Development of Bronchial Adenocarcinoma 11 Years after the Onset of Membranous Nephropathy Associated with Chlorambucil Therapy

M.		Polenaković
L.		Grčevska

Department of Nephrology, Faculty of Medicine, Skopje, Macedonia

Dr. L. Grčevska, Department of Nephrology, Vodnjanska 17, 91000 Skopje (Macedonia)

Dear Sir,

The most common renal lesion noted in patients with carcinoma is membranous nephropathy [1]. Neoplasias are generally discovered within 0-14 months after onset of the nephrotic syndrome. The most commonly associated tumor is lung cancer, with a large predominance of bronchogenic carcinomas over small-cell tumors [1, 2].

We present a 38-year-old man admitted to our Hospital in February 1977 because of slight pretibial edema. He was normotensive, and the renal function was normal. Total protein was 59 g/l, and proteinuria was 2.1 g/l. Percutaneous renal biopsy was performed: uniform and homogeneous thickening of the glomerular capillary walls with minimal cellular proliferation was found on microscopy, with the formation of 'spikes' in some glomeruli. On immunofluorescence microscopy, diffuse granular deposits of IgG (+++) and complement C3 (+++) were seen along the glomerular basement membrane (fig. 1). A relapse of the edema with development of nephrotic proteinuria (8 g/l) occurred in January 1978 and was successfully treated with steroids: proteinuria decreased to 0.5 g/l. In February 1988 nephrotic proteinuria of 6.5 g/l developed again. The chest radiography was still normal. Treatment for membranous nephropathy, described previously by Ponticelli et al. [3], was started. The patient was treated

Fig. 1. Marked deposition of C3 along the glomerular capillary wall. $\times 500$.

tum, and pain in the right hemithorax occurred. Bronchoscopy revealed that the lumen of the right upper pulmonary lobe was completely obstructed by a necrotic, tumorous mass. Histological examination confirmed adenocarcinoma (fig. 2).

We found our case very unusual: development of a bronchial adenocarcinoma 11 years after the onset of the membranous nephropathy. The patient was treated with methylprednisolone 1 g daily during 3 days, steroids 0.5 mg/kg/24 h during the 1st month, and chlorambucil orally 0.2 mg/kg/24 h during the 2nd month. Treatment with chlorambucil was stopped on the 21st day because of severe pancytopenia (red blood cell count 1,800,000/mm³, white blood cell count 1,700/mm³). Three months later, the patient started expectoration of blood-stained spu-

Fig. 2. Bronchial biopsy specimen showing neoplastic malignant cells forming irregular glandular structures. HE. $\times 200$.

pathy, after two relapses of the disease. In the literature periods ranging from 0 to 14 months after onset of a nephrotic syndrome have been reported [1, 2]. There was also an unusual association between the start of the chlorambucil therapy and the occurrence of pancytopenia and the carcinoma. It is well known that cytotoxic drugs may have a direct oncogenic effect [3], but besides leukemias, other malignancies, specially carcinomas, were not reported. The associations between underlying malignant disease, the form of glomerulopathy, and chlorambucil treatment remain unclear in this patient.

References

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