Abstract

Estrogen receptors (ER's) were determined by agar gel electrophoresis in 105 human mammary tumor biopsies. Fifty-three tumor specimens revealed measurable amounts of receptor, and 64% of these patients showed an objective remission after endocrine treatment. If we also include cases with partial remission, previous response, and arrested growth but no actual remission, the benefit rate increases to 87%. The corresponding percentage in the ER-negative groups is 13%. In a retrospective study of 42 patients with human breast cancer, a correlation between ER finding and remission rate after chemotherapy was found. Of the ER-negative patients, 71% showed an objective remission after polychemotherapy, whereas only 43% of the ER-positive cases revealed such remission. The presented data are discussed with special regard to their clinical relevance.

Introduction

Only 30% of unselected patients with advanced breast cancer respond to endocrine therapy, irrespective of the therapy schedules (either surgical endocrine ablation or treatment with steroids or antisteroids). Today because of the fundamental work of Jensen et al. (3) a predictive test for selecting patients before treatment is available. This receptor determination concept is now, especially after the Bethesda meeting in July 1974 (5), generally accepted.

For tumor tissues that contain no or very low concentrations of receptor, less than 10 fmol/mg tissue protein, the situation seems to be clear. These patients have autonomous tumors and have practically no chance to respond to any kind of endocrine treatment. They require polychemotherapy. The problem is the so-called receptor-positive group. We can expect objective remission rates of between 55 and 65% for ER-positive patients. This correlation is rightly regarded as disappointing, but in this connection we must realize what an objective remission means: as recently pointed out by Stoll (7), a 50% decrease in the size of a lesion is correlated to a kill rate of cells of about 99%. Usually, we call a finding of less than this 99% tumor cell kill a failure, and so the finding of steroid receptors would be called "false positive."

On the other hand, results published by Brunner et al. (1) and others showed that patients with no change in their disease after polychemotherapy might gain the same survival time as the responders. Therefore, a steady state of tumor growth is not necessarily a clinical failure.

In this paper we discuss our receptor-positive cases in this direction. Another point of great clinical interest was given by M. Lippman. He first showed a correlation between ER status and remission rate after polychemotherapy. A similar trend was reported by R. King.

In this paper we analyze our data from a retrospective study.

Materials and Methods

ER's were determined by agar gel electrophoresis according to the method published previously by Trams and Maass (6).

Results and Discussion

One hundred five tumor tissues of human breast cancer were assayed for ER; 53 tumor specimens revealed measurable amounts of receptor (Table 1). The rate of objective remissions, following the European Organization for Research on Treatment of Cancer criteria, in our material is 64%. If we introduce cases with partial response, previous response, and no change of growth, the benefit rate increases to 87%. In our opinion these tumors must be somewhat hormone sensitive. Therefore, the endocrine therapy had been absolutely ineffective in 13% of the ER-positive cases. The corresponding percentage in the negative group is 87%.

This observation on the objective remission showed that we need more parameters than the ER status only to get a better correlation. Besides other possibilities [we only make reference to the measurement of the progesterone receptor, first published by McGuire et al. (6), and the nuclear ER, as published by Laing et al. (4), or the important differentiation between the 4S and 8S receptor complex first discussed by Wittliff et al. (9)], we must also take clinical parameters into consideration. It is generally known that patients with visceral metastases are unfavorable for endocrine treatment and, therefore, the domain of polychemotherapeutic schedules. Therefore, in our material (Table 2) the number of patients with visceral metastases is relatively high in unresponsive ER-positive patients.

Patients in the first years after menopause also seem to be unfavorable cases for endocrine treatment, although the receptor data are not different from those in the postmenopausal group. Our material is summarized in Table 3. Thus, the special endocrine situation of the breast cancer patient obviously plays a role, as pointed out by Bulbrook et al. (2).

* Presented at the First Innsbruck Meeting, January 1978, Innsbruck, Austria.

1 Presented at the John E. Fogarty International Center Conference on Hormones and Cancer, March 29 to 31, 1978, Bethesda, Md. Supported by DFG, Sonderforschungsbereich 34, "Endokrinologie."
2 The abbreviation used is: ER, estrogen receptor.
At the first Innsbruck meeting (1978), another point of discussion was given by M. Lippman and R. King. They both pointed out that there is a correlation not only between ER status and hormone sensitivity in tumor cells, but also between ER finding and remission rate after chemotherapy. Table 4 shows our latest data from a retrospective study, those of M. Lippman and the comparable data of R. King. The poor results of chemotherapy in ER-positive patients, a concept that should be confirmed by further studies, shows the importance of measuring steroid receptors in breast cancer.

Chart 1 shows our present proceeding. Receptor determination is, of course, a necessary step within the process of clinical decision-making, but, furthermore, as mentioned earlier, we have to introduce clinical parameters. Patients with estrogen and progesterone receptors in their tumors are divided into 2 groups: patients with rapidly growing tumors of poor differentiation who need a rapid therapy effect, or patients with extensive visceral metastases who should be treated by a combined chemo- and endocrine therapy. The remaining receptor-positive group of patients can be treated with an endocrine method alone as a first step and, if effective, with further steps. Although data concerning clinical experience with ER-positive and progesterone-negative cases are limited, in such cases combined treatment procedures are also recommended. Patients lacking both receptors are candidates for a cytotoxic polychemotherapy.

References


2. Bulbrook, R. D., Greenwood, K. C., Hayward, J. L. Selection of Breast-Cancer Patients for Adrenalectomy or Hypophysectomy by Determination of Urinary 17-Hydroxycorticosteroids and 


Some Comments on the Necessity of Receptor Determination in Human Breast Cancer

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