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لم ترد بالأصل

HOSSAM MAGHRABY

IMMUNOHISTOCHEMICAL ESTIMATION OF PROGESTERONE RECEPTORS IN ENDOMETRIAL HYPERPLASIA AND ENDOMETRIAL CARCINOMA

THESIS

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RATIONAL AND BACKGROUND

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Incidence of endometrial cancer is increasing. standardized mortality rate per 100,000 women was 9.66 for endometrial cancer. For this reason better indices for prognosis and therapy selection are required (Key et al., 1988).

Because endometrial cancer belongs to the category of hormone dependent neoplasias, endocrine indicators such as female steroid receptors have been expected to serve a new basis for categorization of patients with endometrial cancel as far as prognosis and treatment modalities are concerned (Hoffman and Sitteri, 1980).

It is now well known that estrogen and progesterone receptors play a role in the treatment and prognosis of breast and endometrial carcinomas (Marc et al., 1992).

Estrogen receptor (ER) and progesterone receptor (PR) content of endometrial carcinomas correlate with a variety of clinicopathological parameters (Stage, histological grade, etc.) prognosis, and survival. (Palmer et al., 1988).

The progesterone receptors have only recently been studied by immunohistochemical methods (Ferenczy et al., 1989).

Receptor status of both estrogen and progesterone receptors related most strongly to histologic grade of tumor, with well differentiated tumors more likely to be receptor positive and to have a higher absolute receptor content. Similarly, a less invasive tumor was more likely to have a higher estrogen and progesterone receptor content. The relationship between low receptor content and advanced stage was significant. Quantitative rather than qualitative receptor study values in stratification of future treatment protocols to prevent their effect on survival from producing bias in results (Palmer et al., 1988).

In large tumors not only can receptor content varies across a tumor but even receptor status can varies from positive to negative across an individual tumor. The follow up of the patients indicate possible clinical significance of a heterogeneous receptor distribution across a tumor. Clinically it is not easy to determine whether an advanced local tumor is slow growing or aggressive. Multiple biopsies of such tumors for determination of functional receptor status may be useful. These tumors which are receptor positive throughout, reflect a relatively good prognosis whereas variation in receptor status across the tumor may be associated with poor prognosis. In conclusion assay of functional receptors from different parts of large endometrial cancers may be a measure of both hormone sensitivity and prognosis (Castagnetta et al., 1987).

Estrogen and progesterone are known to modulate endometrial proliferation and differentiation via their receptors. Several studies have indicated that prolonged estrogenic stimulation, unopposed by progesterone, may promote the development of endometrial hyperplasia, atypical hyperplasia, and adenocarcinoma (Key et al., 1988).

Most women with hyperplasia do not have a significantly increased risk for developing an endometrial cancer and will respond favorably to progestational thereby. In contrast, endometrial hyperplasia with cytological atypia often progresses to carcinoma and shows unfavorable response to progesterone. When endometrial adenocarcinoma has developed, the proliferation character of this disorder has become irreversible. For histopathological evaluation of endometrial atypical hyperplasia, a marker that could better identifies patients at increased risk for cancer would be very helpful and this marker might be used as a prognostic indicator for progression once adenocarcinoma has developed (Ehrlich et al., 1988, Ferenczy et al., 1989 and Palmer et al., 1988).

Hormone responsiveness of endometrial epithelium has been shown to depend strongly on interaction with the stroma, suggesting autocrine and paracrine action between these cell types. Stimulated by steroids, the stroma produces growth regulating factors which control epithelial cell differentiation and function. Such stromal-epithelial interaction may also play a role in the formation of proliferative disorders of the endometrium (Marc et al., 1992).

The presence of functional PR has been correlated with response to progestational therapy. The extensive PR staining that found in endometrial hyperplasia explains why these lesions can be brought to secretory differentiation by progestational therapy in 100% of cases. The less extensive steroid receptor immunoreactivity in endometrial atypical hyperplasia suggests that this lesion may be less sensitive to progestational therapy rather than hyperplasia (Ferenczy et al., 1989).

Endometrial hyperplasia, atypical hyperplasia and adenocarcinoma with increasing epithelial atypia are correlated with a progressive loss of steroid receptor content. Stromal cells in atypical hyperplasia and well differentiated adenocarcinoma exhibit a relative loss of PR content as compared with epithelial cells, and in atypical hyperplasia the decrease in stromal receptor content is not in parallel for ER. and PR. Therefore defects in hormonal interactions between stromal and epithelial cells are associated with neoplastic transformation of endometrial proliferative lesions (Marc et al., 1992).

Many of the patients with endometrial carcinoma and hyperplasia are generally old and frequently have medical illnesses such as diabetes mellitus, obesity and hypertension. For this reason, the so called "adjuvant" hormonal therapy especially in unselected groups of patients is not entirely harmless (Ehrlich et al., 1981, and Shijders et al., 1990).

Recently, monoclonal antibodies specific for the binding with the progestrone receptors have become available. Immunohistochemistry with these monoclonal antibodies allows localization of the steroid receptors at the cellular level (Press et al., 1986).

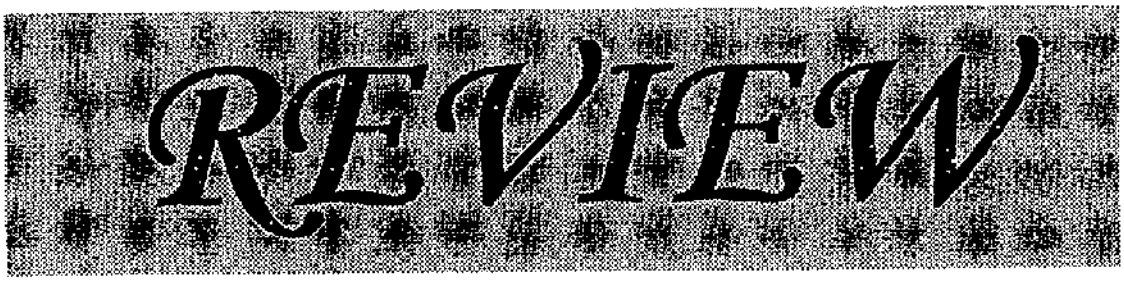
The availability of well characterized reagents and a sensitive immunoperoxidase technique helps in detection and amplification of the few receptor molecules present in individual cells (Green and Jensen, 1982).

OBJECTIVE

1. To find out the correlation between the most adopted standard diagnosis, criteria of progesterone responsive lesions and the progesterone receptor (PR) data assessed by immunohistochemistry.

2. To evaluate the importance of the progesterone receptor data in relation to the histopathological study of these lesions in some Egyptian patients.

3. To study the stromal hormonal receptor pattern in relation to epithelial one in these lesions.


REVIEW