

Ova 03**GRANULOSA CELL TUMOR: A CLINICOPATHOLOGIC STUDY OF 22 CASES**

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From 1965 - 1983 22 patients with granulosa cell tumors were treated at the Gynaecological Department of the University of Cologne. They were admitted to the clinic because of irregular genital bleeding or pain. The existence of a granulosa cell tumor was preoperatively considered only in a few cases, however the high degree of proliferation of the cervical smears from 11 out of 14 postmenopausal patients indicated the presence of an estrogen producing tumor. Hysterectomy and bilateral salpingo-oophorectomy were performed in most cases. 9 patients got additional irradiation, 4 patients additional chemotherapy. In 3 young women only the involved adnexa was exstirpated to prevent infertility.

Pat.	N	Menopause		Stage (FIGO)				Observ. time (months)
		pre n=8	post n=14	I n=16	II n=0	III n=5	IV n=1	
NED	11	7	4	10	0	1	0	25-231
DT	9	1	8	5	0	3	1	10-80
DOR	2	0	2	1	0	1	0	

DT: died from tumor

DOR: died from other reasons

7 of the patients who died of the disease had polymorphic tumors with numerous mitotic figures. Apparently monomorphic granulosa cell tumors have a better prognosis, however the histological data cannot predict the survival outcome in individual cases. Therefore hysterectomy and bilateral salpingo-oophorectomy is advised in all cases (except young childless patients with stage I lesions) supported by adjuvant radiation or chemotherapy.

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Ova 04**OVARIAN TOXICITY OF CYCLOPHOSPHAMIDE IN MONKEYS**

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Cyclophosphamide (cy), an alkylating agent used in the treatment of a variety of neoplastic and non-neoplastic diseases produces early menopause, or premature ovarian failure. Because premature ovarian failure is a significant adverse effect of chemotherapy it is important to explore its mechanism. The experiments reported here were designed to characterise the effect of cy on the non-human primate ovary at different phases of the ovarian cycle. Normal cycling cynomolgus monkeys were treated with cy iv at a dose of $1g/m^2$, equivalent to the dose used in humans, either prior to or following the LH surge. All monkeys were bled daily to determine LH, FSH, oestradiol and progesterone by RIA. Thus, a total of 16 treatment cycles was studied in 11 monkeys. Control data were obtained from untreated monkeys. Monkeys treated after the LH surge had normal luteal phases and the follicular phase of the subsequent cycle was also normal. Treatment 1 day prior to the LH surge decreased both LH and progesterone secretion, the subsequent cycle was not disturbed. Treatment 2 to 4 days before the gonadotrophin surge produced a rapid and complete inhibition of oestradiol secretion, which lasted for more than 20 days; in the luteal phase of those monkeys, progesterone production was abolished. These data demonstrate that ovarian sensitivity to cy varies with the cycle. The sensitivity of the follicular phase is consistent with the known toxic effects of cy on rapidly proliferating cells. It is not known, if treatment during the luteal phase will prevent premature ovarian failure; however, the decreased endocrine disruption indicates that ovarian toxicity is reduced and therefore synchronisation of cy treatment with the luteal phase should be attempted. Univ.-Frauenklinik Grosshadern, Marchioninstr. 15, D-8000 Muenchen 70

Ova 05**MONITORING OVARIAN CARCINOMA WITH CA 125, CA 19-9, CA 15-3 AND CEA IN SERUM, ASCITES AND TUMOR TISSUE**

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The antigens CA 125, CA 19-9, CA 15-3 and CEA were evaluated in 823 sera from 207 patients (pts) with advanced ovarian carcinoma. Follow up studies have been performed in 96 cases (period 2 - 26 months).

CA 125	CA 19-9	CA 15-3	CEA
90%(185/207)	32%(58/183)	45%(48/107)	14%(27/179)

Raised serum concentrations (sc) of CA 125 were found depending on histological type: serous 96%(126/131), mucinous 53%(8/15), anaplastic 91%(19/21), endometrioid 91%(20/22), fallopian tube 100%(5,5). We found a good correlation between tumor mass and sc in 87%(88/99) of pts with large tumor mass (CA 125 > 100 U/ml). Sc > 100 U/ml were found in 4/14 cases with small tumor mass. Progression was indicated by rising Ca 125 sc in 82% (42/51), 28% of these preceded the clinical diagnosis 2 - 12 months. A few cases with single raised sc of CA 19-9 (5/183) and CEA (2/179) or CA 15-3 (1/107) were found. In 22 pts we found normal sc of CA 125. 14 were also negative for CA 19-9, CA 15-3 and CEA.

Immunohistochemistry stained positive in tumor tissue in 83%(33/40) for CA 125, 45%(18/40) for CA 19-9 and 55%(22/40) for CEA. Only a certain portion of each tumor stained positively, in maximum 70% of tumor cells. High sc correlated well with a high percentage of positively stained tumor cells.

In 9 pts serum samples and ascites were examined simultaneously. The mean value of CA 125 in ascites was markedly higher than in serum. Serum: 736 U/ml, ascites 1.229 U/ml. In monitoring advanced ovarian carcinoma CA 125 is superior to CEA, CA 19-9 and CA 15-3. Simultaneous determination of other markers than CA 125 did not show any advantage.

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Ova 06**INDICATION AND TECHNIQUE OF OVARIAN TRANSPOSITION TO PRESERVE OVARIAN FUNCTION IN PATIENTS UNDERGOING IRRADIATION**

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There is still some controversy whether preservation of ovarian function in young patients with Hodgkin's disease undergoing irradiation can best be achieved by oophorectomy or ovarian transposition (Gynecologic Oncology - Controversies in Cancer Treatment, Ed. S.C. Ballon, Hall, Boston 1981). This question cannot be answered from the literature because most of the patients in the past only had irradiation and no chemotherapy. There is strong evidence that the combination of both is likely to result in ovarian failure, depending on age and drug combinations (S.J. Horning et al., New Engl. J. Med. 304, 1377, 1981).

Having transposed ovaries in patients with pelvic tumors successfully, we started transposition in patients with Hodgkin's disease in combination with a modified radiation protocol. Conventional radiation will result in a calculated dose by scatter and penetration which is not tolerable in pretreated patients (approx. 4,8 Gy). Because of this an inverted Y-irradiation field is recommended in cases of limited disease. Calculated dose distributions in these patients, however, my nevertheless effect severely ovarian function. 3 patients have been treated until October 1985, two of them without measurable changes in plasma steroids and gonadotrophins. The case reports including the actual technique of ovarian transposition are presented.

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