Nephrotic Syndrome Associated with Liver Metastasis of Rectal Cancer

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Dear Sir,

The most common renal lesion associated with carcinoma is membranous nephropathy [1]. We present an unusual case of non-membranous nephrotic syndrome associated with liver metastasis of a rectal cancer.

A 66-year-old Japanese man was admitted to the surgical ward on September 17, 1992, because of edema of the lower extremities. His medical history revealed that a rectal cancer, i.e., a moderately differentiated adenocarcinoma, had been resected on October 7, 1991. Although the serum tumor markers CA19-9 and carcinoembryonic antigen (CEA) were mildly increased, abdominal CT scan and ultrasonography initially revealed no evidence of relapse or of metastasis of the rectal cancer. The nephrotic syndrome was diagnosed, and prednisolone, 30 mg daily for 1 month, was administered without improvement.

The patient was referred from the surgical to the medical ward on November 24, 1992. Edema of face and lower extremities was present. Daily urinary protein excretion was 15-25 g without occult blood or sugar. Blood urea nitrogen was 58 mg/dl, creatinine 1.6 mg/dl (142 µmol/l), total cholesterol 279 mg/dl, total protein 4.3 g/dl, albumin 2.3 g/dl, aspartate aminotransferase 36 IU/l, alanine aminotransferase 29 IU/l, alkaline phosphatase 147 IU/l and creatinine clearance 35.4 ml/min. A renal biopsy was performed on November 26, 1992 (yield 22 glo-meruli per specimen). Eleven glomeruli showed minor abnormalities: 3 showed mild to moderate segmental mesangial proliferation: 2 showed segmental mesangiolysis, and 5 were completely sclerosed (fig. 1). Immu-nofluorescent study revealed no significant deposition of immunoglobulins or complements. Electron microscopy demonstrated the effacement of foot processes of the epithelial cells. No electron-dense deposits were detected in the glomerular basement membrane (fig. 2). The dose of prednisolone was increased from 30 to 60 mg daily on December 2, 1992. Nevertheless, the intravenous administration of albumin and diuretics was required to maintain sufficient urine output.
Because serum levels of CA19-9 and CEA were elevated to 1,184 U/ml and 12.6 ng/ml, respectively, the patient was reexamined for a possible relapse or metastasis of the rectum cancer. Some small tumors were observed in the right lobe of the liver by CT scan and ultrasonography. Transcatheter arterial embolization (TAE) was performed to treat these tumors on December 22, 1992. After TAE therapy the serum levels of the tumor markers declined and proteinuria gradually decreased. Partial remission of the nephrotic syndrome was achieved with a daily excretion of 2-3 g of urinary protein without systemic edema. Biopsy of the liver tumor revealed an adenocarcinoma considered to be a metastasis of the rectal cancer. As the serum tumor markers increased again, a reservoir catheter was implanted on February 10, 1993, for the intermittent arterial infusion of 5-fluorouracil (5-FU). Although the serum level of CA19-9 and CEA respectively increased to 13,224 U/ml and 105.6 ng/ml in December 1993, the patient has remained free from the nephrotic syndrome.

Our patient seemed to have a minimal-change nephrotic syndrome or a related disorder such as focal segmental glomerular sclerosis, in that massive proteinuria occurred during the nephrotic period without the deposition of immunoglobulins or of complements in the glomeruli, and without diffuse changes in the mesangium or glomerular basement membrane. Minimal-change nephropathy, commonly associated with Hodgkin’s disease, is rarely associated with carcinomas [1]. Meyrier [2] noted that 16 cases of minimal-change nephrotic syndrome associated with carcinomas have been reported, including their two cases. In the case of membranous nephropathy associated with cancer, several reports have suggested the importance of tumor-associated antigens or of antibodies to these antigens in glomerular deposits [3-4]. With respect to minimal change nephrotic syndrome in Hodgkin’s disease, a disorder of T-lympho-cyte function has been implicated, and the humoral elaboration of a substance, possibly a lymphokine, may alter glomerular permeability [5]. We hypothesize that an immuno-logical disturbance was provoked in our patient by the metastasis of rectal carcinoma to the liver. It is interesting that the nephrotic syndrome was not associated with the primary rectal cancer, but rather with the occult metastasis to the liver.

Prednisolone therapy given alone did not relieve the massive proteinuria. However, TAE therapy combined with prednisolone led to a partial remission of the nephrotic syndrome. Surgical removal of the tumor, radiation therapy, or chemotherapy have

Fig. 1. Light microscopy of renal biopsy. PAS. × 300. A Minor abnormalities. B Segmental mesangial proliferation. C Segmental mesangiolyis.

Fig. 2. Electron microscopy of renal biopsy. Effacement of foot process of the epithelial cells. No electron-dense deposits are seen. × 8000.
been shown to induce remission of the nephrotic syndrome when the cancer is cured [1]. Our patient displayed a remission of the nephrotic syndrome despite only a minor response of the liver metastasis to TAE therapy. We believe the histological findings and clinical course of our patient were unique compared with those previously reported in cases of nephrotic syndrome associated with cancer. They also illustrate the complex etiology of the nephrotic syndrome.

References