211

p53 PROTEIN DETECTED BY IMMUNOHISTOCHEMISTRY IN MALIGNANT EPITHELIAL OVARIAN TUMORS

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136 ovarian epithelial carcinomas were studied by immunohistochemistry for p53 protein expression from paraffin-embedded tissue. Positive staining (present in 44%) was associated with the serous histological type (p=0.002), a higher than the median S-phase fraction size determined by DNA flow cytometry (p=0.02), and poor histological grade of differentiation (p=0.04), but not with the FIGO stage, age at diagnosis, or DNA ploidy. Cancers with positive staining had only a 17% 5-yr and 9% 15-yr survival rate as compared with 42% 5-yr and 36% 15-yr survival rate corrected for intercurrent deaths among the rest of cases (p=0.002). In a multivariate analysis positive p53 staining was associated with poor survival together with less than radical surgery, and advanced FIGO stage.
Key words:Ovarian cancer,Survival,p53protein

212

CYCLOPHOSPHAMIDE-CISPLATIN /CPM-CDDP/ VERSUS CYCLOPHOSPHAMIDE-CARBOPLATIN /CPM-CPL/ WITH AND WITHOUT ANTIEMETIC ZOFRAN IN THE TREATMENT OF ADVANCED OVARIAN CANCER /ST.III-IV./

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Two combinations of chemotherapy agents with and without administration of the antiemetic Zofran /GLAXO/ were compared for therapeutic effectiveness on 83 patients with advanced ovarian carcinoma. Forty-two patients were treated with cyclophosphamide-cisplatin /CPM-CDDP/ and 41 patients with cyclophosphamide-carboplatin /CPM-CPL/. In the CPM-CDDP treated group 32 /76,2%/and in the CPM-CPL treated group 34 /84,0%/ responded to cytostatic therapy. The median progression free interval was a bit longer in the CPM-CPL /14 months/ than in the CPM-CDDP /12 months/ treatment group. The median survival was 26months and 23 months in favor of the CPM-CPL therapy . Addition of Zofran caused significantly better antiemetic effect in both combinations of chemotherapy agents than other steroid derivates /Oradexon, Metypred/.

213

DOLICHOL AS A TUMOUR MARKER IN OVARIAN CANCER CONTROL

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Ovary contains the highest concentration of Dolichol (Dol) in human tissues, Dol is responsible for the state of cell membranes and synthesis of N-glycoproteins. In cancer patients, urinary Dol have been reported to be 5 to 40 times the normal values, suggesting a metabolic abnormality of Dol in patients with metastatic cancer (Pullarkat et al., 1984). With fokus on a tumour marker, the present study was carried out to estimate blood and urinary levels of Dol in ovarian cancer patients with different stages of the process. The samples obtained from 28 patients (45-50 years old). Dol in blood and urine was assayed by HPLC (Turpeinen, 1986). The amounts of Dol in healthy women's blood and urine are 136,5 ± 6,9 ng/mL and 7,6 ± 0,5 μg/mmol creatinine respectively. Blood Dol concentration incresed at stage Ib up to 36%, at stage Ic up to 68%, at stage IIb up to 75 %, making up 285,4 ± 12,8 ng/mL at stage III. Urinary Dol concentration increased statistically significantly at stage Ic (ascite with tumor cells) up to 124%, making up 47,9 ± 2,4 μg/mmol creatinine at stage IIb (the beginning of metastatic spreading). Chemotherapy with adriamycin and 5-FU decreased blood and urinal Dol levels at stages IIa - IIc. The interest drawn to the employment of Dol as a marker is explaned by the fact that known ovarian cancer markers are glycoproteins (CA-125 and TAG-72). There is reason to suggest that markers detected in ovarian cancer may evidence of the prime dolichyl phosphate cycle disorder. Dolichol appeared in urinary excretion as well as in blood is one of the first manifestations of this disorder.

214

OVEREXPRESSION OF THE ONCOGENE *C-ERBB-2* IN OVARIAN CANCER: A NEW PROGNOSTIC FACTOR

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To date, there are no prognostic factors in ovarian cancer that adequately account for tumor biology and disease behavior. In recent years, some reports have described the prognostic significance of the amplification and overexpression of the oncogene *c-erbB-2* in various human cancers. Concerning ovarian cancer, this is still a matter of discussion. In the present study, tumor tissue of 275 patients treated for ovarian cancer at our between 1982 and 1992 was department immunohistochemically analyzed for overexpression of c-erbB-2-encoded transmembrane protein p185. In 19% (51 of 275 cases) p185 overexpression was detected. The percentage of p185-positive cases varied from 7 to 46 % according to histological subtype. Patients with p185-positive tumors had a significantly worse prognosis (p = 0,001); median survial was 20 months compared with 33 months for p185-negative tumors. In the Cox proportional hazards regression, p185 overexpression was identified as an independent prognostically relevant factor. These results suggest that overexpression of oncogene *c-erbB-2* in ovarian cancer characterizes a group with unfavorable tumor biology and a significantly worse prognosis.

Key Words: Ovarian cancer - c-erbB-2-oncogene - Prognosis.

215

CISPLATIN AND TREOSULFANE CHEMOTHERAPY IN THE TREATMENT OF METASTATIC OVARIAN CANCER -LOW VERSUS HIGH DOSE

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The combination of Cisplatin 100mg/m² and treosulfane 5g/m² is a promising chemotherapy in the treatment of metastatic ovarian cancer. In order to minimalize the side effects of this chemotherapy without any loss of effectivness 92 patients were treated in a prospective randomised trial after maximal primary surgery either with cisplatin 50mg/m² and treosulfane 5g/m² (low dose) or cisplatin 100 mg/m² and treosulfane 5g/m² (high dose) four times in monthly intervalls. 44 patients belonged to the low dose group, 48 patients to the high dose group. After this treatment 23 patients of the low dose group and 33 patients of the high dose group underwent a second look surgery. The remissionrate of the low dose group was 41% compared to the 50% remissionrate of the high dose group. 70% of the low dose group patients and 60% of the high dose group patients develloped recurrences within a median disease free intervall of both 11 months. Side effects were more frequently regarded in the high dose group. Concerning remissionrate and recurrences high dose chemotherapy achieved better results. Survival and side effects did not show a significant difference between the two randomized groups.

216

AGE, MENOPAUSAL STATUS, HISTOLOGICAL GRADE, SURGICAL STAGE AND SURGICAL CLEARANCE: INDIPENDENT PROGNOSTIC FACTORS IN EPITHELIAL OVARIAN CANCER.

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OBJECTIVES: to identify favourable characteristics as independent prognostic factors for the overall survival of patients with epithelial ovarian cancer.
DESIGN: A retrospective multivariate analysis of 110 patients, treated by the same oncological team over a period of ten years (1983-1993)
SETTING: department of Gynaecology and Clinical Oncology, Derriford Hospital, Plymouth U.K.
RESULTS: The patients were divided in three age groups. The first group (21-40) had the best 5 year survival rate (80%), the second group (41-60) the worst (23%) and the third one group (61-80) (33%) respectively (P:0,006). The pre-menopausal group achieved a 57% 5 year survival rate againist only 23% in the post-menopausal group (P: 0,0009). Surgical staging according to the FIGO classification was a strong prognostic factor with survival varing from 100% for stages Ia, Ib to 15% and 13% for stages IIIc and IV respectively (P≤ 0,0001). Histological grade I, II and III had 72%, 22% and 6% respectively, 5 year survival rate. Complete surgical clearance produced an 86% survival, less than 2 cm residual tumor clearance 25% and more than 2 cm 7%. None of the patients with inoperable tumors survived 5 years.
CONCLUSION: Early diagnosis and optimal surgery are the cornerstones in the treatment of ovarian cancer. The elderly patients should be offered full and prompt treatment, since they are expected to do better than the middle age group.