Why to Measure Estrogen Receptor Status in Breast Carcinomas?

Pages with reference to book, From 132 To 133

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Why to measure estrogen receptors (ER) in the first place, how to measure it and to determine what is required of the test. These are the questions most commonly asked regarding estrogen receptor determination. Several clinical studies have established the value of estrogen receptor assays of carcinoma breast in predicting the response to endocrine (anti-estrogen) treatment[1,2]. has now been conclusively demonstrated that the ability to respond to these treatments in breast cancer is associated with the presence in tumours of ER and especially to progesterone receptors (PR)[3]. It has been suggested that since the synthesis of PR results from estrogenic action, the presence of PR denotes a functional ER and thus its measurement with ER can be of greater value than the measurement of ER alone[4]. The prognostic impact of ER status is still under investigation but seems to indicate that significant amounts of ER in breast tumours are associated with longer overall and possibly with a longer disease free survival[5,6]. Since cells normally dependent on estrogen contain a similar receptor, the presence of this protein may reflect the degree of differentiation of the cells. The question now being investigated is whether ER status is of prognostic significance in itself or only in relation to tumour grade! controversy persists[7]. Another important question is commonly asked regarding clinical responses obtained with hormonal treatments, of which anti-estrogen (tamoxifen) administration is the most usual is that they are not infrequently followed by recurrence. Several possibilities have been proposed to explain these failures and the most convincing explanation is that a tumour consists of both ER positive and negative clones and that after hormonal therapy, only ER negative clones survive and grow[8]. However, this cannot explain the fact that most recurrent tumours are still ER positive[9]. It is hypothesized that ER may be absent in tumour stem cells even in ER positive clones, only being expressed in the course of cellular differentiation[10]. It is proposed that after some cell divisions and while still retaining some proliferative capacity the ER start to get expressed[11]. This induces the expression of PR. Once PR is synthesized and binds progesterone, it inhibits several genes related to cellular proliferation. This explains the growth characteristics of most breast cancers, e.g., inwell differentiated ER+ /PR+ tumours PR expression would determine a feedback inhibition on ER+ cells and would slow down the growth process. Since many poorly differentiated tumours do not express ER and consequently PR, they would remain insensitive to the blocking action of PR. Considering very high incidence of breast carcinoma pathologists must do everything possible to assist with breast carcinoma management. Evaluation of estrogen and progesterone receptor status which aids patient management and prediction of prognosis is an important first step. The dextran coated charcoal (DCC) assay has been considereb the gold standard for hormone status determination but it is problematic, requires specialized equipment and is expensive. In addition abundant fresh/frozen tissue is required. Immunohistochemical methods of ER and PR determination overcomes many of these drawbacks. It is relatively inexpensive and requires no specialized equipment and can be performed at a community hospital level. Only minute samples are required including FNA's. Only disadvantage is that it is semi-quantitative. However, as management decisions appear to be made on a positive or negative receptor basis the riced for exact quantification may not be essential. There are still some important technical issues regarding immunehistochemical (IHC) analysis of ER e.g., no consensus exists regarding howto score or report results. Nearly every imaginable method of scoring has been tried. In addition none of these methods has been directly related to clinical outcome. In my opinion arbitrary semi-quantitative

scoring of Il-IC staining as we routinely do in our laboratory is valuable atleast for quality control and for performing correlative inter-laboratory studies[12]. ln summary despite the rapid growth of information much remains to be clarified about the role of these receptors in health and disease and regarding best method to determine it.

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