9410 POSTER

Anti-apoptotic Effect of Decoy Receptor 3 in Human Malignant Fibrous Histiocytoma Cells

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Background: Decoy receptor 3 (DcR3) is a soluble secreted protein which belongs to TNF receptor superfamily, and inhibits Fas/Fas ligand (FasL) apoptotic pathway by binding to FasL competitively with Fas. Previous studies have reported that overexpression of DcR3 is detected in various human malignancies, and that DcR3 plays an important role on tumour progression. We previously reported that DcR3 overexpression was observed in human osteosarcoma and malignant fibrous histiocyoma (MFH) cells, however, the role of DcR3 in musculoskeletal tumours has not been studied. The purpose of this study was to evaluate the effect of DcR3 inhibition in Fas/FasL apoptotic pathway in human MFH cells.
Methods: TNMY1, human MFH cell line that expresses the high level of DcR3, was used in this study. TNMY1 cells were transfected with either DcR3-siRNA or control siRNA. After siRNA transfection, each cell was cultured in medium with or without FasL, and cell proliferation assay was performed at 0, 24 and 48 hours of incubation. Also, cell lysate was collected from each transfected cell which was treated with or without FasL, and we performed immunoblot analysis to evaluate the expression of DcR3, Fas and apoptosis-related proteins, such as Caspases and PARP.
Results: DcR3-siRNA transfection sufficiently suppressed DcR3 expression in TNMY1 cells compared with control cells without affecting Fas expression. FasL treatment significantly decreased cell proliferation in DcR3-siRNA transfected cells compared with control cells after 24 and 48 hours of incubation. Apoptosis-related proteins, cleaved Caspase-3 and cleaved PARP, were detected in cells which were treated with FasL after DcR3-siRNA transfection, however both proteins were not observed in control cells.
Conclusions: Previous studies revealed that DcR3 blocks Fas/FasL apoptotic pathway by binding to FasL competitively with Fas, and that overexpression of DcR3 is associated with tumour progression in various human malignancies. However, the role of DcR3 in musculoskeletal tumours is still unknown. In this study, we demonstrated that FasL treatment with DcR3 inhibition caused a svnergistic cytotoxic effect and induced apoptosis in human MFH cells. These results suggest that DcR3 may have an anti-apoptotic effect via inhibiting Fas/FasL apoptosis pathway in human MFH, and that DcR3 may be a potent therapeutic target for human malignant musculoskeletal tumours.

9411 POSTER

Coexistence of GISTs With Other Malignancies − More Than a Simple Coincidence?

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Introduction: Over the last decade, several changes occurred in the diagnostics, treatment and understanding of pathogenesis in gastrointestinal stromal tumours (GISTs). However, their coexistence with other malignancies of different origin remains a challenging situation during the clinical treatment course.
Methods: Patients diagnosed for GIST in our centre were identified retrospectively. A subgroup, associated with other types of malignancies, was selected and the clinical, pathological (macroscopic, microscopic, and immunohistochemical) features and the clinical follow-up were statistically analysed.
Results: Thirty four (24 male, 10 female) of 85 GIST patients (40%) were associated with other malignancies (n = 38) in the period 2000–2009. The mean age was 69.7 years (range 56−86). GIST-associated malignancies were: stomach (n = 7), rectal (n = 5), oesophageal (n = 4), pancreatic (n = 4), colon (n = 3), papilla (n = 2) and oro-/hypopharyngeal (n = 2) adenocarcinoma, as well as plasmacytoma (n = 2), melanoma (n = 2), prostate (n = 2) and urothelium adenocarcinoma (n = 1), hepatocellular carcinoma (n = 1), neuroendocrine tumour (n = 1), thyroid cancer (n = 1) and non-Hodgkin lymphoma (n = 1). The majority of GISTs occurred in the stomach (65%) and small intestine (29%), with rare occurrence in the rectum (3%) or esophagus (3%). In the majority of cases (82.5%), GISTs were asymptomatic and were accidentally found during diagnostic or therapeutic procedures for associated malignancies. Open surgery was performed in 32 cases, laparoscopic surgery or endoscopic therapy in 2 cases. GIST's size ranged from 0.1 to 9 cm (mean size: 2.2 cm) and all of them had a low (<5/50HPFs) or absent mitotic activity. CD117 was expressed in 82.5% and CD34 in 70.5%. Twenty nine tumours (85.3%) were classified as very-low- or low-risk tumours. Imatinib mesylate was administered in 2 patients. During follow-up (range 3–117 months, mean: 33.7 months), 2 patients suffered from local recurrence (n = 1) or distant metastases (n = 1) of GISTs. Postoperative mortality was 5.8%. Eight patients (23.5%) died of associated malignancies, one patient for other reasons.
Discussion: The coexistence of GISTs with other malignancies should draw the attention of clinicians towards these accidentally findings. Little is known about the possible common origin of GISTs and associated malignancies. The prognosis in this combination of tumours is usually not determined by the GISTs. Therefore treatment algorithms should be focused on the prognostic relevant malignancy.

9412 POSTER

Brain Metastasis in Sarcoma − Presentation, Treatment Strategies and Survival in This Rare Clinical Setting

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Background: Brain metastasis (mets) is rare in sarcoma. Risk factors, optimal management strategies and therapeutic outcomes of such metastases are not well studied. We aimed to evaluate the incidence, clinical characteristics and treatment outcomes of parenchymal brain mets in patients (pts) with sarcoma.
Methods: Single center retrospective analysis. Overall survival was calculated from diagnosis of brain metastasis to time of death.
Results: Thirteen pts (1.7%) with complete electronic medical records were identified from our sarcoma database. Median age was 55 yrs (range, 21−71 yrs), 8 were males. Histology of the primary sarcoma was undifferentiated pleomorphic sarcoma (6 pts), uterine leiomyosarcoma (2 pts), epithelioid sarcoma, embryonal rhabdomyosarcoma, alveolar soft part sarcoma, Ewing's sarcoma and osteosarcoma (1 pt each). Synchronous brain mets were identified in 3 (23%) pts while 77% subsequently developed brain mets at a median of 19 months (mths) (range 6−90 mths) after initial diagnosis. Five (38%) pts had solitary brain metastasis while 62% developed multiple lesions. Four (31%) pts underwent aggressive therapy for brain mets, defined as either surgical resection (1 pt) or multimodality treatment (1 pt had chemotherapy plus whole brain radiotherapy [WBRT]; 2 pts had surgical resection plus WBRT). The remaining 9 pts received conservative treatment with WBRT alone (7 pts), chemotherapy alone or best supportive care (1 pt each). Median overall survival (OS) for the entire cohort was 4.0 mths (95% CI 1.3−6.7). Median OS for pts who underwent aggressive therapy vs conservative approach was 4.0 mths vs 3.6 mths respectively (p = 0.234). Of note, in 10 pts who died, 90% had progressive systemic disease which contributed significantly to mortality. There was no clear association between histological subtype of sarcoma and median OS due to small sample size.
Conclusion: Brain mets in sarcoma is rare, usually co-exists with significant systemic disease and is associated with a grave prognosis. In our study, there was no significant difference in OS between pts treated with an aggressive vs conservative approach. Progressive systemic disease was a main cause of death. Achieving better systemic disease control may be important in influencing outcome in pts with sarcomatous brain mets. Better risk stratification and selection of patients who may benefit from aggressive/multi-modality treatment is needed.

9413 POSTER

Primary Localized Gastrointestinal Stromal Tumours (GIST) of the Duodenum − a French Sarcoma Group (FSG) Retrospective Review of 84 Patients (pts)

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Background: Duodenal GIST represents only 3−5% of all GISTs. Clinicopathologic data are mainly derived from small series. We conducted a retrospective analysis of duodenal GISTs over the past 17 years.
Methods: Pts with localized duodenal GISTs were identified in two ways: a group of 75 pts reported via survey from 20 FSG centers, and a group of 9 pts enrolled in the BFR14 trial.