Hormone Receptors in Pulmonary Lymphangiomyomatosis

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Summary: Biochemical assays have demonstrated the existence of hormone receptors in lung tissue from patients with pulmonary lymphangiomyomatosis (LAM). This finding is the biologic corollary to the finding that LAM responds to hormonal therapy. We have examined lung tissue from two patients with LAM for estrogen and progesterone receptors by immunohistochemistry and a biochemical assay. Although specimens from both patients were negative for estrogen receptor activity by the biochemical assay, positive stain of estrogen receptors was observed in both patients with immunohistochemistry.

Key words: lymphangiomyomatosis (LAM) — estrogen receptor — progesterone receptor — immunohistochemistry — open lung biopsy

Introduction

Pulmonary lymphangiomyomatosis (LAM) is a rare disease characterized by the widespread proliferation of immature smooth muscle cells within the lung. Hormonal influences are thought to be important in the pathogenesis of this entity since LAM occurs in young women who are generally of childbearing age and since pregnancy (Yockey et al. 1986; Hughes and Hodder, 1987), or estrogen supplementation (Shen et al. 1987) may exacerbate the disease. Hormonal manipulation, such as oophorectomy or administration of progesterone, has emerged recently as a therapeutic option in this disease. The possibility of hormonal control of smooth muscle proliferation in LAM has recently led inves-

tigators to more thoroughly examine the presence of hormone receptors in this disease (Yockey et al. 1986). Frozen tissue is analyzed frequently for the presence of estrogen and progesterone receptors by biochemical assays. However, results obtained in LAM using this technique have been variable, and a number of cases have been negative (Colley et al. 1989). In the present study, an immunohistochemical approach was used, in addition to a biochemical assay, for the detection of hormone receptors in tissue samples obtained from two patients.

Materials and Methods

Two patients (Patient 1, 34-year-old female; Patient 2, 39-year-old female) with

histologically proven LAM were studied. Lung biopsy specimens were obtained by thoracotomy performed for the initial diagnosis. The biopsies were obtained in both instances prior to the initiation of hormonal treatment. A portion of the biopsy specimen was frozen immediately in liquid nitrogen; the remainder was fixed in 10% phosphate-buffered formalin, embedded in paraffin blocks, cut into 4 μ m thick sections, and mounted on glass slides. Subsequently, these sections were deparaffinized with xylene and graded alcohols and subjected to hematoxylin-eosin (H & E) staining.

Estrogen and progesterone receptor antigens were analyzed by an enzyme immunoassay (EIA) sandwich technique (Abbott ER-EIA and Abbott PgR-EIA monoclonal kit; Dainabot, Tokyo, Japan) that was performed on frozen tissue samples from the lung. A concentration of estrogen or progesterone receptor antigen greater than 3.4 fmol/mg protein was considered positive (Brentani et al. 1984).

Immunohistochemical studies were performed on frozen tissue using the

peroxidase-antiperoxidase technique and the following antibodies: monoclonal anti-estrogen receptor antibody (Abbott ER-ICA; Dainabot, Tokyo, Japan) and anti-progesterone receptor antibody (Abbott PgR-ICA; Dainabot, Tokyo, Japan). The sections were examined by light microscopy.

Results

The biochemical assay by EIA demonstrated the presence of progesterone receptors and the absence of estrogen receptors in the pulmonary tissue from the two patients with LAM (Table 1). However, immunohistochemical staining demonstrated both progesterone and estrogen receptors in smooth muscle cell nuclei which contained darkly stained progesterone receptors and more weakly stained estrogen receptors (Fig. 1). Uninvolved smooth muscle cells in the vascular and bronchial walls were negative for both progesterone and estrogen receptors.

TABLE 1.
Biochemical assay and immunohistochemical results for two patients with LAM

Patient	EIA (fmol / mg protein)		Immunohistochemistry	
	PgR	ER	PgR	ER
1	36	<3.4	++	+
2	5.1	<3.4	++	+

PgR: progesterone receptor; ER: estrogen receptor; ++: marked ; +: mild

Fig. 1. Immunohistochemistry of hormone receptors in a patient (Patient 1) with LAM. Progesterone receptors are indicated by (A) and estrogen receptors are indicated by (B). original magnification $\times 100$.

Discussion

Hormone receptor analyses in lung tissues of LAM patients using biochemical assays have been reported previously (McCarty et al. 1980; Brentani et al. 1984; Dishner et al. 1984). However, there are no reports comparing the results of biochemical and immunohistochemical assays. The immunohistochemical staining was more sensitive than the biochemical assay and demonstrated the coexistence of estrogen and progesterone receptors in proliferative smooth muscle cells. This result suggests that hormone receptor analysis by biochemical assays alone

is inadequate for detecting estrogen and progesterone receptors. The results of hormone receptor analysis have been considered in the context of hormonal therapy. However, Taylor and colleagues have shown that there is no apparent correlation between the presence of progesterone and estrogen receptors and the response to hormonal therapy (Taylor et al. 1990). Our study reveals, however, that previous attempts to correlate the existence of hormone receptors and the response to hormonal therapy may have been flawed by inadequate assays.

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