for clinical characteristics, radiologic appearance, skeletal-related events (SREs) and plasma ET-1.
Results: The median age was 60 years (range 29 to 71). There were 11 males and 8 females. Major pathologic types were poorly-differentiated adenocarcinoma and signet-ring cell carcinoma. Radiologic appearance included 12 osteoblastic, 5 mixed, and 2 osteolytic pattern. There was no case which developed major SREs, being at least complicated with radiation to bone, pathological fractures, or hypercalcemia. Out of 19 patients with skeletal metastases, 11 patients developed hematological complications, including microangiopathic hemolytic anemia (MAHA), disseminated intravascular coagulation (DIC). In contrast, reviewing non-skeletal metastases (n = 89), there was only two cases with hematological complication. Plasma ET-1 level was measured in 6 out of 19 patients with skeletal metastases. The levels in the skeletal metastases were 2.416±0.6 pg/ml, mean±SD (n = 6), which were higher than those in non-skeletal metastases, 1.817±0.4 pg/ml, mean±SD (n = 7). In addition, serum ALP levels were also high in 6 patients that ET-1 were measured (1245±424 U/L, mean±SD, n = 6).
Conclusions: Our study shows that the major SREs are uncommon in gastric cancer and that their skeletal metastases are characterized as associations with hematologic complications. It suggests that higher plasma level of ET-1 is correlated with skeletal metastases in gastric cancer, as it previously studied in prostate cancer by others.

6640 POSTER

Enhancer of zeste homolog 2 expression is associated with tumour cell proliferation and metastasis in gastric cancer

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Background: Polycomb group proteins are transcriptional repressors that silence specific sets of genes through chromatin modification. The enhancer of zeste homolog 2 (EZH2), considered a member of the polycomb group proteins, plays an important role in cell proliferation and cell cycle regulation. EZH2 is overexpressed in aggressive forms of prostate, breast, bladder, and endometrial cancer. However, the role of EZH2 expression in gastric cancer has not yet been fully determined. This study was conducted to investigate the mechanisms of carcinogenesis and the clinical value of EZH2 expression in gastric cancer.
Materials and Methods: We analyzed EZH2 expression using western blot in AGS, MKN-28, SNU-16, SNU-484, SNU-601, and SNU-638 gastric cancer cell lines. After transfection of for EZH2 siRNA in MKN-28, the change of cell cycle related molecules was assessed by western blot. Expression of EZH2, Ki-67, and p53 was determined by immunohistochemical staining of tissue microarrays from specimens of 137 cases of resected gastric cancer.
Results: Among 6 cell lines we found high expression of EZH2 in all gastric cancer cell lines. RNA interference of EZH2 induced up regulation of p53 and down regulation of cyclin D1 and cyclin E. High EZH2 expression was observed in 60.6% of gastric cancers and in 6.7% of non-neoplastic gastric tissues ($P < 0.01$). 40.1% were positive for p53. High EZH2 expression correlated with Ki-67and p53 expression and was significantly associated with distant metastasis and non-signet ring cells.
Conclusions: These results suggest that high EZH2 expression is associated with tumor cell proliferation and metastasis.

6641 POSTER

Elevated expression of cyclooxygenase-2 is a negative prognostic factor for disease free survival and overall survival in patients with gastric carcinoma

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Background: Cyclooxygenases regulate the production of prostaglandins and play a role in tumor development and progression. The authors investigated the prognostic impact of expression of the cyclooxygenase (COX) isoform, COX-2, on disease-free survival and progression-free survival in patients with primary gastric adenocarcinoma (any pN any pT) without distant metastasis as well as the association between COX expression and other clinicopathologic parameters.
Methods: A cohort of 194 patients with gastric cancer (123 males 87 women) without distant metastasis who underwent R0 gastric resection were enrolled in this study. Immunoistochemical immunoreactivity was assessed by the intensity of staining and percentage of positivity areas. Association between factors including clinico-pathological variables and COX-2 scores, were assessed by χ^2 and Student t test. Survival rates were calculated using Kaplan-Majer method and the difference between the groups were analyzed by log-rank test.
Results: A correlation between COX-2 expression, grading and advanced penetration dept (mean COX-2 expression 74% in early gastric cancer (EGC) versus 52% in non-EGC, $p = 0.0017$). There was an association between COX-2 expression and the presence of lymph-node metastasis ($p < 0.0001$, χ^2). We also observed a significant association between COX-2 expression and relapse of disease ($p = 0.05$ KM) but not with poor survival.
Conclusions: High COX-2 protein expression, serosal invasion (pT3-pT4), and presence of lymph-node metastasis are poor prognostic factors in patients with gastric carcinoma without distant metastasis. COX-2 expression in any percentage strongly correlates with lymph-node invasion and penetration dept, so it may indicate tumor aggressiveness. The current data suggest that increased expression of COX-2 may play a role in the progression of primary gastric carcinoma. It remains to be investigated whether treatment with selective inhibitors of COX-2 may be an additional therapeutic option for patients with breast carcinoma.

6642 POSTER

Gap junctional intercellular communication influences the cytotoxic effect of docetaxel in esophageal cancer cells

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Background: Gap junctional intercellular communication (GJIC) mediated by connexin (Cx) plays the important role to maintain homeostasis in multicellular organisms. GJIC has also been reported to be associated with positive therapeutic aspect, such as the bystander effect in HSV/TK gene therapy. The aim of this study was to investigate the influences of GJIC in the cytotoxic effect of anticancer drug in esophageal cancer cells.
Materials and Methods: Human esophageal squamous cell carcinoma cell line (KE-10) without GJIC capacity was transfected with connexin 32 gene (Cx32), and cytotoxic effect of docetaxel (DOC) was investigated in KE-10 and Cx32-transfected KE-10 (KE-10/Cx32). Moreover, the cytotoxic effect of DOC was further examined when GJIC was blocked in KE-10/Cx32 cells.
Results: Restoration of GJIC capacity was confirmed by dye-transfer assay in KE-10/Cx32. Cytotoxic effect of DOC in KE-10/Cx32 increased by 40% compared to that in parental KE-10. Enhancement of cytotoxity of DOC in KE-10/Cx32 was abandoned when exposed with the GJIC blocking agent. MDR gene and its protein, which plays the key role in the drug resistance of DOC, was not observed in both KE-10 and KE-10/Cx32.
Conclusions: These data suggest that gap junctional intercellular communication in esophageal cancer cells has the positive influence on the cytotoxic effect of DOC.

6643 POSTER

Anti-proliferative effect of SOCS-1,-3 through the suppression of JAK/STAT and P38 MAPK signaling pathways in gastric cancer cells

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Background: Cytokines and growth factors are important regulators of cell differentiation and proliferation and their signal transduction is negatively regulated by the suppressors of cytokine signaling (SOCS) family proteins. Elevated serum levels of interleukin-6 (IL-6) cytokine correlates with enhanced disease progression and recurrence in patients with gastric cancer. In this study we investigated an anti-proliferative effect of SOCS-1,-3 gene delivery in gastric cancer cells *via* the inhibition of IL-6 signaling.
Material and Methods: Six gastric cancer cell lines (MKN7, MKN45, MKN74, NUGC-3, NUGC-4, AGS) were used in this study. IL-6 levels in culture supernatants were measured by ELISA. Levels of the IL6-activated proteins STAT3, P38 MAPK and PI3-Kinase protein in cell lines was determined by Western blot analysis. The *in vitro* anti-proliferative effect of SOCS-1/-3 adenovirus-mediated gene delivery in cultured gastric cancer cell lines was measured by MTT assay.
Results: Elevated levels of IL-6 in NUGC-3 (1271 pg/ml) and AGS (159 pg/ml) cell culture supernatants compared to MKN7, MKN45, MKN74 and NUGC-4 cell lines (barely detectable levels) correlated with enhanced phosphorylation of STAT3, P38 MAPK and AKT proteins in NUGC-3 and AGS cells. Ectopic expression of SOCS-1/-3 significantly reduced cell proliferation to 12 % in NUGC-3 cells ($p < 0.0001$) and to 10 % in AGS cells ($p < 0.0001$) compared to control cells at day 5. SOCS-1 gene delivery also reduced cell proliferation in MKN45 (a low IL6-producing cell line). The inhibitory effect of SOCS-1/3 delivery on cell proliferation in NUGC-3, AGS and MKN45 cells correlated with decreased levels of phosphorylation of