Conclusion: Colorectal cancer expresses strongly a variety of tumour antigens which are involved in recurrence and metastatic processes

1122 POSTER

The value of follow-up in resectable colo-rectal cancer after adjuvant therapy

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The aim of post-operative follow-up in colo-rectal cancer (CRC) patients (pts) is to detect recurrences while resectable with the possibility of improving survival. Benefit in long-term survival is still controversial while exhaustive follow-up is expensive and bothersome for patients.

Methods: Between 1993 and 1997 we followed up 399 pts (225 males, 174 females) with resectable CRC (207 colon, 192 rectum) after adjuvant therapy. The mean age was 59 years (33-78). Pathological stages: Colon: EII 65, EIII 142; rectum: EII:81, EIII:111. Adjuvant treatment: the main schedule in colon cancer was Levamisole + 5-Fluorouracil (Lev + 5FU) in 87%. and in rectum was 5FU (500 mg/sqm/day x 5d every 4 w x 8 cycles) in 85% + pelvic radiotherapy in 98%. The follow-up consisted on:CEA and clinical examination every 3 months(m) the first 2 years, every 4 m the third year, every 6 m the 4th and 5th year and annually thereafter; abdominal ultrasonography (AUS) every 6 m for the first two years and yearly afterwards; chest roentgenogram annually; colonoscopy every 2 years; rectoscopy annually the first 2 years and abdominal CT scan at 12 and 24 m in rectum. If CEA elevations were detected, cross-sectional imaging was done. Mean of follow-up was 48 m.

Results: Recurrences were detected in 126 of 377evaluable pts (4 lost of follow-up while free of disease and 18 deaths for other reasons):16 locorregional (L), 94 systemics (S) and 16 L+S. The 86.4% of those were detected within the first 3 years. The main indicator of recurrence was: CEA in 84 pts (64%), CT in 12pts (9.6%)and clinical in 19 pts (15.2%). 39 pts (31%) underwent rescue surgery for recurrent disease: 6 L (37.5%); 31 S (32.9%); 2 L+S (12.5%). From the total of recurrences 38 envolved liver as unique site, from these, 23 (61%) underwent rescue surgery. At the end of this study (Feb 01) 19 pts are still alive: 12 (30.7%) free of disease and 7 (17.9%) with a 2nd recurrence. Median of survival when rescue surgery was performed was 35m (16.2-53.8) versus 11m (8-14) when it was not possible ($p<0.001$).

Conclusions: Postoperative follow-up in CRC with high risk of recurrence is useful, specially in the first three years. With a less exhaustive follow-up based in CEA, clinical examination and a rational postoperative imaging, we have achieved a great number of rescatable recurrences and an obvious benefit in time of survival in these patients

1123 POSTER

Association of p27 and TGF-β expressions with colorectal cancer: an immunohistochemical study

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Introduction: TGF-β1 has been demonstrated to be an inhibitor epithelial cell growth and it is commonly over expressed in solid malignancies. Down regulation of p27, a cyclin dependent kinase inhibitor is associated with aggressive behavior in some tumors. We analyzed immunohistochemically TGF-beta and p27 expression levels in human colorectal carcinomas associated with inflammatory bowel diseases e.g. colitis ulserosa (CU) and polyposis coli.

Methods: Formal in fixed-paraffin embedded sections from randomly selected 15 CU cases with epithelia dysplasia in various degrees, 25 colorectal adenocarcinoma (Cca) arise in polyposis coli (PC) were immunostained with a monoclonal antibody against TGF-beta and p27 proteins immunoactivity was evaluated without any clinico-pathologic knowledge. p27 analysis was recorded as p27 labeling index. TGF-beta analysis was revealed as intensity of staining, (+/+++).

Results: There were not any significant differences in TGF-beta levels in normal epithelia and CU group. It's found significant TGF-beta over expression in Cca group ($p<0.05$). The p27 labeling index in normal colorectal mucosal epithelia was 94.3%3.2%(meanSD), and in UC was 68.3%±5.4% ($p<0.05$). It was also found significantly reduced p27 expression in Cca group (25.05%8.5%) and PC group (41.07%2.6%)($p<0.05$). Reduced p27 expression and TGF-beta over expressions were associated with invasion level and histological grade in Cca group.

Conclusion: This study showed that the posttranslational reduction of levels of p27kip1, which mediates TGF-beta growth inhibition, provides an additional means for colorectal adenocarcinoma cells to escape negative growth regulation by TGF-beta.

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A phase II study of irinotecan (CPT-11) alternated with a weekly schedule of oxaliplatin (L-OHP), high-dose leucovorin (LV) and a 48-hour infusion 5-fluorouracil (5-FU) in patients with metastatic colorectal cancer (MCRC)

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Purpose: In an our previous phase II study we have verified that the efficacy of CPT-11 alternated with a weekly-times-four schedule of high-dose LV and a 48-hour infusion 5-FU is comparable to that of regimens with drugs given together, but at lower costs and less toxicity (data in press). In order to improve the infusional part results of regimen, we conducted a phase I trial in which a weekly administration of L-OHP was added (Ann Oncol, in press).

Methods: We tested the activity of a regimen consisting of a weekly-times-four schedule of L-OHP (65 mg/m^2), high-dose LV (150 mg/m^2) followed by a 48-hour 5-FU infusion (2300 mg/m^2) alternated with CPT-11 (350 mg/m^2). A cycle was to be performed every eight weeks. Twenty-five consecutive patients (M/F, 12/13) with measurable MCRC, aged 26–74, PS (ECOG): 0/1/2, 8/15/2 entered our study. Metastatic sites: liver (64%), lung (24%) and lymph nodes (16%).

Results: All patients were evaluable for toxicity and 15 for response. The objective response rate was 47% (7 of 15 patients; 1 complete and 6 partial responses). An additional 53% of the patients had stable disease. After a median number of 3 cycles per patient no toxic deaths occurred. The incidence of grade 3–4 toxicity per patient in any cycle was: mucositis 8%, and diarrhea 40% for the infusional part; diarrhea 4% and neutropenia 24% for the CPT-11 part of regimen. No patient stopped the treatment due to neurotoxicity.

Conclusions: These preliminary results suggest that our schedule is feasible and highly active: the overall tumor growth control rate is 100%. The reported data stimulate us to continue the study and up-dated results will be presented.

1125 POSTER

Elevated serum VEGF levels in colorectal cancer patients correlate with poor survival

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Purpose: Vascular endothelial growth factor (VEGF) is an angiogenic cytokine involved in tumor progression and metastasis. In this study, we evaluated the clinical usefulness of circulating VEGF concentrations in colorectal cancer.

Methods: Serum VEGF concentrations were determined in the sera of 61 healthy controls and 67 patients with colorectal cancer by an enzyme linked immunosorbent assay and associated these levels with clinicopathological features and patient survival.

Results: Colorectal cancer patients showed significantly higher serum VEGF levels compared with healthy controls. Serum VEGF levels correlated significantly with degree of tumor differentiation, disease stage, tumor invasion depth, and the presence of lymph node and distant metastases. Univariate analysis showed significantly lower survival rate for patients with elevated serum VEGF levels. Multivariate regression analysis showed that the prognostic value of serum VEGF level was not independent of tumor stage.

Conclusion: Serum VEGF levels in colorectal cancer patients reflect the presence of advanced and metastatic tumor and their determination might be clinically useful.