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Serum cytokine levels in human papilloma virus (HPV)-related cervical disorders

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Purpose: to assess the difference, if any, between serum levels of interleukin 6 (IL6), tumour necrosis factor alpha (TNFα), c-reactive protein (crp) and ferritin in patients with different HPV-related cervical disorders.

Methods: IL6, TNFα, crp and ferritin were measured (single determination, standard methods) as follows: in 24 pts seen at diagnosis (9 with cervical dysplasia, CIN I–III; 15 with condilomata), mean age 32.5; 11 disease-free pts, mean age 28.2, seen at a follow-up visit for previous dysplasia (5) and condilomata (6).

Results: mean values are plotted in the table.

NV	IL6 pg/ml 3–8.5	TNFα pg/ml 3–20	CRP mg/dl <1	FERR ng/ml 15–155
CIN-D	6.9	18.1	0.4	21.5
CIN-DF	4.6	21.2	0.4	40.9
COND-D	5.4	20.4	0.8	26.2
COND-DF	3.5	17.3	0.6	34.5

(COND = condilomata, D = at diagnosis, DF = disease-free)

No difference was observed by Student's t test among the mean values measured in the 4 subgroups, although there was a slight trend towards abnormal values for crp, IL6 and TNFα in the CON-D pts.

Conclusion: neither in situ cervical cancer nor condilomata secondary to HPV infection seem to induce any significant alteration in the circulating levels of cytokines and acute phase reactants.

955 PUBLICATION

Treatment of endometrial stromal sarcoma

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Purpose: Different treatment modalities of endometrial stromal sarcoma (ESS) were evaluated.

Methods: 50 patients with ESS were included in the study. The mean age was 46.5 years. Stage I tumor was in 28 (56%) patients, stage II – in 7 (14%), stage III – in 8 (16%) and stage IV – in 7 (14%) patients. Twenty four patients were only operated on. Hysterectomy and bilateral salpingo-oophorectomy were performed. Twenty one patients were applied combined treatment modalities, 13 of them – operation and chemotherapy, 3 – operation and radiotherapy (external radiation to the primary tumor zone and regional nodes) and 5 – operation, chemo- and radiotherapy.

Results: 45 patients were followed up. Five-year disease-free survival was 55.6% and ten-year – 26.7%. Five- and ten-year survival after surgical treatment was 66.7% and 33.4%, respectively, after combined treatment – 42.9% and 19.1%, respectively. The data aren't significant. ESS spread to the ovaries, pelvic lymph nodes and to the omentum in 37.5%, to the para-aortic lymph nodes in 25%, to the vagina in 12.5% of cases.

Conclusion: We consider it's necessary to perform radical hysterectomy and bilateral salpingo-oophorectomy in stage I ESS and radical hysterectomy, bilateral salpingo-oophorectomy, and omentectomy in stage II–III ESS. If there are positive retroperitoneal lymph nodes and if there is spread to the omentum, ovaries, or vagina postoperative radiotherapy and chemotherapy should be applied.

956 PUBLICATION

Monocyte chemoattractant protein-1 serum levels in ovarian cancer patients

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Purpose: To evaluate MCP-1 serum levels in patients with ovarian cancer and to determine its value as differentiation marker and prognostic marker.

Methods: MCP-1 serum levels were determined in 48 patients with primary and 38 with recurrent ovarian cancer, 67 patients with benign ovarian cysts, and 42 healthy women by using a commercially available ELISA.

Results: Median MCP-1 serum levels in patients with primary ovarian cancer, recurrent ovarian cancer, benign ovarian cysts, and in healthy women were 535.6 (range 129.6 to 1200) pg/mL, 427.3 (range 193.4 to 1101) pg/mL, 371.2 (range 222 to 986.8) pg/mL, and 318.7 (range 241.3 to 681.4) pg/mL, respectively (Mann-Whitney U-test, $p < 0.001$). Univariate logistic regression models revealed a significant influence of MCP-1 serum levels on the odds of presenting with ovarian cancer versus benign cysts and versus healthy women, respectively ($p < 0.001$; and $p < 0.001$, respectively). In a multivariate logistic regression model, both MCP-1 and CA 125 revealed statistical significance on the odds of presenting with ovarian cancer versus benign cysts ($p = 0.05$, and $p < 0.001$, respectively). Elevated MCP-1 serum levels prior to therapy were not associated with disease free and overall survival (log-rank-test, $p = 0.2$; and $p = 0.7$, respectively).

Conclusion: MCP-1 might play a role in the natural history of ovarian cancer and might serve as differentiation marker between benign ovarian cysts and ovarian cancer, providing additional information to the established tumour marker CA 125.

957 PUBLICATION

Hypoxic abdominal perfusion plus chemosensitivity guided chemotherapy using ATP-bioluminicence assay as an effective therapy for recurrent ovarian cancers

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In order to increase response rates and improve survival of recurrent ovarian cancer patients we developed new strategies such as isolated hypoxic abdominal perfusion (HAP) to increase locoregional drug concentrations and individualization of chemotherapeutic regimens by using an ATP-bioluminicence sensitivity assay.

Material and Methods: Between 10/94 and 12/98 44 consecutive patients were treated by three different protocols: *Group A:* 11 pts., 2 cycles of HAP using Novantron (20 mg), Cis-platinum (75 mg) and Germanin (2000 mg) as cytostatics. *Group B:* 21 pts., 2 cycles of HAP using Mitomycin (20 mg), Cis-platinum (75 mg) and Treosulfan (7.500 mg) combined with 1 cycle intraaortic infusion of the same drugs. *Group C:* 12 pts., 3 cycles of an individualized treatment plan after chemosensitivity testing using ATP-bioluminicence assay – most drugs were given during HAP procedure.

Results: The three groups were well balance in terms of age, Karnofsky-index, UICC-stage: Group A: 58.1 y, 89.1, III 45%, IV 55%; Group B: 58.2 y, 86.2, III 67%, IV 33%, Group C: 56.3 y, 89.2, III 58%, IV 42%. No specific side effects could be observed. In most cases side effects were mild not exceeding WHO grade II. Remission rates were as follows: A: 45% CR 2, PR 3/11; B: 57% CR 6, PR 6/21; C: 92% CR 4, PR 7/12. The following survival rates after 12 and 24 months could be observed: Group A: 50%, 40%; B: 76%, 57%; C: 100%, 92%. This difference in survival was statisticly significant with p-value <0.00001.

Summary: Hypoxic abdominal perfusion is a therapeutic tool leading to increased regional drug concentrations hight enough to break through resistance in recurrent ovarian cancer patients. The combination of regional chemotherapy and individualisation of chemotherapeutic protocol will lead to an increase in response rate and prolongation of survival. Further studies have to confirm these encouraging results.

958 PUBLICATION

Expression of proteins – Products of genes involved in apoptosis regulation in epithelial tumors of ovarian cancer patients with different sensitivity to anticancer drugs

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Drug resistance represents one of the main reasons of failure in treatment of malignant tumors. Many anticancer drugs affect cancer cells by the induction of apoptosis. We have studied the expression of p53 and bcl-2 proteins affecting apoptosis and p-glycoprotein (product of mdr gene) in cells of epithelial ovarian tumors with different sensitivity to anticancer drugs

The sensitivity of cancer cells to cisplatin, cyclophosphane, thiophosphamide and doxorubicin has been assayed in vitro by the degree of SH-group inactivation in the tissue of the tumors due to the action of these drugs. The expression of the above-mentioned proteins has been studied immunohystochemically by PAP-technique in cryostat sections. The specimens of 20 patients with malignant ovarian cancer of different hystology have been analysed. The p53 expression has been shown in majority of the tumors under study with the most intensive reaction being observed in the cells of the least sensitive tumors. Most tumors do not express bcl-2