□ SHORT COMMUNICATION □

Marked Reduction of Proteinuria after Eradication of Gastric *Helicobacter pylori* Infection in a Patient with Membranous Nephropathy: Coincidental or Associated?

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Membranous nephropathy is a common cause of nephrotic syndrome in adults. It is thought to be mainly a primary or idiopathic form; however, it may also be secondary to many other diseases (e.g., infections, drugs, neoplasms, and autoimmune diseases). Here, we describe a patient with membranous nephropathy, whose nephrotic-range proteinuria was markedly reduced after the eradication of gastric *Helicobacter pylori* infection.

A 34-year-old Japanese woman was admitted because of proteinuria and hematuria. She had no remarkable medical history (i.e., urinary abnormalities or hypertension); however, two months prior to admission she was noted to have urinary abnormalities and iron-deficiency anemia at a routine health examination. She also complained of dyspepsia; thus, gastric endoscopy was performed, which revealed no ulcers, but histologically revealed *H. pylori* infection in the gastric mucosa. On admission, laboratory examination revealed microcytic anemia (hemoglobin, 9.9 g/dl), hypoalbuminemia (2.7 g/dl) and nephrotic range-proteinuria (4.8 g/day) without active urinary sediments. Renal biopsy revealed normocellular glomeruli with mild capillary wall thickening. Immunofluorescent microscopy disclosed granular deposits of IgG and C3 on the capillary wall, but no deposits of IgA, IgM, C4, or C1q. Electron microscopy revealed small and discrete electron-dense subepithelial deposits without surrounding glomerular basement membrane reactions, indicating stage I membranous nephropathy. Immunohistochemistry with anti-*H. pylori* antibodies revealed that the positive staining was found only in the gastric mucosa, but not in the glomeruli from her biopsy specimens (1). Taken together, the fact that the serological studies (e.g., complements, anti-nuclear antibodies, and hepatitis B/C) yielded negative/normal results, and that she had not taken any medications, her membranous nephropathy was regarded as an idiopathic

form.

She showed dyspepsia and iron-deficiency anemia with negative results of fecal occult blood tests, which might have been related to *H. pylori* infection (2); thus, we administered *H. pylori* eradication therapy: lansoprazole, 30 mg twice daily, plus amoxicillin, 0.75 g twice daily, plus clarithromycin, 200 mg twice daily, for 7 days. Four months after this eradication therapy, her gastric symptoms and anemia were improved (hemoglobin, 12.7 g/dl, Table 1), and her urinary protein excretion had markedly decreased (0.76 g/day, Table 1) without any treatments for nephrotic syndrome (e.g., corticosteroids or angiotensin-converting enzyme inhibitors/angiotensin II receptor antagonists, or anti-platelet drugs). Six months after this treatment, the eradication of gastric *H. pylori* infection was confirmed with endoscopic gastric mucosa biopsy. One year after the eradication of the infection, her proteinuria remains decreased at less than 0.3 g/day (Table 1).

It is well-known that approximately 30% of the cases of membranous nephropathy resolve spontaneously; however, the occurrence of spontaneous complete remission of this nephropathy within one year from its onset is thought to be rare (less than 5%) in the untreated patient, as Schieppati et al have reported (3); thus, the eradication of gastric *H. pylori* infection might have contributed to the marked reduction of proteinuria in the present case. The proteinuria associated with membranous nephropathy is thought to be caused by functional impairment resulting from the formation of *in situ* subepithelial immune deposits and complement activation. Therefore, considerable efforts have been devoted to the identification of antigens involved in human membranous nephropathy, and certain antigens (e.g., hepatitis B/C, tumor antigens, and DNA-containing materials) have been identified in the immune deposits in patients with so-called secondary membranous nephropathy; however, the pathogenetic role of these antigens in the development of membranous nephropathy has not been confirmed (4). Nagashima et al have reported the presence of *H. pylori* antigens in the glomeruli of membranous nephropathy patients (1). Moriyama et al also found a significantly higher *H. pylori* infection rate in membranous nephropathy patients than in their control group (5). Further, they reported that eradication of *H. pylori* markedly reduced urinary protein excretions in three of four membranous nephropathy patients who were receiving corticosteroid therapy (5). These reports indicate that *H. pylori* infection might play an important role in the development of this disease. In the present case, the immunohistochemistry findings revealed no deposition of *H.*

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Table 1. Laboratory Findings in the Present Case

Variable	0 mo	2 mo	4 mo	6 mo	8 mo	10 mo	12 mo	reference range
Hemoglobin (g/dl)	9.9	10.7	12.7	13.8	13.8	14.8	15.2	11.3-15
Red blood cells ($\times 10^4/\mu\text{l}$)	496	525	547	525	486	509	532	380-480
MCV (fl)	67	66	74	81	86	86	84	83-100
Total protein (g/dl)	4.7	5.0	4.9	5.3	5.3	5.5	5.8	6.3-8.3
Albumin (g/dl)	2.6	3.0	3.0	3.3	3.1	3.3	3.5	4-5.2
Creatinine (mg/dl)	0.43	0.43	0.44	0.44	0.42	0.42	0.45	0.4-0.8
Blood urea nitrogen (mg/dl)	8	10	9	10	9	12	11	8-20
Total cholesterol (mg/dl)	257	286	241	223	214	199	204	125-220
Urinary total protein (g/day)	4.8	2.0	0.76	0.50	0.72	0.39	0.24	
Ferritin (ng/ml)	3.7	NT	19.7	20.7	NT	NT	48.7	10-80
Notes	GF ↑ Eradication of <i>H. pylori</i> ↑ Sodium Ferrous Citrate (50mg/day)							

mo, months; MCV; mean corpuscular volume; NT, not tested; GF, gastric endoscopy with mucosal biopsy

pylori antigens in the glomeruli. Our patient showed the early stage of membranous nephropathy (Stage I); thus, there is a possibility that enough amounts of *H. pylori* antigens, which can be detected with immunohistochemistry, might not have deposited in our patient's glomeruli. Therefore, the eradication therapy of *H. pylori* could prevent further glomerular deposition of its antigens, which might suppress the progression of membranous nephropathy, resulting in the rapid reduction of proteinuria in our case. Further, there is another possibility that anti-*H. pylori* antibody might react with podocyte antigens to form immune deposits *in situ* under the subepithelium, resulting in the development of membranous nephropathy in our case.

To our knowledge, this is the first case report describing that only the eradication of *H. pylori* infection successfully reduced proteinuria in a patient with nephrotic syndrome caused by membranous nephropathy. However, the question remains as to whether the improvement of nephrotic syndrome was due to eradication of this infection, or spontaneous remission of membranous nephropathy. Therefore, further accumulation of clinical studies including case reports is necessary to confirm whether *H. pylori* infection is a secondary aetiological factor in membranous nephropathy and the eradication of this infection might be an affirmative therapy for membranous nephropathy patients with *H. pylori* infection.

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