

Original Article

Prognostic Values of Estrogen and Progesterone Expression Receptors in Ovarian Papillary Serous Carcinoma

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ABSTRACT

Background and Objectives: Presence of steroid hormone receptors (estrogen and progesterone) in the tumor tissues of various organs correlates with response to therapy and prognosis. Since their role in ovarian cancer is still controversial, in this study we investigated the expression and prognostic value of the estrogen receptor (ER) and progesterone receptors (PR) in ovarian papillary serous carcinoma (PSC).

Material and Methods: In this retrospective study we determined the expression of tissue receptors including tissue samples from 36 patients with stage III ovarian PSC by Immunohistochemistry method. Then ER and PR expression correlated with clinicopathological parameters and possible prognostic impact on ovarian PSC were investigated.

Results: The correlation between age and survey of patients with ovarian PSC and expression of steroid receptor was not significant. Although correlation between severity of expression of PR and mortality rate was not meaningful, the relationship between severity of ER expression and mortality rate was significant ($P=0.02$)

Conclusion: The determination of steroid receptor status may offer additional prognostic information in ovarian carcinoma (PSC).

Keywords: Ovarian cancer, Estrogen receptor, Progesterone receptor, Survival

Introduction

Estrogen and progesterone are important hormones secreted by the ovary acting through specific receptors (1). Tumor tissue expression profiles of these have demonstrated prognostic value in malignancies such as breast, uterine, prostate, and cancers (2).

In contrast to breast tumors, as far as the medical science is concerned, little information concerning estrogen receptor (ER) and progesterone receptors (PR) expression is available for ovarian cancers. Both hormones and their receptors are thought to be involved in the process of tumor genesis in gynecology as well as ovarian cancer (3).

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Although steroid hormones may have an important influence on the tumor genesis and response to treatment and progression of ovarian carcinomas, comprehensive immunohistochemical analyses of tumoral ER and PR expressions in the patient groups in literature representative are scarce (4). Clinical records of 186 patients with ovarian carcinoma who were admitted from 1982 to 1996 showed that the determiners of steroid hormone receptors provide helpful information regarding long term prognosis in patients with ovarian carcinomas (5). Penglec reported that PR is an independent marker, and its over expression association with a favorable prognosis in women with ovarian cancer was observed. While some studies have shown that the expression of PR was associated with a longer progression-free survival in patients with ovarian cancer (6), others have not presented such a benefit. The conflicting findings appear in results may be from various factors including the methods used for detection on the expression of the receptors, case selection, and sample size (7).

Thus, we studied ER and PR tumor expression and their possible prognostic value in ovarian papillary serous carcinoma.

Materials and Methods

In this retrospective study we analyzed expression of receptors (ER,PR) in tissue from women with stage III ovarian PSC referred to our Gynecologic Oncology Centers, (Ghaem hospital , university of medical science , Mashhad , Iran and Omid Hospitals, Mashhad University of Medical Science , Mashhad , Iran from 2005 to 2008 by immunohistochemistry method. The slides of cases were reviewed by a pathologist for tissue adequacy and confirmation of diagnosis, the immunohistochemistry method that we used in our study was PAP method (peroxidase, antiperoxidase) after cutting the paraffin blocks for 2-4 h in room temperature and then different steps of immunohistochemistry staining regard to the factory catalogue . The antibody code PR clone PgR 636 mouse Anti human progesterone, the antibody code N, 15. 75, ER-clone 1D5 MoM Anti human estrogen for positive control of ER and PR markers normal breast tissue was used and for negative control, antibody were omitted in staining process.

Nuclear staining in tumoral cells was assessed. All of patients underwent the same treatment.

We followed them for a period of three years .Specific survival rate was calculated as a percentage

of subjects who survived with the disease free for a definite period , reported as the time diagnosis or treatment until follow-up . The percentage of tumor cells that exhibited nuclear staining for a particular receptor regardless of the intensity was as follows : negative (0) weak (<9%) moderate (10-15%) and strong (>50%). Samples in which more than 10% of cells showed stained nuclei were judged positive. Receptor negative and receptor positive population were compared by chi-square, Fisher exact test, Mann – withney test and kruskal –wallis test analyses were used to identify the correlation between tumor expression receptors and age and survival of patients.

Results

The mean age of 36 patients was 56.61 years (range 35-95 years). All of the patients were in stage III ovarian papillary serous carcinoma .Three years survival was 24.55±16.3 months. Mortality rate of patients was 66.7%. All tumor specimens of patients with PSC expressed estrogen and progesterone receptors.

According to statistical analyses the relationship between the age and survey of patients with ovarian papillary serous carcinoma and tumor expression of estrogen and progesterone receptors was not significant.

(*P* value for ER and age =0.184, for ER and survey >0.093) (*P* value for PR and age = 0.286, for PR and survey > 0.321). Also correlation between the severity of expression of PR steroid receptor and mortality rate of ovarian PSC patients was not significant, but this relationship about ER expression severity was meaningful (*P*<0.02).

Discussion

In the last two decades the prognostic role of the steroid hormone receptors has been the subject of a myriad of publications. Nevertheless, its relevance after long term follow-up of ovarian cancers is still not clear (8).

The latest studies of the analyses of ER/PR status showed that steroid receptors in ovarian carcinoma have significant favorable prognostic values and long disease free-survival (9,10). Especially progesterone positive tumor receptor status is proved to be an independent prognostic variable of improved progression for free-survival among patients with

ovarian cancers. These studies reflect functional effects of steroid receptors (ER, PR) on tumor proliferation, differentiation and cellular apoptosis(11).

Unlike cancers of the breast and endometrium, in which steroid hormone receptor status correlates well with response to hormonal manipulation, a significant impact of tumor receptor status and response to hormonal therapy among patients with epithelial ovarian cancer is not readily demonstrable (12). Schwartz *et al* observed that 4 out of 13 patients treated with tamoxifen as salvage therapy for progressive epithelial ovarian cancer and achieved disease stabilization had borderline or high tumor ER levels(13). Extending these observations, he randomized untreated patients with FIGO stage III or IV epithelial ovarian cancer to treat with cisplatin plus doxorubicin or cisplatin, doxorubicin, and tamoxifen. No statistically significant difference in survival was observed between the two treatment arms when evaluated based on receptor status (13-15). In our study expression of ER and PR in patients with PSC did not have significant correlation with age and survival of patients but the relationship between the severity of ER expression and mortality rate of patients was significant. All of our patients have the same treatment.

Parallel to our results from this study a lack of association between steroid hormone receptor status and response to hormonal therapy was also reported by Rose *et al.* These researchers reported that among 26 valuable patients with ovarian cancer who received either megestrol, tamoxifen, or both as salvage therapy, disease stabilization for 6 months or more, tumor regression was not significantly associated with ER status or PR status. In a Gynecologic Oncology Group Study 23 in which 105 patients with FIGO stage III or IV epithelial ovarian cancer were treated with tamoxifen as second – line salvage therapy, no significant difference in response to therapy based on ER status was observed (16).

These differences about hormone receptors expression may be due to various parameters including case selection, method of immunohistochemistry and sample size, that they should be standardized and it is important to identify reliable prognostic markers in future clinical trial of hormonal therapy in the treatment of patients with ovarian papillary serous carcinoma.

Conclusion

The determination of steroid receptor status may offer additional prognostic information in ovarian carcinoma (PSC).

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