THEORETICAL AND PRACTICAL ASPECTS OF RECEPTOR HORMONE ASSAY IN BREAST CANCER

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SUMMARY

The Authors have discussed the importance of ER/PR assay in breast cancer care. 162 patients were studied. The dextran-coated charcoal technique was used as the standard most readily available. The Authors point out the importance of specimen handling as is shown by time-decay studies, and the differences in ER/PR level at the time of the biopsy and mastectomy cut-section, and its eventual influence to better understanding assay results. The establishment of a center of control between different labs would also help in the development of more exact regimens for cancer care.

During the past years there have been great advances in receptor assay protocols and even though the exact action of re-receptors has not yet been determined, it has been recognized without doubt the importance of the effect that they have on proliferative activity and therapeutic approach in breast cancer.

Hormone receptors were in fact first studied in the 60's by Jensen and Associates. This group of Researchers realized that in tumor target tissues structures were present that bind specific hormones that may be used in the selection of patients for hormonal therapy or adjuvant chemotherapy and also as predictors of cancer recurrence ([9]).

After the first hypothesis numerous methods were devised by different Authors in order to demonstrate estrogen receptors within breast-cancer cells and various opinions were expressed as to which offered better results ([2, 3, 4]).

This paper describes the results we have obtained with a technique which we feel is the most suitable for routine use at the present and has the purpose of discussing its utility, technical problems and limits.

METHODS

Many protocols have been suggested in order to assay this high affinity protein receptors. They all require homogenisation and centrifugation of the tumor and isotopic tracers and depend on the capacity of proteins in the cytosol fraction of tissue homogenates to specifically bind estrogen. The difference between the various methods consists in the technique of the hormone bound to receptors from the amount of free hormone.

The method most widely used and recommended by EORTC is that in which separation of the marked steroids is performed by use of dextran-coated charcoal. We have used this method and will not review the technique since it has been already fully described by other Authors ([2, 3, 4, 6, 15]).

Table 1. — *Percentage of ER/PR assay in 162 patients examined.*

	Cases	%
ER+	76	40.9
PR+	54	33.3
ER−	86	53.0
PR−	108	66.6
Dubious Activity for ER	15	9.2
Dubious Activity for PR	17	10.4

RESULTS

162 patients submitted to mastectomy for carcinoma of the mammary gland have been studied. Most patients were treated in a teaching surgical department of the University of Trieste, the remaining were treated in other Hospitals participating in the Friuli - Venezia Giulia research group.

In regard to positive-negative cut-off values, ER (estrogen receptors) less than 4 femtomoles we considered negative, positive ER above values of 10 femtomoles, PR (progesterone receptors) less than 15 negative, positive that above levels of 15 femtomoles.

In table 1 are listed the frequency percentages for ER/PR cancers. The positives are somewhat elevated for ER, less for PR.

In table 2 are reported the precentages of the cases where both ER/PR are positive and where only ER is positive in relation to PR.

DISCUSSION

We can make the following points.

1) Our results are very close to those obtained by other Authors, for example that of Hawkins, Faherty, Mass and Jensen and Associates. The latter resulted in 117 examined patients where only ER was determined, being 56 cases ER positive and 53 cases ER negative and 8 cases which where difficult to classify. Also out of 56 patients with nodal status only 18 resulted positive, 4 with dubious results and 34 negative cancers ([9, 16, 17]).

2) It is interesting to note that in patients with metastatic tumors the percentage of negative cases is very much elevated. According to various Authors this distribution is due to a lack of receptor synthesis which is thus characteristic of a more advanced stage of relentless emergence of new subpopulations with enhanced metastatic capacities ([11]). No Authors up to date has reported the presence of negative ER/PR in breast cancer with positive nodes ([8, 19]).

3) If we analyse the positive ER's compared to PR we see that,

a) All cases of ER− resulted in PR− too, except for 8 cases which were difficult to classify.

b) Cases of ER positive resulted only in 28.4 percent with positive PR cancers.

4) At present there does not exist a protocol which is completely satisfactory and hopefully there will be further advances in this sense ([5]).

The possibility of eliminating false negatives or false positives such as PR positive with ER negative, can be found not only in better protocols such as monoclonal preparations, but also in handling of the mastectomy specimen. Newsome and associates have demonstrated (fig. 1, 2) that receptor modification varies not only during menstruation or because of subpopulations of tumor cells but also depends on the time taken to obtain and later trasport the specimen to the lab. In this sense it is possible to have results of high

Table 2. — *Comparison of precentage of cases ER+ and PR− with ER+ and PR−.* ER+/PR− or ER+/PR+

	Cases	%
ER+/PR+	46	20.4
ER+/PR−	30	18.5
ER−/PR+	8	4.9

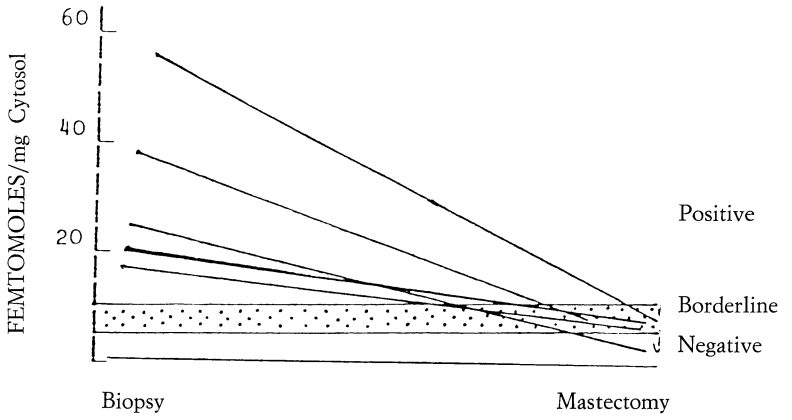

Fig. 1. — Comparison of receptor concentration during biopsy and mastectomy (Newsome and Ass.).

positives during the biopsy compared to specimens taken during the mastectomy. According to these Authors in fact, one of the reasons that negative ER cancer patients response to hormonal therapy could be the result of poor specimen preparation ([13]).

CONCLUSION

Receptor assay as seen by our results and according to other Authors has important clinical aspects. The dextran-coated charcoal protocol is certainly very exact, but not perfect. At the present time it is the only method readily available ([7]). In the last years receptor assay has taken on clinical importance for therapeutic approaches and to avoid surgical procedures in cases of ER negative cancers and within limits to suggest a prognosis ([1, 14]).

To eliminate margins of error that might occur in specimen handling during

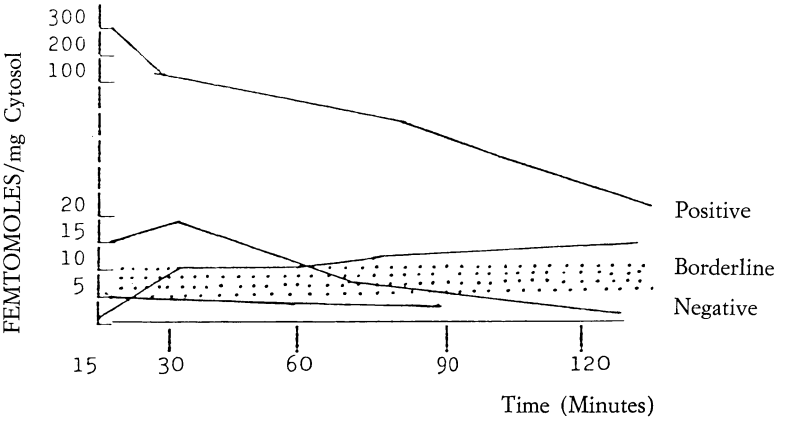

Fig. 2. — Variations in ER concentration of specimens after mastectomy left at room temperature for 15 to 120 minutes (Newsome and Ass.).

the mastectomy and trasport to the lab, we propose a program of checking between different labs and the creation of a " data bank " which would be at the disposition of Oncological Clinics to better prepare a therapy regimen such as the trail to increase the efficacy of cytotoxic chemiotherapy by hormonal synchronization proposed by M. Lippman ([10, 18, 20]).

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