539 POSTER

PSYCHOLOGICAL FUNCTIONING IN CHILDREN WITH CANCER

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Psychological functioning in children 0–18 years old, having various types of cancer, and their families visiting the pediatric oncology unit at Uppsala Akademiska Hospital, during the spring 1995, is investigated.

Patients at least 8 years complete questionnaires measuring self-concept ("I think I am"); depression (CDI) and anxiety (RCMAS). Patients of age 11 or older also complete YSR measuring social/behavioral problems and those >12 years also complete A-COPE assessing coping. Both parents report social/behavioral problems for children 4–18 years (CBCL). For patients 8–12 years old parents assess the child's coping (CHIC). Patient and parent general background data and patient disease related medical data is also collected.

Anxiety, depression, behavioral/social problems, coping and self-concept for the various diagnosis, disease stages/phases and ages will be presented as well as differences/associations between: (1) patient (11–18 years) and parent reports of behavioral/social problems, and (2) mother and father reports of the childs behavioral/social problems (4–18 years) and coping (8–12 years).

540 PUBLICATION

ACTIVITY OF LIVER MONOOXYGENASES IN PEDIATRIC ONCOLOGICAL PATIENTS

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Liver monooxygenases (LMO) metabolize most antitumor drugs and LMO activity is a factor determining their efficacy. For example, anticancer agents are less active and more toxic in patients (pts) with concomitant hepatic damages which result in inhibition of LMO activity. The question is how many pts have low LMO activity. We examined 146 pediatric oncological pts without hepatic pathology by determining half life-time of antipyrin (T1/2 AP). Only 22% pts had high LMO activity, the same as in healthy (T1/2 AP is 5 h and less). 46% pts had moderate LMO activity (T1/2 AP is 5–10 h) and 32%—low LMO activity (T1/2 AP is more than 10 h). Among 36 pts with concomitant hepatic damages the latter group included 63% pts. So about 1/3 of all pts and 2/3 of the pts with hepatic damages cannot achieve optimal effect of chemotherapy regardless of tumor sensitivity. We believe to optimize the drug efficacy LMO inhibited activity should be stimulated to the normal level before chemotherapy and we have already had positive results of the approach.

541 PUBLICATION

POST OPERATIVE MANAGEMENT OF AGGRESSIVE FIBROMATOSIS IN CHILDHOOD

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Summary: Aggressive fibromatosis (also known as desmoid tumors) arise from musculo-aponeurotic tissues and are histologically benign. They are however locally aggressive. Local relapse occurs in 20 to 100% of treated patients and is specially frequent following incomplete resection. We report 9 cases of children treated at Léon Bérard Center between 1979–1991 by surgery and post operative treatment.

Patients and methods: Between 1979 and 1991, 9 children (7 male, 2 female) with aggressive fibromatosis were treated at Léon Bérard Center. Ages ranged from 24 to 204 months. Five were seen at first relapse and 4 were treated in first intent. All specimens were reviewed by the Department of Pathology. (histological confirmation of aggressive fibromatosis was confirmed in all cases). Involved sites of disease include: limbs (4), supraclavicular (2), face (2) and sacrum (1). Initial surgery consisted of wide excision in 7 patients with a macroscopic residual disease, and a microscopic residual disease in 2 cases. Despite partial surgery in 5/9 patients who were treated at other institutions, no further post-operative treatment was proposed and these patients were referred at Centre Léon Bérard with local recurrences following first surgical resection. All of them underwent a record surgery at time of relapse. Four patients were referred for initial diagnosis of desmoid tumors and had an incomplete surgery. Four children were treated with postoperative radiation, 2 with radiation and chemotherapy, 1 child with radiation therapy, chemotherapy and endocrine therapy and 1 with endocrine therapy alone.

Results: Local control: Six patients relapsed within 4 to 12 months from surgery. Three were controlled. Among the controlled patients, 1 received radiation therapy alone (45 Gy), the second received chemoradiation (Ifosfamide, Vincristin, Adriamycin + 45 Gy); the third received Tamoxifen (20 mg/m^2). Second surgery was performed on the 6 patients who failed locally: macroscopic complete resection was performed but with positive margin in 3 cases. Gross residual disease was present in two cases, the last one achieved microscopically complete resection. No additional treatment was administered to the child who underwent a complete resection; he is alive at 10 years follow up. Adjuvant treatment was delivered to 5 patients: radiation therapy alone (2 pts); chemoradiation and TAM (2); chemotherapy alone (1).

Survival: All but one patients are still alive with a 93 months median follow up. Seven of 9 children are free of recurrence at last review. Nevertheless, one is still alive but with active disease. The last one died of disease 28 months after the initial surgery by locally uncontrolled tumor.

Conclusion: Primary treatment is surgical resection and should be as complete as possible. This is difficult to achieve. No patient in our study was completely resected. Most of children relapsed after the initial surgery and patients may died as a consequence of locally uncontrolled tumor. Theses findings confirm that fibromatosis are aggressive tumor which warrant aggressive therapy. Local control may be achieved with adjuvant "aggressive" treatment such as radiotherapy.

Other gastro-intestinal tumours

542 ORAL

THE FATE OF 100 CONSECUTIVE RESECTIONS FOR CARCINOMA OF THE OESOPHAGUS AND G.O. JUNCTIONS WITHOUT HOSPITAL MORTALITY

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From 01.01.1992 until August 1993, 100 consecutive resections for carcinoma of the thoracic oesophagus and the gastrooesophageal junction were performed in our institution without hospital mortality (83 O - 17 O). Mean age was 62.07 years (42–90 years). There were 34 squamous cell-, 64 adenocarcinomas and 2 leiomyosarcomas. Extensive 3 field lymphnode dissection was performed in 41 patients, 2 field dissection in 17 patients. A Ro situation was obtained in 81 patients. Mean operation time was 7 hrs (3–11 hrs). Mean blood loss 1540 cc (200–3500). *Results:* Thirty two patients had a completely uneventful postoperative course. Postoperative complications included: pulmonary: 39, cardiac: 15, infectious: 22, phychoneurological: 16. There were two anastomotic fistulae treated conservatively. One thoracic duct leakage was treated conservatively. Two patients suffered from recurrent nerve paralysis. Ten patients had to be admitted in ICU with a mean stay of 27 days (2 d.–83 d.). Mean hospital stay for all patients was 21.6 days (8 d–101 d). pTNM staging was as follows: stage I: 11, stage II: 24, stage III, 33, stage IV: 32 (Distant LN: 22, liver 4, liver-lung: 2, lung: 3). Overall 3-year actuarial survival is 45% being 51% for the extensive lymphnode dissection

group. Median survival is 27 months. Six months and 1 year survival is 89% and 71% respectively. Stage related 3 year actuarial survival was for stage I: 91%, stage II: 50%, stage III: 53% and stage IV: 20%. Late mortality was cancer related in 41 patients: distant metastasis: 23, distant metastasis + locoregional recurrence: 10, locoregional recurrence: 8. Quality of survival of the 55 survivors showed an excellent or good feeding capacity in 49 (89%) patients. Nine patients developed an anastomotic stricture treated with a mean of two dilatations. Weight status showed a mean decrease of −7.3 kg (−33 kg to +10 kg) as compared to the preoperative weight and −3. kg (−26 kg to 17 kg) as compared to the patients ideal weight. Final Visick score was grade I: 34 (61%), II: 11 (20%), III: 7 (12%), IV: 3 (5.4%). *Conclusion:* Today oesophagectomy for carcinoma can be performed with a minimum mortality and acceptable morbidity. Risk factors have to be judged individually especially in relation to radicality of associated lymphadenectomies. Survival is as expected stage related but even in distant lymphnode metastasis acceptable prolonged palliation is obtained with excellent to very good functional outcome in the majority of patients justifying resection or primary treatment in absence of gross tumour spread or solid organ metastasis.

543 ORAL

THE ROLE OF INTRA LUMINAL BRACHYTHERAPY IN TREATMENT OF CANCER OF THE OESOPHAGUS

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A prospective, non-randomized study was performed in 201 patients with inoperable cancer of the oesophagus. 101 were treated with palliative reason with Intra Luminal Brachytherapy (ILB), (n = 56), or combined External Beam RadioTherapy (EBRT) and ILB, (n = 45). 100 patients were treated with Radical Radiotherapy: group 1) 50 Gy EBRT + 2 × 7.5 Gy ILB, (n = 54), group 2) 60 Gy EBRT + 2 × 6 Gy ILB, (n = 46).

Results: ILB as single modality treatment results in good, life long improvement of dysphagia. Median survival is 3.4 months and 1-year overall survival 5%. EBRT + ILB has equal effects, with median and 1-year overall survival of 4.7 months and 13% respectively.

Treatment related complications were rare. In the radical group 50 Gy + 2 × 7.5 leads to a median, 1- and 2-year survival of 9.3 months, 40% and 13% respectively. For 60 Gy + 2 × 6 this was 11.8 months, 43% and 31%. Complications were mild.

Conclusions: Intraluminal Brachytherapy is save and effective in palliation for carcinoma of the oesophagus. Results with intraluminal brachytherapy alone are comparable with combination of EBRT + ILB. In Radical Radiotherapy increasing EBRT dose from 50 to 60 Gy + ILB 2 × 6 Gy increases local control as well as overall survival.

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ECF IS A HIGHLY ACTIVE REGIMEN WITH LOW TOXICITY SUITABLE FOR NEOADJUVANT TREATMENT OF OESOPHAGOGASTRIC CANCER

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Initial trials with ECF demonstrated a 71% response in oesophagogastric cancer with modest toxicity, renewing interest in neoadjuvant therapy. We now report our experience of 235 consecutive patients treated between 1989 and 1994. All diagnoses were histologically proven. The regimen comprises epirubicin 50 mg/m^2 and cisplatin 60 mg/m^2 3 weekly × 6–8 with protracted venous infusion 5-FU 200 mg/m^2/d throughout. Responses were evaluated with CT scan and gastroscopy. 173 patients had metastatic disease and 62 had locally advanced disease (LAD). Measurable response occurred in 135/220 (61%, 95% CI 55–68%) with CR in 11% and PR in 50%. Symptomatic response occurred in 50–85%. Quality of life was improved or maintained in most patients. Toxicity was modest; 22% grade 3/4 leucopenia and 14% grade 3/4 non-haematological toxicity. There were 6 treatment related deaths, all during the first 3 years. 29 patients with LAD who responded proceeded to surgery. 19 (66%) had a potentially curative resection; histological CR was demonstrated in 6 (32%). Overall median survival was 256 days. Patients with LAD and ECOG performance status 0–2 had a median survival of 404 days with a 1 year failure free rate of 40%. We conclude ECF is a highly active regimen with acceptable toxicity that can render locally advanced tumours operable. This potential is being evaluated in the MRC "MAGIC" trial comparing ECF before surgery with surgery alone.

545 ORAL

SECOND MALIGNANCIES (SM) IN ESOPHAGEAL CANCER (EC) AFTER COMBINED MODALITY TREATMENT: IMPLICATIONS FOR FOLLOW-UP AND CHEMOPREVENTION

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From 5/85 to 12/92, 101 consecutive patients (median age: 61 yrs), with locally advanced EC received a combined chemoradiotherapy treatment, Sixty-one pts were treated with FU + CDDP × 4 cycles and concurrent RT (50 Gy) and 40 pts with 2 courses of the same regimen plus concurrent RT (30 Gy) followed by surgery. Overall survival (OS) at 6 yrs was 22%. In 14 pts EC developed after a previous neoplasm and they were excluded from the analysis. In the remaining 87 pts with primary EC (OS 23% with a median follow up of 77 mos) a total of 12 pts (median age 67 yrs, range 49–79) developed a SM after a median of 27.5 mos (range 7–83) from the diagnosis of EC: 4 epidermoid head and neck cancers, 3 gastric adenocarcinomas (1 early gastric cancer), 1 distal esophageal adenocarcinoma, 2 non small cell lung cancers, 1 colon adenocarcinoma, and 1 vaginal squamous cell carcinoma. Actuarial cumulative risk for SM at 2, 4, and 6 yrs is 6%, 17%, and 23% respectively. Total incidence rate was 6% with an age-adjusted incidence of SM 3 times higher than that of primary cancer in the general population. The high incidence of SM in long-term survivors with EC strongly supports a prolonged follow-up oriented to the early detection of SM. This population with high rate of SM should represent an optimal model to assess the role of chemoprevention.

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ADVANCED GASTRIC CANCER: COMPARISON OF FAMTX (5FU, ADRIAMYCINE, METHOTREXATE) VERSUS ELF (ETROPOSIDE, 5 FU, LEUCOVORIN) VERSUS FUP (INFUSIONAL 5 FU + CISPLATIN). RESULTS FROM AN EORTC TRIAL OF THE GITCCG AND THE ARBEITSGEMEINSCHAFT FÜR INNERE ONKOLOGIE (AIO)

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FAMTX, shown superior to FAM (*J Clin Oncol* 1991;9:827) has been compared to ELF (*Sem Oncoll* supp2, 1990) and FUP (*Eur J Cancer* 1994;**30A**:1263). Eligibility criteria included locally advanced and/or metastatic gastric cancer, measurable, evaluable or non measurable disease, performance status O-2, age < 76 years and adequate organ functions. A total of 373 pts were randomized by 52 institutions. This preliminary analysis is based on 274 eligible pts. Grade 3–4 toxicities were (ELF-FUP-FAMTX): vomiting 8-25-10%; mucositis 3-13-10%; leucopenia 6-4-7%; thrombocytopenia 0-4-2%. There were 5 toxic deaths (2 FUP and 3 FAMTX). The median number of cycles was 4 (1–8), 4 (0–6) and 3 (0–6) respectively. Extramurally reviewed objective response (OR) in 132 assessable pts with measurable disease was; ELF 21%; FUP 27%; FAMTX 20%. SD was achieved in 35%, 41% and 42% respectively. Downstaging with subsequent resection was achieved in 0/15, 2/18 and 4/16 respectively. Median survival was 7, 8, 7 mths respectively. *In conclusion* no significant differences in response or survival were detected. The low OR rate may be due to the number of pts receiving no (3%) or only one cycle of chemotherapy (12%, 14% and 20% respectively) and to the number of institution which entered less than 4 pts (n = 19).

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IMPROVEMENTS IN SURVIVAL AND CLINICAL BENEFIT WITH THE USE OF GEMCITABINE (GEM) AS FIRST-LINE THERAPY FOR ADVANCED PANCREATIC CANCER: A RANDOMIZED TRIAL

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Following phase II clinical observations that patients with pancreas cancer experienced improvement in disease-related symptoms with GEM, a quantitative definition of clinical benefit (CB) was developed as a primary efficacy measure (Andersen, 1994, *Proc ASCO* 13:461). CB has