Minimal-Change Nephropathy and Malignant Thymoma

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A 56-year-old man had fever, precordial pain, and a mediastinal mass. The mass disappeared two months later and the patient remained asymptomatic for 2½ years. At that time a full-blown nephrotic syndrome developed, with minimal-change glomerulopathy. The chest x-ray film showed the reappearance of a giant mediastinal mass. On biopsy of the mass, malignant thymoma was diagnosed. Association between minimal-change disease and Hodgkin's disease is well known, while the association with malignant thymoma has not been previously reported. The relationship between malignant thymoma and minimal-change disease is discussed, and a possible pathogenic mechanism involving cell-mediated immunity is proposed.

Nephrotic syndrome is a well-recognized systemic manifestation of neoplastic diseases. Approximately 70 percent of the carcinomas associated with nephrotic syndrome represent immune-complex membranous glomerulopathy, while minimal-change glomerulopathy is predominantly associated with Hodgkin's disease. We report the first case of minimal-change disease associated with malignant thymoma.

CASE REPORT

A 56-year-old man was admitted to Meir General Hospital, Kfar-Saba, Israel, in May 1974, because of fever and pre-

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CHEST, 77: 5, MAY, 1980

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Figure 1. Huge polycyclic mass in left hemithorax is fused with left border of heart and great vessels.

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The patient was readmitted on November 1977 with a full-blown nephrotic syndrome. The chest x-ray film at that time showed a giant polycyclic mass in the left hemithorax (Fig 1). Laboratory examination disclosed massive proteinuria (20 gm/24 hr), hypalbuminemia (1.8 gr/100 ml), hypercholesterolemia (350 mg/100 ml), and increased plasma level of creatinine (2.1 mg/100 ml). Immunologic studies revealed normal levels of immunoglobulins, normal counts of T-lymphocytes and B-lymphocytes, and normal levels of C3 and C4 of the serum complement; however, there was a marked increase in immune complexes equal to 56.9 percent by the method of inhibition of antibody-dependent cell-mediated cytotoxicity. Renal venous occlusion by thrombosis or infiltration with tumor was ruled out by a normal renal venogram.

Percutaneous renal biopsy was performed, and minimal-change disease was diagnosed by electron microscopic studies (Fig 2 and 3). The immunofluorescent stains with fluorescein-labeled anti IgM, IgG, IgA, and complement were negative. On exploratory thoracotomy a solid friable mass was exposed, occupying most of the left upper lobe and adherent to the pericardium, great vessels, and the thymic region. Histologic examination of the tumor revealed thymoma of lymphocytic type. For technical reasons the whole mass was not resected, but only a great part of it. Treatment with prednisone (80 mg/day) was started shortly after surgery; however, after two months, no improvement of the renal manifestations occurred, while severe muscular atrophy and weakness developed. An abscess appeared in the anterior mediastinum, and the patient began to cough up copious amounts of blood and purulent sputum. Klebsiella pneumoniae and Escherichia coli were cultured from the sputum. Because of this complication, therapy with irradiation was postponed. The patient died several days later from severe pneumonia and renal failure. Permission for postmortem examination was not given.

**DISCUSSION**

Various glomerulopathies can be associated with carcinomas, Hodgkin’s disease, and other lymphoproliferative disorders, as well as other malignant and benign tumors. 1 In neoplastic disease, minimal-change disease is predominantly associated with Hodgkin’s disease. 1-3 There are several hypotheses regarding the pathogenesis of minimal-change disease associated with Hodgkin’s disease. One of the most attractive was suggested by Shalhoub. 4 According to Shalhoub, minimal-change disease is a manifestation resulting from the dominance of the immune system by a clone of abnormal T-lymphocytes which produces circulating lymphokine toxic to the glomerular basement membrane and thus altering its permeability to protein.

Several clinical observations support the theory that minimal-change disease is associated with an existence of alterations in cell-mediated immunity: (1) Remissions in minimal-change disease and Hodgkin’s disease were reported after measles. 5,6 (2) Cell-mediated immunity is modified by measles, 7 suggesting a similar mechanism for minimal-change disease and Hodgkin’s disease, which may be a lymphoreticular cellular mechanism. (3) Predominance of minimal-change disease in Hodgkin’s disease suggests a relation between cell-mediated immunity and Hodgkin’s disease.

**FIGURE 2.** Visceral epithelial cellular cytoplasm reveals microvillous proliferation as sign of glomerular proteinuria (uranyl acetate and lead citrate, × 12,000).

**FIGURE 3.** Complete fusion of foot processes along surface of whole glomerular tuft. No electron-dense deposits or proliferation of cells is detected (uranyl acetate and lead citrate, original magnification × 45,000).
and minimal-change disease. Antibody response to type-3 pneumococcal polysaccharide can be enhanced in patients with minimal-change disease by treatment with antithymocytic globulin, suggesting the presence of abnormal suppressor T-lymphocytes. Based on these clinical observations an association between minimal-change disease and thymoma was predicted by Shalhoub; however, to the best of our knowledge, this association has not been described in the literature.

In our case, additional circumstantial evidence supports the fact that minimal-change disease was a paraneoplastic process, rather than a coincidental event. Minimal-change disease in elderly patients is rare and generally occurs in relation to malignant disease other than thymoma. When minimal-change disease is the only disease in the elderly patient, it is usually responsive to steroid therapy. The minimal-change disease presented in this case was resistant to steroid treatment, suggesting a possible interdependence of this nephropathy with the malignant thymoma, which does not respond to steroid therapy. Remission of Hodgkin's disease also results in a remission of minimal-change disease in these patients. Unfortunately, in our case, this was not achieved, since the thymoma was unresectable. The minimal-change disease developed late in the course of the thymic malignant disease. An explanation might be that the mutant clone of lymphocytes originated towards the end of the course of the disease.

In conclusion, this case provides further indirect evidence that minimal-change disease might be the result of an imbalance in cell-mediated immunity. Nevertheless, until an experimental model for minimal-change disease induced by disorders of cell-mediated immunity is created, our assumption concerning the mechanism underlying this clinical observation remains hypothetical.

ACKNOWLEDGMENT: We wish to thank T. Moalem, M.Sc., M. Becker, Ph.D., and Professor A. Klajman for performing determinations of levels of circulatory immune complexes.

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Massive Hemoptysis Secondary to Pulmonary Arteriovenous Fistula
Treatment by a Catheterization Procedure


Massive pulmonary hemorrhage secondary to an acquired arteriovenous fistula is a rare event associated with high mortality. Cotton wads mounted on steel coils were inserted by percutaneous catheter and successfully occluded a pulmonary arteriovenous fistula in a patient who had massive hemoptysis and contraindications to thoracotomy.

Massive pulmonary hemorrhage is life-threatening and associated with high mortality. Suffocation occurs in 50 to 100 percent of patients treated without operation. The most common causes of hemoptysis are tuberculosis, arpergilliosis, bronchial tumors, and bronchiectasis, but pulmonary arteriovenous fistulas, multiple or single, are well-documented causes of massive hemoptysis.

Various nonoperative treatments of massive hemoptysis have been attempted. None has been uniformly successful, and mortality rates approximate 85 percent. Operation is the treatment of choice, but contraindications to surgery include inadequate pulmonary function, inability to locate the site of bleeding, bronchial carcinoma with involvement of the mediastinum, multiple bleeding sites, or severe coagulation deficiencies.

The following case illustrates a new method of managing massive hemoptysis from a pulmonary arteriovenous fistula without thoracotomy.

CASE REPORT

A diagnosis of single left ventricle, L transposition of the great arteries, and pulmonic stenosis was made at cardiac catheterization at age four years in a 15-year-old boy who had been cyanotic at birth. At age five, a Glenn anastomosis was performed for palliation of cyanosis and polycythemia. During the summer of 1977, he developed progressive dyspnea, cyanosis, and polycythemia. In October 1977, he had his first episode of hemoptysis which terminated spontaneously.

MASSIVE HEMOPTYSIS AND PULMONARY AV FISTULA

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