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Laparoscopic fluorescent diagnostics of peritoneal dissemination of ovarian cancer with Alasense

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The aims of the study were working out the regime of fluorescent diagnostics (FD) with second-generation photosensitizer Alasense (5-aminolevulenic acid, NIOPIC, Russia)(AS) during standart laparoscopy in patients with ovarian cancer (OC) in frames of 2 stage of clinical trials, evaluating the efficacy, toxicity and safety of FD with AS.
Materials: Fluorescent diagnostics (FD) using Alasense as photosensitizer during standart laparoscopy have been provided in 10 patients with T1–4 stage ovarian cancer of different histology for evaluating the completeness of response after previous complex therapy or in cases of suspicion of recurrence of disease. Previous complete clinical and instrumental investigation (ultrasound, computer tomography) showed no signs of peritoneal metastases or liquid in peritoneal cavity in these patients.
AS was given per os in dose 20 mg per kg of body weight in 150 ml of water solution. Laparoscopy in white light and FD with detecting of the fluorescence zones, borders of metastases dissemination and intensity of accumulation of AS in metastases of ovarian cancer and adjusting tissues has been provided 4 hours after AS administration with Spectral-fluorescent Complex (He-Ne-laser, wavelength 633 nm) with CCD-camera.
Results: We've found intensive fluorescence zones on peritoneum in 9 patients, the number of zones in patients was from 1 till 7, the sizes of it from 0.2 till 0.9 cm. Most of this places were not suspicious for metastases in white light. Biopcies were taken from all fluorescence zones for cytological and histological examination. Morphological verification of metastases of ovarian cancer has been got in 8 patients in all samples, in 1 case – endometriosis has been found in biopsy by histology. No skin phototoxicity and other side effects were found after AS administration or during laparoscopy with FD.
Conclusion: Our experience show pronounced efficacy of laparoscopic FD with alasense comparing to traditional one in white light for early evaluating of peritoneal dissemination of ovarian cancer with high specificity and sensitivity.

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Beneficial effect of chemotherapy on CD8+ T cell responses in advanced ovarian cancer

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Development of potent $CD8^+$ T cell responses is crucial for efficient anti-tumour responses in several types of cancer and is the main aim of cancer immunotherapy. Combination of immunotherapy with chemotherapy is an emerging new approach with promising results in some settings [1]. The objective of our study was to establish a method for monitoring $CD8^+$ T cell function in cancer patients in order to provide basic information about immunological changes during chemotherapy. T cell function of 21 patients with advanced ovarian cancer (FIGO III-IV) was assessed by cytokine flow cytometry following stimulation of 42 PBMC samples with a panel of synthetic viral peptides in vitro, consisting of pan-Caucasian epitopes. $CD8^+$ T cell responses were significantly lower in patients with high levels (>200 U/ml) of Ca125 (marker of tumour load and progression) than in those with low Ca125 levels ($p = 0.0013$). Longitudinal studies of nine patients showed, after the full course of chemotherapy, 5/9 patients in remission displayed potent $CD8^+$ T cell responses, while 4/9 patients in progression displayed low or falling T cell responses, pointing towards a correlation between T cell function and clinical response. Most importantly, the magnitude of the $CD8^+$ T cell response showed a significant correlation with progression free survival (univariate analysis, $p = 0.011$). Our results show for the first time that $CD8^+$ T cell function is not permanently suppressed in advanced cancer and chemotherapy may result in improved immunological functions. The underlying mechanism is likely to be complex, including the release of dead tumour cells for uptake by the immune system, and overcoming the immunosuppressive effects of the tumour. Identifying these elements will make it possible to design better chemo-immunotherapy protocols.

References

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966 PUBLICATION

Detection of human papillomaviruses and Epstein-Barr virus in ovarian malignancy

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The role of HPV and EBV infection in ovarian cancer is unclear. The aim of this study was to investigate association between "low risk" and "high risk" HPV types, EBV and epithelial ovarian cancer by screening ovarian tumor tissues for presence of HPV DNA.
Materials and Methods: The patients group consisted of 67 epithelial ovarian carcinomas (52 serous adenocarcinomas and 15 mucinous adenocarcinomas). The mean age of the patients was 57 years (range 20–85 years). The control group consisted of 25 nonmalignant ovarian tissues collected from 25 women (mean age 56; range 41–69) with uterine pathology undergoing pelvic surgery. DNA was isolated from snap-frozen ovarian tumor tissues and polymerase chain reaction (PCR) kits were used to detect the presence of the "low risk" HPV types (6, 11, 42, 53, 54), the "high risk" HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 55, 58, 59, 66, 68, 73, 83) and EBV in tumor DNA samples.
Results: HPV DNA was detected in 51 (76%) of the 67 tumor DNA samples. Only 2 or 8% of normal ovarian tissue samples were positive determined by PCR ($p < 0.001$). There was no correlation between HPV infection and histological type of ovarian cancer. The positive rate is 75% of serous adenocarcinomas and 80% mucinous adenocarcinomas ($p > 0.05$). Among samples of epithelial ovarian carcinomas more frequently were revealed HPV-18 (30%), 52 (30%), 55 (27%), 83 (18%) and 39 (16%) types. HPV 73, 31, 51, 45, 33, 66, 68 and 16 types were detected 12%; 10%; 9%; 6%; 5%; 3%; 3% and 3% of the tumor tissue samples respectively. HPV-35, 58, 59 types and "low risk" HPV types were not identified in any ovarian cancer. HPV-18 type was significantly higher in mucinous adenocarcinomas (80%) compared to serous cancer (15%) ($d < 0.001$); HPV-52 (36.5%) and 55 (32.7%) types – in serous adenocarcinomas compared to mucinous cancer (7% and 7% respectively) ($d < 0.01$). EBV DNA was present in 38.8% of the ovarian cancer specimens (in 46.2% of serous and in 13.3% mucinous adenocarcinomas) and in 12% of nonmalignant ovarian tissues ($d < 0.01$). Moreover a 28.4% prevalence rate was demonstrated for association of EBV and HPV, namely HPV-52 (17.9%), HPV-55 (13.4%) and HPV-18 (6%) types.
Conclusions: Our results support an association between HPV-18, 52, 55, 83 and 39 types, EBV and epithelial ovarian malignancy. The prevalence of HPV and EBV infection in ovarian cancer is much higher than normal ovarian tissues, suggesting that both viruses may play a role in the development of ovarian cancer.

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HPV DNA detection and the shedding of viral infected cells in the blood of women with cervical cancer

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Purpose: Detection of HPV DNA in blood samples of patients with Squamous Intraepithelial Lesion (SIL) and Invasive Cervical Cancer (ICC).
Methods: Blood samples were collected from 163 patients with cervical neoplasia. Using PCR and two pairs of specific HPV primers, the presence of HPV DNA was tested in all samples from cases with SIL and ICC with (ICC-P) and without parametrial involvement (ICC-NP)
Results: HPV DNA was found in 25 (15.3%) of 163 patients. The medium age of patients with HPV DNA presence were 49.8 ± 19.6 and 45.2 ± 12.8 for patients with HPV DNA absence ($P = 0.105$). An association was found between the detection of the HPV DNA presence and the severity of the cervical lesion: In SIL lesion we could detect HPV DNA in 6 (7.7%) of 78 patients, 6 (20.7%) in 29 with ICC-NP and 13 (23.2%) in 56 with ICC-P. Using SIL group as reference a statistical significant difference was found for ICC ($P = 0.009$), ICC-NP ($P = 0.058$) and ICC-P ($P = 0.011$).
Conclusion: Our results demonstrate an association between the severity of the cervical lesion and the HPV DNA presence in peripheral blood, particularly in invasive cervical cancer with parametrial involvement. Further studies may help to understand the real meaning of the shedding of HPV infected cells in the blood of women with cervical cancer.