

Different Glomerulopathies Accompanying Non-Small-Cell Lung Cancer

SAIME PAYDAS, M.D.¹, BARIS SOYDAS, M.D.¹, SEMRA PAYDAS, M.D.¹,
MUSTAFA BALAL, M.D.¹, SEYDA ERDOGAN, M.D.², AND ILHAN TUNCER, M.D.²

Abstract

The coexistence of lung cancer and glomerular lesion is not commonly reported. Malignancy-related glomerulopathy is commonly membranous glomerulonephritis. Other glomerulopathies are seldom reported. We report two cases presenting with non-small-cell lung cancer, acute renal failure and nephrotic syndrome secondary to membranoproliferative glomerulonephritis and amyloidosis.

Key Words: Lung cancer, malignancy, glomerulopathy, proteinuria.

NEOPLASM-RELATED NEPHROTIC SYNDROME has been recognized for years. Nephrotic syndrome is rare in the course of carcinomas. Lymphoproliferative diseases are the most common neoplasms accompanying nephrotic syndrome (1). The renal lesion of paraneoplastic nephrotic syndrome usually presents as membranous nephropathy, membranoproliferative glomerulonephritis (MPGN), minimal change disease, focal segmental glomerulosclerosis and the other glomerulopathies (2). Coexistence of lung cancer and glomerular lesion is not commonly reported. We report two cases presenting with non-small-cell lung cancer, acute renal failure and nephrotic syndrome secondary to membranoproliferative glomerulonephritis and amyloidosis.

Case 1

A 48-year-old-man was admitted to our hospital with cough, purulent sputum, dyspnea and lower extremity edema of one-month duration. He had a 60-pack/year smoking history. Physical examination on admission revealed a temperature of 37.5°C, pulse rate of 92/min, respiratory rate of

25/min, and blood pressure of 150/90 mm Hg. Other significant physical findings were the absence of respiratory sound in middle and upper zones of the left lung, moist rales bilaterally and prominent edema on the lower extremities. Chest X-ray showed a well-defined opacity filling the left middle and upper lung, and bilateral moderate pleural effusion. Computed tomography (CT) revealed a 12 × 9 cm mass in the left middle and upper lung and infiltrating the pleura. The complete blood count was unremarkable except for normochromic normocytic anemia (hemoglobin: 8 g/dL). Additional biochemical tests revealed hypoalbuminemia (1.8 g/dL), dyslipidemia and significant proteinuria (10 g/day) with granular and hyalin casts in urinary sediment. The erythrocyte sedimentation rate was 20 mm/h. Serum levels of C3 and C4 were found to be lower than normal limits: 45 mg/dL (normal: 55–120) and 10 mg/dL (normal: 14–51), respectively. Tests for antistreptolysin O titer, anti-nuclear antibody, cryoglobulins, hepatitis C antibody, hepatitis B surface antigen and HIV were negative. The pathological diagnosis of the tumor specimen obtained by CT-guided (fine-needle) aspiration was non-small-cell lung carcinoma (Fig. 1).

Radiotherapy was begun with 60 Gy towards the left hemithorax. Protein- and salt-sparing diet, furosemide (180 mg/day), amlodipine (10 mg/day) and ceftriaxone (2 g/day) were started. On the tenth day of hospitalization, deterioration of renal function (as evidenced by an increase in blood urea

Departments of ¹Internal Medicine and ²Pathology, Cukurova University Faculty of Medicine, Adana, Turkey 01330.

Address all correspondence to Saime Paydas, M.D., Cukurova University, Faculty of Medicine, Department of Internal Medicine, 01330 Adana, Turkey; e-mail: spaydas@cu.edu.tr

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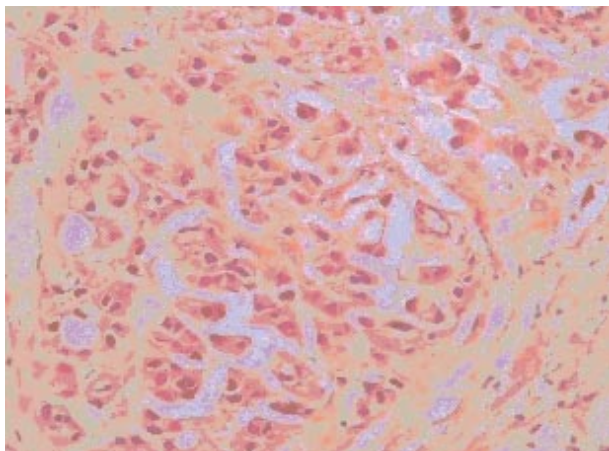


Fig. 1. Adenocarcinoma of the lung with gland forming.

nitrogen and serum creatinine) was detected (BUN: 105 mg/dL, normal: 8–20 mg/dL; Cr: 2.8 mg/dL, normal: 0.7–1.1 mg/dL). Ultrasonography and Doppler ultrasonography did not show evidence of obstruction, hydronephrosis or renal vein thrombosis. Subsequent renal biopsy was consistent with MPGN. Methylprednisolone (1 mg/kg/day), dipyridamole (225 mg/day) and aspirin (100 mg/day) were added to therapy for renal failure and nephrotic syndrome. However, the patient died on the 20th hospital day due to pulmonary failure from sudden massive pleural effusion.

Case 2

A 50-year-old man was referred to our hospital with nausea, vomiting, generalized edema, renal failure and proteinuria. Renal function tests had been within normal limits one year earlier (BUN: 23, Cr: 1.2). Non-small-cell lung carcinoma (stage IIIB adenocarcinoma) had been diagnosed by fine-needle aspiration (FNA) on the left upper lung two years earlier. He had been treated with combination of radiotherapy (60 Gy to left hemithorax and mediastinum) and chemotherapy (every 4 weeks for 6 courses, using gemcitabine and cisplatin). Physical examination findings were generalized edema and no breathing sound on the upper zone of the left lung. Chest X-ray and CT of the lung showed a 10 × 10 cm mass in the left upper lung and mediastinal lymphadenopathy. Abnormal laboratory findings were as follows: serum level of albumin 1.6 g/dL, creatinine clearance of 8 mL/min, and proteinuria of 6 g/day. Renal biopsy showed amyloid deposition, secondary (AA) type (Figs. 2 and 3). Medical history was unremarkable for chronic infectious diseases like osteomyelitis, rheumatoid arthritis, familial hypotension or neuropathy and familial Mediterranean fever. Exami-

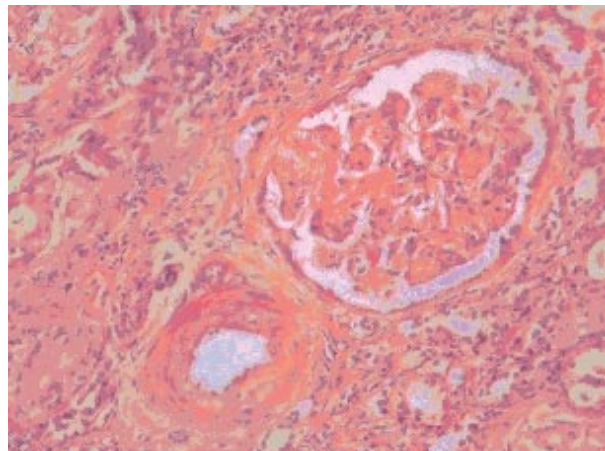


Fig. 2. Glomerulus with prominent mesangial and vascular deposition of amyloidosis (HEX 400).

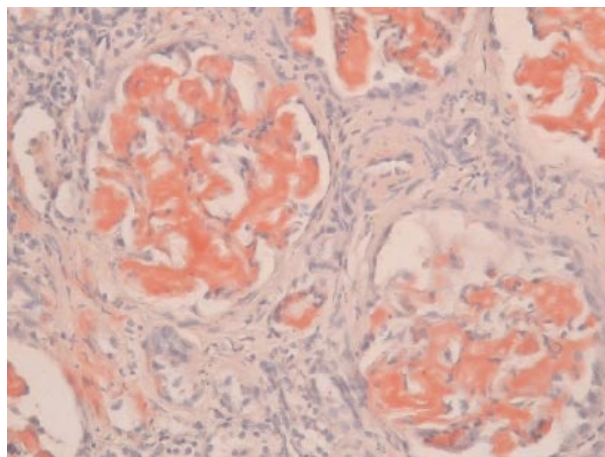


Fig. 3. Amyloid deposition with Congo-red stain (Congo-red × 400).

nation of amyloid deposition in lung tissue taken by FNA could not be done due to technical reasons. Renal function of the patient deteriorated progressively and required hemodialysis. Surgical resection of lung tumor was recommended for relief of paraneoplastic syndrome; however, the patient refused surgical intervention.

Discussion

Paraneoplastic nephrotic syndrome is seen concurrently with cancer diagnosis in 40% of cases and after the diagnosis of cancer in 20% of patients (3). In both of our cases, nephrotic syndrome was detected after the diagnosis of non-small-cell lung cancer. Membranous nephropathy is the most commonly seen glomerular lesion among cases of paraneoplastic nephrotic syndrome. However, the patient in case 1 had MPGN and the patient in case 2 had amyloidosis. Both these entities are reported

uncommonly, especially amyloidosis, which is seen very rarely; only a few cases have been reported so far (4).

The pathogenesis of paraneoplastic nephrotic syndrome has been thought to involve the production of cancer-related antigens, with subsequent damage to the glomerular basement membrane by antigen-antibody complexes. An alternative hypothesis is that an auto-antibody produced in response to the malignancy may cross-react and damage the glomerular basement membrane (3). MPGN, which is usually found in conditions of chronic infection or systemic disease, has rarely been seen in the course of carcinoma (5). It is assumed that the glomerular injury in patients with cancer and MPGN is mediated by circulating immune complexes, composed at least in part of tumor-associated antigens that may cryoprecipitate (6). Generally, the nephrotic syndrome completely resolves when the malignant disease can be treated curatively with chemotherapy and/or radiotherapy or surgery (7–9). Some immunosuppressive drugs (corticosteroids, cyclosporin and azathiopurine) have been found to be useful in a few cases (10). Our patient with membranoproliferative glomerulonephritis (case 1) died soon after treatment due to hypoxic-hypercapnic respiratory failure. For this reason there was insufficient time to observe the effect of immunosuppressive therapy.

Secondary amyloid (AA) deposition, found at renal biopsy in our second case, is unusual. In the literature, tumor-associated amyloidosis is frequently seen to be the AA type in renal cell carcinoma (4). Amyloid in association with tumors is usually primary amyloid (AL), and this has been described with bronchial tumors. However, there is one case report of carcinoma of the bronchus and renal AA amyloidosis (11) and there are some reports of amyloid deposits in basal cell carcinoma with permanganate resistance but without AA protein (12). It is speculated that intratumoral amyloid deposition could have a neoplastic origin rather than be a secondary amyloidosis. Amyloid may originate from the tumor cells as a result of tumor apoptosis (13, 14). In our case, the tumor could not be resected due to the patient's rejection of surgery, so we had no chance to determine the effect of tumor removal on the amyloidosis. Finally, nephrotic syndrome and renal failure did not improve. In this patient, amyloidosis could not be related to lung cancer. But we did not discover any etiology for renal amyloid deposition in his detailed medical history and laboratory evaluation. The second patient was also treated with nephrotoxic drugs such as cisplatin for 4 months. If he had had renal failure due to amyloidosis before

lung cancer, the renal failure could have appeared earlier. But we cannot exclude other possibilities related to renal amyloidosis. In the literature, basal cell carcinoma and related amyloidosis seldom appear together (15). Earlier, we reported a case with basal cell carcinoma, tumoral amyloid deposition, renal failure and severe proteinuria. In that patient, renal failure and proteinuria regressed with tumoral resection and colchicine therapy (16).

In summary, we report two cases of non-small-cell lung cancer with nephrotic syndrome due to membranoproliferative glomerulonephritis and deposition of AA amyloidosis. These are rare occurrences, and the presence of renal pathology in cases with lung cancer produces a poor outcome.

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