

16

KALLIKREINS 6 AND 10 AS PROGNOSTIC MARKERS OF OVARIAN CANCERS

V. Barak, Y. Sherman, V. Doviner, D. Edelman and E.P. Diamandis
Immunology Lab., for Tumor Diagnosis, Oncology Dep., Pathology Dep., Hadassah University Hospital, Jerusalem, Israel and Pathology and Laboratory Medicine Dep., Mount Sinai Hospital, Toronto, ON.

BACKGROUND: Previous studies indicated that two members of the human kallikrein (KLK) family, KLK6 and KLK10 are differentially expressed in epithelial ovarian cancers and may serve as independent adverse prognostic markers. The expression of both KLK6 and KLK10 in these studies was determined by measuring the level of the kallikreins in ovarian cancer cytosolic extracts. Both kallikreins correlate with unfavorable prognosis in late-stage ovarian cancer. These studies also report a general positive immunohistochemical expression of both kallikreins in the cytoplasm of ovarian cancer cells of epithelial origin.

In the present study, we examined in detail the nature of the immunostaining in the tumor cells of various ovarian neoplasms and evaluated the correlation between its intensity and the histological sub-typing and grading of the tumor, with the aim of defining the potential use of the differential expression as a morphologic prognostic marker in this tumor group.

EXPERIMENTAL DESIGN: We analyzed specimens from 15 normal ovarian tissues, 20 ovarian tissues with benign epithelial neoplasms, 16 with various mesenchymal tumors and 35 with carcinomas of various histological sub-types. We employed KLK6 and KLK10-specific polyclonal rabbit antibodies and avidin-biotin to localize KLK6 and KLK10 respectively, by immunohistochemistry.

RESULTS: Both kallikreins were markedly expressed in the cytoplasm of carcinoma cells of various histological types and grades. They were missing altogether in normal stromal cells, in normal cells as well as tumor cells of mesenchymal origin, and only negligibly expressed in cells of the epithelial component of benign ovarian neoplasms.

The staining intensity in the positive carcinoma cells was found to differentiate well between the main two histological sub types, so that the serous papillary carcinoma portrayed, in general, a higher staining intensity than the mucinous carcinoma.

Comparison of the staining characteristics in the various sub-groups (as defined by histological grading), revealed a tendency towards increasing intensity of expression with higher the tumor grade, being particularly accentuated in foci of anaplastic carcinoma.

CONCLUSIONS: Our results indicate that the immunohistochemical expression of both KLK6 and KLK10 in ovarian cancers follows the path of the classical morphological criteria for tumor aggressiveness, and may prove to be a useful prognostic tool for more accurately defining the future biological behavior and therapeutic response of these tumors. However, additional clinical-pathological-immunohistochemical correlation studies are required in order to assess and confirm the reliability of the expression of these kallikreins as a morphologic prognostic marker for ovarian epithelial cancers.