2909 POSTER

Expression of insulin growth factor-1 receptor (IGF-1R) is associated with cancer stem-like cells and tumor microenvironment

M. Joonsalu[1], M. Kase[2], A. Minajeva[3], J. Junninen[3], T. Metsaots[3], K. Niinepuu[3], M. Vardja[1], S. Kase[4], T. Asser[5], J. Jaal[1]. *[1]Tartu University Hospital, Department of Radiotherapy and Oncological Therapy, Tartu, Estonia; [2]East-Tallinn Central Hospital, Clinic of Internal Medicine, Tallinn, Estonia; [3]University of Tartu, Faculty of Medicine, Tartu, Estonia; [4]Riga Stradinš University, Faculty of Medicine, Tartu, Estonia; [5]Tartu University Hospital, Neurology Clinic, Tartu, Estonia*

Background: IGF-1R and its activation sustain cancer growth and progression. Moreover, IGF-1R is necessary for cancer cell stemness which is a key feature for cancer cell renewal. The aim of the study was to assess the IGF-1R expression and its association with CD133+ stem-like cells and tumor microenvironment in one of the most aggressive brain tumors − glioblastoma multiforme (GBM).
Methods: Surgically excised GBM tissues (n = 42) were histologically examined for overall extent of inflammation (score 1−3, based on typical appearance of inflammation, including presence of edema and inflammatory cell infiltration) as well as for overall proportion of necrosis (%) and microvascular proliferations (MP; low, medium, high). All histological parameters were assessed by an experienced pathologist. After immunohistochemistry, the number of IGF-1R-positive (IGF-1R+) cells and the proportion of CD133-positive (CD133+) GBM stem-like cells (%) were determined. Both immunohistochemical parameters were examined in 6 randomly taken microscopic fields by 2 independent researchers. Expression of IGF-1R was correlated to CD133+ stem like cell proportion and other parameters.
Results: In individual GBM samples, the extent of inflammation varied, being in the whole group 1.9±0.7 (mean±SD). The mean proportion of necrosis of the entire study group was 38%±31% (mean±SD) and the overall proportion of MP was low-medium in 39% and high in 61% of GBM patients. Immunohistochemical parameters were examined by 2 independent researchers whose results were in good accordance ($R = 0.8$, $p < 0.0001$). The number of IGF-1R+ cells per microscopic field was 1.8±0.7 (mean±SD). The proportion of CD133+ stem-like GBM cells varied greatly between patients, being from 0.5% to 82%. The mean CD133+ proportion was 33%±24% (mean±SD). A positive association was found between the number of IGF-1R+ GBM cells and the proportion of CD133+ stem like cells ($p = 0.036$). The number of IGF-1R+ GBM cells correlated positively also with the extent of inflammation ($p = 0.026$) and necrosis ($p < 0.005$), as well as with the proportion of MP-s (0.02).
Conclusion: The expression of IGF-1R is associated with cancer stem-like cells and depends on GBM microenvironment. More IGF-1R+ cells were present in tumor tissues with more pronounced inflammatory reaction, extensive necrosis and angiogenesis. Further studies are needed to clarify whether GBM stem-like cells can be influenced by modification of IGF-1R signaling and tumor microenvironment. This work was supported by grant IUT2−4.
No conflict of interest.

2910 POSTER

Assessing primary brain tumour recurrences using (18)F-FET PET-CT scanning − an Australian perspective

S. Angelides[1]. *[1]Westmead Hospital, Nuclear Medicine, Earlwood, Australia*

Background: Anatomical imaging modalities and (18)F-FDG PET scintigraphy are limited in their ability to differentiate brain tumour recurrences from other pathologies such as radiation necrosis.
The aim of this study was to evaluate the capacity of O-(2-(18)F-fluoroethyl)-L-tyrosine ((18)F-FET) to detect primary brain tumor recurrences.
Methods: Forty-five patients with a suspected brain tumour recurrence based on MRI findings were investigated by (18)F-FET PET and (18)F-FDG-PET within 3 wk. Region-of-interest analyses were performed on co-registered PET/MRI images. The presence of tumor and the discrimination of anatomic structures on (18)F-FET PET and (18)F-FDG-PET images were visually determined. Patients were followed-up for at least six months (range 6−40 months) post-scan acquisition, and the clinical outcomes were correlated to the initial findings.
Results: (18)F-FET-PET scans were positive in 36 cases and negative in 9 cases. In all nine "negative" cases, the (18)F-FDG scans were also reported as normal, and the patients remained disease-free at follow-up (range 6−26 months). Of the "positive" cases, 6 patients also demonstrated avid (18)F-FDG uptake in the culprit lesions, in a pattern highly-suggestive of disease recurrence. Each of these patients succumb to their disease within 14 months of the scan. In the remainder of the cases, (18)F-FDG uptake was either graded as normal or equivocally increased. Disease recurrence (histological and/or clinical) was confirmed in 34 of the 36 patients with increased (18)F-FET uptake.
Conclusion: A negative (18)F-FET-PET scan confers a favourable clinical outcome. Conversely, a positive scan is usually, but not universally, associated with tumour recurrence. Further, (18)F-FET PET is superior to (18)F-FDG for biopsy guidance and determining appropriate management.
No conflict of interest.

2911 POSTER

Cis-diamminedichloroplatinum penetration into the cerebrospinal fluid of the lateral ventricle, postoperative cavity and lumbar subarachnoid space with or without pre-intravenous mannitol administration in patients with brain metastasis from lung cancer

H. Nakagawa[1], M. Yamada[1], M. Tamura[1], M. Yoshida[1], M. Shindo[1], H. Nishiyama[1], T. Tomi[1], S. Sakai[2]. *[1]Nozaki Tokushukai Hospital, Neurosurgery, Daitou, Osaka, Japan; [2]Nozaki Tokushukai Hospital, Surgery, Daitou, Osaka, Japan*

Introduction: We reported that the repeated intravenous infusion of cis-diamminedichloroplatinum (CDDP) prevented the local recurrence of metastatic brain tumors after total excision surgery. However, the data regarding CDDP distribution in the cerebrospinal fluid (CSF) after an intravenous CDDP is not available. On the other hand, hypertonic intracartoid infusion has been reported to enhance delivery of the drug to the brain. Therefore, we evaluated the penetration of total platinum (Pt) into the CSF, both with or without hypertonic intravenous infusion, on the total Pt distribution in the plasma and the CSF.
Patients and Methods: Total Pt levels in plasma and CSF's were determined immediately after the intravenous infusion of CDDP (80mg/m^2) for 1 hour, with and without pre-intravenous infusion of 20% mannitol (200ml), in 11 patients with brain metastasis resulting from lung cancer. CSF samples were obtained via Ommaya reservoirs that were placed in the anterior horn of the lateral ventricle (CSF-V) and the post-operative cavity (CSF-C). Spinal CSFs (CSF-L) were also obtained in the last 4 patients of the series via a spinal drainage. CDDP was infused intravenously at 13:00 hours to eliminate the influence of circadian variation. Plasma and CSFs were sequentially sampled after intravenous CDDP infusion, and their Pt levels were analysed for Pt content by using the atomic absorption spectroscopy. The area underneath the concentration time curve (AUC) was calculated for plasma and CSF using the moment method.
Results: The AUC for total Pt in plasma showed a significantly higher level with the infusion of mannitol compared with the infusion without mannitol ($p < 0.01$, paired t-test). Total Pt levels (AUCs and peak concentrations) in CSF-C were much higher than those in CDF-V and CSF-L, both with and without the infusion of mannitol. The ratios (%) of CDDP penetration into the CSF (CSF AUC/plasma AUC) were much higher for CSF-C than for CSF-V ($p < 0.0001$), both with and without mannitol infusion. However, the CSF penetration ratio with the mannitol infusion did not significantly differ from the ratio without the mannitol infusion. Thus, the infusion of mannitol did not significantly increase the penetration ratio of total Pt.
Conclusion: Ratios (%) of total Pt penetration into CSF-C (CSF-C AUC/plasma AUC) reached approximately 30%, leading to the killing of tumor cells. However, hypertonic intravenous infusion did not enhance delivery of the CDDP to the CSF.
No conflict of interest.

2912 POSTER

Failure pattern and survival after carmustine implant and concurrent chemo-radiation in newly diagnosed glioblastoma multiforme patients

R. Dandamudi[1], S. Giridharan[1]. *[1]University Hospitals of North Midlands NHS Trust, Cancer Centre, Stoke-On-Trent, United Kingdom*

Background: In the UK, since the publication of National Institute for Health and Care Excellence (NICE) guidelines in 2007, there has been an increase in the usage of Carmustine implants after maximal (>90%) safe resection of newly diagnosed glioblastoma multiforme (WHO Grade 4 Glioma). There is published retrospective evidence that most relapses occur locally after adjuvant chemo-radiation with Temozolamide. Our objective is to investigate the relapse patterns and survival in newly diagnosed glioblastoma multiform patients treated with multi modality