Pulmonary Lymphangiomyomatosis—Past, Present, and Future—

Key words: lymphangiomyomatosis/lymphangioleiomyomatosis (LAM), hamartoangio-myomatosis (HAM), chylothorax

Pulmonary lymphangiomyomatosis (LAM) is an uncommon chronic debilitating disorder of unknown etiology afflicting women of childbearing age, characterized histologically by proliferation of atypical smooth muscle cells in the lungs, pleura, mediastinum, thoracic duct, and retroperitoneum (1). Silverstein coined the term of pulmonary lymphangiomyomatosis in 1974 (2) and more recently the term of lymphangioleiomyomatosis has been used as synonymously (3). The acronym LAM is commonly used to denote both terms. However, the actual disease now referred to as LAM has been known for a long time. Since Rosendal published the paper “diffuse myomatosis and cystic formation in the lung” in 1942 (4), this disease has been given various names.

Yamanaka and Saiki were the first to report LAM in Japan in their account of three cases in 1970 (5). They described the disease as hamartoangiomyomatosis (HAM) and stressed its distinct differences from chronic obstructive lung disease. The term HAM refers to the hamartoma-like hypertrophy of smooth muscle tissue growing in areas where the smooth muscle tissue is not normally found, a condition distinct from muscular hyperplasia with simple proliferation of collagen fibers. The term is reasonable, but Yamanaka and Saiki’s report was not in English so, the term has not been used widely outside of Japan. Subsequent literature on the disease in Japan has included reports on 36 cases in 1986 by Onodera (6), 65 cases in 1991 by Saiki and Ibata (7), 45 cases in 1995 by Kitaichi (8), and 65 cases in 1997 by Izumi (9). However, there was some overlapping of cases in these reports, and the total number of cases confirmed in Japan is about 150.

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There have only been a few cases of this type in Japan. For example, among the 41 cases reported by Kitaichi et al, only 2 showed this condition (8). Furthermore, Japanese cases had a better survival than the Western cases (8). One of the reasons for the fewer involved organs and good survival in Japanese cases may be the universal health coverage for the entire Japanese population and detection of the disease in earlier stages because of the higher frequency of visits to medical facilities in Japan. The high availability of CT in Japan may contribute to the early detection of LAM.

Since LAM is a disease of women of the childbearing age, ovariectomy and hormone therapy have been attempted, but no efficacy has been shown. In the reports by Kitaichi (8) and Izumi (9), there were no differences in survival between treated and untreated groups. The only effective therapy against LAM is considered to be lung transplant (11); transplants are being conducted in Western countries. The best time to perform the transplant is a difficult decision since the progression of the disease is very slow in many cases.

Though LAM is a very rare disease, the poor prognosis in the young women that it afflicts is making it a growing social concern worldwide, especially in the USA. In 1996, the LAM Foundation was established in Cleveland to promote the study of the disease. In June 1997, a Workshop on Lymphangiomyomatosis was held jointly by the Office of Rare Disease Research and the Office of Research on Women’s Health in the Department of Lung Diseases of the National Heart, Lung, Blood Institute (NHLB). Registration of LAM cases on an international basis was started for the following purposes: 1) study of the progression of LAM; 2) classification of pathological stages; 3) cooperative research on the treatment; 4) exchange of study material. Furthermore, the LAM Foundation, NHLB, and Columbia University jointly held the 1999 LAM Symposium on the topic of Molecular Mechanisms of Lymphangiomyomatosis in New York City in November 1999. The results of future international cooperative research on this rare disease are awaited.

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