518 PUBLICATION

WHOLE ABDOMINOPELVIC RADIOTHERAPY IN EPITHELIAL OVARIAN CANCER: A RETROSPECTIVE STUDY OF 48 PATIENTS

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Aim: To assess results and morbidity of whole abdominopelvic irradiation (WAI) in ovarian cancer.

Patients and methods: From January 1983 to December 1992 48 patients (pts.) with median age of 54.2 years, who presented epithelial ovarian cancer, were treated with WAI in our department. Patients were staged according to FIGO classification: stage I 9 pts., stage II 10 pts and stage III 29 pts. All pts. have had primary surgery; 41 out of 48 pts. have received chemotherapy (CT) and only 38 pts. have had second look laparotomy with debulking surgery in 18 pts. WAI consisted of whole abdominal dose of 22 Gy (at 1.6 Gy per fraction) and a total pelvic dose of 40 Gy; whereas the paraortic lymph nodes were boosted to a dose of 30 Gy. The series was divided in 3 groups: the first 22 pts. underwent macroscopically complete surgical resection at first laparotomy; in the second group 12 pts. had no residual disease after CT and or second surgical removal. Finally 14 pts. had histologically proven residual disease before radiation therapy.

Results: The median follow up was 48 months. For all pts, overall survival was 60.64% and overall survival in groups 1, 2 and 3 was respectively 81.14%, 62.86% and 28.57%. Six pts experienced small bowel complications requiring surgery.

Conclusions: High dose WAI is an effective treatment for patients with minimal residual disease with an acceptable complication rate.

519 PUBLICATION

TREATMENT OF PERITONEAL CARCINOSIS USING HYPERTHERMIC INTRAPERITONEAL PERFUSION

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The peritoneal surface is the second most common anatomical site for recurrence by gastrointestinal and ovarian cancer; 50% of all patients treated for gastric, ovarian or colo-rectal cancer present a "Peritoneal Carcinosis". 50% of patients with PC die without other metastases. Treatment of PC is controversial. Surgery is usually impractical because of its multiplicity and often microscopic size; systemic chemotherapy (CT) is inefficacious because cytotoxic agents do not penetrate into the peritoneal surface in good concentration; intra-peritoneal CT is inefficacious for the low penetration of drugs into the nodule of carcinosis (not more than 1–3 m) in normothermia. Since 1985 Fujimoto *et al.* showed that intraperitoneal hyperthermic perfusion (IPHP) combined with CT is effective in treatment of Peritoneal Carcinosis. We treat peritoneal carcinosis with Intraperitoneal Hyperthermic Perfusion with high doses of CDDP + MMC. Preliminary results in tern of toxicity and responses are impressive according to the data of the literature. The authors report their experience on this new treatment in a disease considered incurable up today.

This work has been supported by AIRC, contribution 1994.

520 PUBLICATION

FIRST-LINE CHEMOTHERAPY WITH CARBOPLATIN, CISPLATIN AND CYCLOPHOSPHAMIDE (C.C.C) IN ADVANCED OVARIAN CANCER (AOC)

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The combination of C.C.C was delivered to 30 patients with AOC. Of these patients 24 had suboptimally debulked and 6 had optimally debulked tumors. C.C.C regimen was given as follows: Carboplatin 200 mg/m^2 d1, Cisplatin 60 mg/m^2 d2 and Cyclophosphamide 550 mg/m^2 d1, 2 q 4 weeks, for 6 cycles. Of 24 patients with sub-optimally debulked, measurable disease 23 (96%) had a clinical response, including 18 (75%) with clinical complete response (CR), of whom 15 underwent a second look laparotomy. Macroscopic CR was found in 10 (42%) patients of whom 6 (25%) had a pathologic CR. After a median follow-up duration of 16 months median survival is pending. For all 30 patients, grade IV leucopenia was noted in 50% and leucopenic fever in 23% of the patients. Grade IV thrombocytopenia was noted in 20%. No other grade III–IV toxicity was noted. There was no toxic death. 90–100% of planned dose was administered to 87% of pts, while 13% received 80–89% of the planned dose. C.C.C is active and safe in ovarian cancer.

521 PUBLICATION

OVARIAN CARCINOMA AFTER LONG-TERM OVULATION INDUCTION-REALITY OR COINCIDENCE?

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In September 1994 thirty-nine years old woman was admitted for lower right abdominal pain. During 1993/1994 there were 7 ovulation inductions with hMG/hCG followed by either artificial insemination of IVF-ET procedure, the last one in April. Complaints dated from that time. Lower right abdominal pain persisted and even worsened after treatment with antibiotics and hemotherapeutics. After preoperative evaluation adnexectomy was performed. Multilocular highly differentiated serous papillary cystadenocarcinoma was found, displaying moderate nuclear atypia and small areas of clear-cell differentiation, with foci of necrosis and stromal microinvasion. Elevated serum CA-125 levels at the time of operation slightly decreased four weeks after (from 145 IU/ml to 124 IU/ml). Serum concentrations of CA-125 were within normal range between 6^{th} to 8^{th} postoperative week. Nine weeks after operation, at the end of December, severe metrorrhagia occurred and curettage was performed. Histological evaluation of the obtained material showed papillary cystadenocarcinoma endometrioides endometrii G_1NG_1. Serum CA-125 were extremely elevated to the values of 1360 IU/ml. In January 1995 hysterectomy, adnexectomy and omentectomy were performed. There were no apparent metastatic features during the operative procedure. In order to assess current knowledge of the potential excess risk of ovarian carcinomas associated with ovulation induction, a Medline search of the literature was performed. It was confirmed that up to December 1994 there are eleven cases of ovarian malignancies after ovulation induction. Our patient is the twelfth one.

522 PUBLICATION

TREATMENT OF ADVANCED OVARIAN CANCER (AOC). FROM PLATINUM COMPOUND TO TAXOL: AN INDIAN EXPERIENCE

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From Jan. '91 patients with AOC have been treated with P (400 mg/m^2 Q 4 W × 6) and cyclophosphamide (C) (600 mg/m^2 Q 4 W × 6). Between Jan. '91–Oct. '94 19 patients with AOC (St. III c = 15, St IV = 4) median age 53 yrs (36–73) were treated with PC Protocol. 15/19 had primary debulking, of which 5 were suboptimal. 4/19 received PC primum only 1/4 subsequently had suboptimal interval debulking, 3 progressed on therapy. Median Progression free interval for the group is 8 mths (1–47 range). There was no neurotoxicity, nephrotoxicity, Myelosuppression was minimal (gr I–II). PC although standard and well tolerated treatment survival remains suboptimal. Taxol (T) has been identified as an active agent in salvage therapy in AOC. T is being indigenously manufactured in India (Inlaxel, Dabur India ltd.) and available for use since Nov. '94. We have treated so far 2 patients of AOC primarily with P (300 mg/m^2 Q 4 W × 6) and T (135 mg/m^2 escalated to 175 mg/m^2 Q 4 W × 6). T is given as 3 hrs infusion followed by 1 hr infusion of P with premedication. The toxicity of TP is acceptable in the above doses. No cardiotoxicity, nausea gr I–II, myelosuppression gr I–II, arthralgia and myalgia managable with mild analgesic and mild autonomic disturbances were observed. We intend to escalate further the dose of T till such point where myelosuppression is manageable without support of growth factors, the target being higher dose intensity for better survival advantage. The data will be updated till Sep. '95 & discussed.

523 PUBLICATION

TOLERABILITY OF PAGLITAXEL (TAXOL®) IN PLATINUM PRETREATED ADVANCED OVARIAN CANCER PATIENTS

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Forty-four pts entered this non-randomized phase II study. The pts were treated with TXL (3-hour iv infusion) 175 mg/m^2 as second- (n = 23) or third-line (n = 13) chemotherapy or with TXL 135 mg/m^2 as fourth-line chemotherapy (n = 8). Standard premedication was required. All the pts are evaluable for toxicity and 35 are evaluable for objective response. An objective remission was observed in 17 (16 PR + 1 CR)/34 evaluable pts (50%). The median TTP was 28 weeks. The hematological toxicity was mild: grade 3 leukopenia in 8/44 pts (18%); gr. 3 alopecia was universal. Gr. 2–3 paresthesias were observed in 20 pts (45%), while treatment-related pain (abdominal pain, arthralgia, myalgia) was

observed in 25 pts (57%). Hypersensitivity reactions occurred in 12 pts (27%); in 2 cases (4%) the reaction was severe (gr. 3 and 4). Partial bowel obstruction occurred within 30 days from TXL administration in 6 pts (14%): the relationship with chemotherapy was uncertain. Overall 8 pts (18%) stopped TXL treatment because of adverse events: 5 hypersensitivity reactions, gr. 3 paresthesias in one case, partial bowel obstruction in 2 cases. In our opinion pts with constipation or bowel subobstructive condition at the beginning of TXL treatment should be carefully selected and monitored.

524 PUBLICATION

CISPLATIN (C) + IFOSFAMIDE (I) FOR PATIENTS WITH OVARIAN CARCINOMA (O.C.) WITH PRIOR CARBOPLATIN (CBT) + CYCLOPHOSPHAMIDE (CTX) CHEMOTHERAPY

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Thirty patients (pts) aged 55 (45–68) 8/30 with refractory and 22/30 with recurrent O.C. received C:100 mg/m^2 day 1 and I: 5 g/m^2 over 3 days as second line therapy. Staging at first diagnosis was: stage III 24 cases, stage IV 4 cases. After primary surgery all pts were treated with CBT + CTX for six courses. Eight pts had early tumor recurrence within 6 months while 22/30 had tumor recurrence 1–2 years after first line chemotherapy. Objective response was achieved after 4 courses in 2/8 pts with resistant tumors (PRS of 4 and 6 mo duration) while 8/22 pts with tumor recurrence responded with 2 pathology CRS and 6 clinically and laboratory confirmed $\geqslant$ PRS. Time to progression was 8 mo (6–12) all pts expired within 16 months. Myelotoxicity was moderate because of GCSF or GM-CSF post chemotherapy administration. Neurotoxicity was moderate also except for one case with Grand-mal most probably due to (I). With a (33%) response rate C + I as second line is at least as effective as newer drugs. However, the major determinant of response to C + I was the progression free interval from first line chemotherapy. This interval may be an indicator for deciding Cisplatin Taxanes or both drug administration in recurrent O.C.

Paediatric oncology

525 SIOP Award lecture

THE CONSEQUENCES OF THE TREATMENT OF CHILDREN WITH CANCER. SUCCESS OR FAILURE/DO WE YET KNOW THE ANSWERS?

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Survival rates for children treated for cancer have continued to rise from the 1950's to the present day and for most diagnoses are now in excess of 50%, reaching 90% in some categories. These results have not been achieved without unwanted consequences which have long term implications for the health status of the survivors and health care costs for the community. Patients treated in the 1950's and 1960's demonstrate the long term effects of surgery and radiation therapy while more recently chemotherapeutic sequelae have increased in importance and frequency. The interaction of radiation and chemotherapy was poorly understood in the earlier decades but is now well documented.

As more intensive protocols are introduced using many different drugs it is likely that the long term survivors of the future will have as yet unrecognised complications. Even the survivors from the earlier years continue to develop new problems and need ongoing regular surveillance. The psychological problems associated with the diagnosis, long periods of intensive life threatening treatment and continuing uncertaintity of outcome add to the sequelae. A multidisciplinary approach to follow up is as necessary as it is in the initial treatment period. The optimum method of insuring that this monitoring is effective is still being evolved and requires repeated revision. Guidelines have been developed which require clinicians to check each patient on an individual basis and provide a simple method of regular review. If used systematically they should reduce the chance of missing as yet undescribed problems and allow these essentially healthy young adults to control and modify their own lifestyle.

526 ORAL

THE SIOP WILMS' TUMOR (WT) TREATMENT (TRT) STRATEGY AND RESULTS: A REPORT OF THE SIOP WILMS' TUMOR TRIAL AND STUDY COMMITTEE

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The advantage of a preoperative Trt, in non metastatic WT, in terms of surgical tumor rupture (< 5%) and chances for a favorable stage (stage I rate >50%), avoiding the need for rediotherapy (Rth) to cure, have been proven through the SIOP trials 1 and 5 and the optimal duration of a 4 weeks Actinomycin D + Vincristine (AV) preoperative chemotherapy (CT) has been established in SIOP 9. Lymphnodes invasion and unfavorable histology (UH), known to be of pronostic value and still determinable in preop-treated tumors, were considered in scheduling SIOP 6 and 9 postoperative Trt. Through randomized trials risk adapted treatment groups have been defined. Stage I: 1 post-op. and 2 maintenance AV courses are sufficient, 3-year disease free survival (DFS) = 85% and survival (S) = 95%. Stage II N0 non UH: no Rth needed, 3-drug CT using AV + Epirubicin (AVE), abdominal recurrence rate <4%, DFS = 84%, S = 92%. Stage IIN1 and III non UH: abdominal Rth and 3-drug AVE CT needed, DFS = 73%, S = 92% .Stage over I with UH: 4-drug CT using AVE + Ifosfamide DFS 49%.

527 ORAL

MOPP/ABVD AND RADIOTHERAPY IN THE TREATMENT OF PEDIATRIC HODGKIN'S DISEASE (HD)

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The aim of this paper is to assess: (1) results of combined approach (MOPP and/or ABVD and radiotherapy) in the treatment of HD in childhood and (2) factors proved to be prognostically significant. *Patients and methods:* During the period 1980–1984, 163 children aged 3 yrs–19 yrs (Me = 12 yrs) were treated for HD. There were 102 boys and 61 girls, in clinical stage I: 31 pts; II 88 pts; III 35 pts. and IV 9 pts. Histologically, the majority of children were diagnosed to have mixed cellularity (53) and nodular sclerosis (49). Mediastinal involvement was noticed in 58.5% pts and presence of systemic symptoms in 41.5%. All children received MOPP and/or ABVD and radiotherapy in "sandwich" regimen or after chemotherapy. Six cycles of chemotherapy where given in 106 pts, four in 45, and more than six cycles in 12 pts. Radiotherapy was applied on supervoltage units (TCT or Linear accelerator 10 MeV) using various techniques—the most often extended fields. *Results and conclusions:* During the follow up period from 1 yrs up to 15 yrs (Me = 8.1 yrs) overall survival rate is 96.5% and disease-free survival rate is 88.5%. In multivariate analysis, among 6 factors (age, sex, presence of systemic symptoms, bulky mediastinum, number of involved areas, hystologic subtype), advanced clinical stages and mediastinal involvement are deemed to be of the most importance for outcome. Based on these factors favourable and unfavourable subgroups are defined. Combined therapy (more or less intensive) should be designed according to subgroups. In pts with good prognosis (majority in our group) main goal is to decrease the risk of long-term treatment-related toxicity without