Few cases of nephrotic syndrome have been associated with sarcoidosis. Membranous glomerulonephritis predominates as the pathological basis of nephrotic syndrome [1-4]. Less frequent lesions of proliferative glomerulonephritis [5, 6], amyloidosis [7] or focal glomerulosclerosis [8-10] have also been observed. Both the heterogeneity and the rarity of glomerular involvement could suggest that the association between glomerulonephritis and sarcoidosis might be fortuitous. However, several immunological facts suggest a relationship between both diseases.

We report a 31-year-old male who was hospitalized in July 1991 because of asthenia, anorexia, chest pain, and leg edema. His blood pressure was 120/60 mm Hg. The urinary sediment was normal, proteinuria was 8.3 g/24 h, serum creatinine 1.03 mg/dl and creatinine clearance 86 ml/min. Serum protein was 5.9 g/dl, albumin 2.1 g/dl, and cholesterol 639 mg/dl. Erythrocyte sedimentation rate was high and serum calcium concentration was normal. Chest radiographs disclosed reticulonodular pulmonary images distributed in a homogeneous bilateral pattern and bilateral hilar and laterotracheal adenopathies. Tuberculine test was negative and repeated searches for Mycobacterium tuberculosis gave negative results. The material obtained from bronchial biopsy showed the presence of a large number of gigantocellular granulomas without caseous necrosis, characteristic of sarcoidosis. In addition, there was lymphocytosis (46%) in the fluid recovered by bronchoalveolar lavage (normal 7 ± 2%). Determinations of lung lymphocyte subpopulations by flow cytometry showed a large number of activated T cells (CD3 + DR +, 58%). Pulmonary function tests showed a restrictive syndrome, and alveolar capillary diffusion capacity of carbon monoxide was decreased. A gallium-67 scan showed diffuse captation in both lungs. A computed tomography scan of the abdomen and pelvis showed negative results. Plasma level of the angiotensin-converting enzyme was elevated to 292 U/ml (normal values: 8-52). The kidneys were of regular shape and normal size. A percutaneous renal biopsy disclosed focal segmental glomerulosclerosis (fig. 1). Tubulointerstitial or vascular lesions were not observed. Immunofluorescence studies were negative. Treatment with prednisone 60 mg daily was initiated which resulted in a dramatic improvement of the constitutional symptoms. One month later, there was resolution of the pulmonary reticulonodular pattern, but the bilateral hilar lymphadenopa-thies persisted. The plasma level of angiotensin-converting
enzyme was 130 U/ml, and proteinuria declined to 4.2 g/day. On October 9, on a regular review, proteinuria was 3 g/24 h, total serum protein and albumin had become normal, and the plasma level of angiotensin-converting enzyme was 63 U/ml. Over the following 5 months, proteinuria disappeared and prednisone was progressively reduced and discontinued. Mediastinal adenopathies disappeared 9 months after the onset of the disease.

The present report documents a patient with simultaneous occurrence of pulmonary sarcoidosis and nephrotic syndrome secondary to focal segmental glomerulosclerosis. To our knowledge, only 3 cases of focal segmental glomerulosclerosis during sarcoidosis have been reported previously [8-10]. The question as to whether sarcoidosis and focal segmental glomerulosclerosis are related entities cannot be resolved on the basis of our current knowledge. In our patient, the evolution of nephrotic syndrome clearly paralleled that of sarcoidosis, supporting the relationship between the granulomatous disease and the glomerular lesion. In addition, the nephrotic syndrome resolved when prednisone therapy was effective in treating active sarcoidosis. This case lends more support to the theory of the pathogenetic involvement of T-cell dysfunction in minimal-change nephropathy and focal segmental glomerulosclerosis [11]. Pulmonary sarcoidosis is a chronic granulomatous disorder of unknown etiology, characterized by a T lymphocyte-mononuclear phagocyte inflammatory process in the lower respiratory tract, interstitial granulomata, and distortion of the alveolar, bronchiolar, and vascular walls. T lymphocytes composing the lung inflammation spontaneously release interleukin-2 and the T-cell growth factor and spontaneously proliferate [12]. Minimal-change nephropathy and focal segmental glomerulosclerosis are thought to be related to T-lymphocyte dysfunction [13]. Disturbances in the production of some cytokines could lead to an increase in glomerular permeability [14]. Local excess of interleukin-2 or related substances or oversecretion of interleukin-1 could alter glomerular permeability [13-15]. Further support for a lymphokine-mediated pathogenesis of nephrotic syndrome is indirectly provided by the response of both conditions to corticosteroids, which are known to exert an effect upon T-cell-mediated lymphopoiesis as well as being able to block the production of lymphokines. The fact that prednisone therapy of this patient was accompanied by a rapid clinical response of the systemic manifestations associated with suppression of angiotensin-converting enzyme synthesis in the lung [16], and concomitantly, with remission of nephrotic syndrome is consistent with the concept that corticosteroids are capable of suppressing a factor produced by activated T lymphocytes.

In summary, immunological abnormalities in some patients with sarcoidosis may lead to nephrotic syndrome. Lymphokines, humoral factors derived from pathological tissues or from activated lymphocytes may be responsible for the renal lesions.

References


