is extremely unusual as a complication of treatment with NSAIDs [1, 2]. This form of glomerulopathy was reported in association with diclofenac [4, 5], phenylbutazone [6], ketoprofen [7], and fenoprofen [8]. The pathogenesis of MN in these cases has not been elucidated [8]. Concomitant interstitial nephritis (IN) might have contributed to the development of MN, but Campistol et al. [5] reported isolated MN without IN after ketoprofen treatment. Interstitial nephritis

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was also absent in our case, but the protein-uria developed after oxaprozin treatment, and decreased after withdrawal of the drug without addition of steroid. Therefore, oxaprozin might have contributed, at least in part, to the development or progression of MN in our case. To our knowledge, oxaprozin-associated NS has not been reported [9]. We would stress that urine protein should be carefully monitored during treatment with any kind of NSAIDs. Our case also suggests that NS during NSAIDs treatment is not necessarily dependent on MCNS or IN.

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Nephron 1996;74:439-440

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