Poster presentations (Mon, 24 Sep, 14:00−17:00)
Paediatric oncology

1408 POSTER

Identification of bipotential cells in both neuroblastic primary tumours and neuroblastoma bone marrow metastasis

S. Acosta, E. Rodriguez, C. de Torres, I. Garcia, C. Lavarino, H. Beleta, J. Mora. *Hospital Sant Joan de Deu, Developmental tumor laboratory, Esplugues de Llobregat, Spain*

Background: Neuroblastic (NBT) tumors are derived from neural crest stem cells. Double staining cells by neurofilament and calcyclin have recently been proposed as NBT tumor precursor cells. However, in our hands, neurofilaments are expressed in both glial and neuroblastic cells. Instead, we found specific neuroblastic and glial markers in the GD2 membrane staining and nuclear calcyclin immunostaining, respectively. In this study, we searched for GD2/calcyclin coexpressing cells in primary NBT and bone marrow metastasis.
Methods: Immunofluorescence for membrane GD2 (neuroblastic lineage) and nuclear calcyclin (glial lineage) was used independently and simultaneously looking for GD2/calcyclin double stained (bipotential) cells. Fresh frozen sections (n = 11) and bone marrow metastasis specimens (n = 5) were investigated. Endothelial cells were identified by CD34 immunostaining.
Results: GD2 staining was detected in all neuroblastic cells. Calcyclin was detected in the stromal-glial bundles and endothelial cells. 8 of the 11 NBT were evaluated for double staining and 3 different populations were identified: GD2+/calcyclin− neuroblastic cells, GD2-/calcyclin+ Schwannian-like cells and some GD2+/calcyclin+ population, which included neuroblastic-like cells but also some of cells within the stromal bundles. The double staining neuroblastic subpopulation did not form clusters and was surrounded by GD2+/calcyclin− neuroblasts.
All metastatic bone marrow specimens analyzed showed double stained cells in the neuroblastic aggregates. Most cells in such aggregates were GD2+/calcyclin− and only few double staining cells were present.
Conclusions: The presence of neuroblastic cells which coexpress glial and neuronal lineage markers in neuroblastic primary tumors and metastasis shows their bipotential capacity, but it remains unclear whether these cells are undifferentiated neuroblasts giving rise to sustentacular cells or, otherwise, they are multipotential cells maintaining the malignancy of the tumor.

1409 POSTER

Differential expressed genes in favourable versus unfavourable neuroblastoma tumors

F. Abel, A. Wilzen, T. Martinsson. *Biomedicine, Clinical Genetics, Göteborg, Sweden*

Neuroblastoma (NB), a childhood tumor originating from neural crest cells in the sympathetic nervous system, has a complex biological heterogeneity depending on clinical stage and age at diagnosis. In order to screen for genes involved in tumour development, a global micro array expression analysis was performed on six NB tumours (three favourable and three unfavourable). Data indicated that the expression levels of several important players in the noradrenalin biosynthesis pathway were significantly lower in unfavourable NB tumours compared to favourable. The 92 most significant genes with a fold change above 2.0 between groups were picked out for verification with real-time PCR (with TaqMan Low Density Array cards, Applied Biosystems) on tumours included in the micro array study. Thirteen additional tumours were also analyzed by real-time PCR in order to explore if the expression pattern is applicable to a larger group. The preliminary results show that transcripts encoded by solute carrier family 6 (SLC6A2), transcription factor AP-2 beta (TFAP2B), and chromosome 5 open reading frame 13 (C5ORF13) all show a distinct down-regulated pattern in unfavourable tumours versus favourable. The protein encoded by SLC6A2 is an important mediator in the noradrenalin biosynthesis pathway. Both TFAP2B and C5ORF13 (also known as P311) are known to induce the expression levels of cell-cycle regulator P21. Also, TFAP2B has been shown to regulate expression of genes required for development of tissues of ectodermal origin, such as neural crest. These findings insist us to further explore these genes and their involvement in neuroblastoma development and progression.

1410 POSTER

Frequent impact of ^{18}F-fluorodeoxyglucose positron emission tomography on the staging of children and adolescents with alveolar rhabdomyosarcoma

E. Kabickova[1], D. Sumerauer[1], E. Drahokoupilova[1], E. Cumlivska[2], M. Kyncl[2], L. Krskova[3], R. Kodet[3], J. Votrubova[4], O. Belohlavek[4]. *[1]University Hospital Motol, Ped.Hematology and Oncology, Prague 5 Motol, Czech Republic; [2]University Hospital Motol, Radiological Techniques, Prague 5 Motol, Czech Republic; [3]University Hospital Motol, Pathology and Molecular Medicine, Prague 5 Motol, Czech Republic; [4]Na Homolce Hospital, Nuclear Medicine, Prague 5 Motol, Czech Republic*

Background: Alveolar rhabdomyosarcoma (ARMS) is an aggressive soft tissue tumour with a characteristic translocation involving chromosomes 2 and 13. It is usually found in adolescents, and typically arises in large muscles of the trunk and extremities. Accurate staging is important, in order to reserve the combined modality treatment to those children who might benefit from it. The most difficult patients to treat are those with metastases, they have a five-year survival rate <30%. FDG-PET is a new imaging method; its diagnostic criteria are based on the metabolic activity of tumour cells. In this study we assess the usefulness of ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) in the detection of metastatic disease in children and adolescents with ARMS.
Materials and Methods: Over a period of 5 years twelve patients with ARMS (median age 15 years, range 8.7−18.5 years) were prospectively recruited into the study. PET findings were correlated with standard staging including CT, ultrasound, bone scan and bone marrow examination. Discordant findings were verified by MRI. No patients presented with brain or pulmonary metastases.
Results: One third (4/12) of staging PET scans was concordant with conventional staging. PET was found to be more sensitive for detecting of nodal, skeletal and soft tissue involvement. In eight patients PET revealed 11 additional ARMS manifestations (3 distant lymph nodes, 5 multifocal bone lesions, and 3 soft tissue infiltrates) and correctly upstaged 5 of 12 children (42%). No false-positive results were observed. Sensitivity for PET and standard staging methods was 100% and 44%, specificity 100% and 100%, and accuracy 100% and 58%, respectively. Clinical management was changed in 42% of patients as a result of FDG-PET findings.
Conclusions: Our results showed that whole-body FDG-PET might improve and simplify the current staging procedure in ARMS. PET should be recommended as a screening method prior to other conventional used imaging modalities to plan a rational staging protocol. Large multicentric prospective studies are necessary to verify this conclusion.Supported by grant MZ0 CR 64203

1411 POSTER

Impact of FDG-PET for staging of pediatric solid tumours: comparison with conventional imaging modalities

A. Hosono[1], A. Makimoto[1], A. Kawai[2], N. Tsuji[1], S. Hamanoue[1], F. Nakatani[2], K. Chuman[2], Y. Beppu[2], U. Tateishi[3], T. Terauchi[4]. *[1]National Cancer Center, division of Pediatric Oncology, Tokyo, Japan; [2]National Cancer Center, division of Orthopedic Surgery, Tokyo, Japan; [3]National Cancer Center, division of Diagnostic Radiology, Tokyo, Japan; [4]National Cancer Center, division of Cancer Screening, Tokyo, Japan*

Background: Pediatric solid tumors are sometimes difficult to visualize correctly with conventional imaging such as computed tomography (CT) or magnetic resonance imaging (MRI). Accurate initial assessment of the extent of disease and precise evaluation of the effect of treatment are critical to deliver appropriate therapy. Metabolic imaging using ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) has become a widely used test for the staging of many malignancies in adults, but there is scarce information with this imaging modality in patients with pediatric malignancies. With these considerations in mind, this study was undertaken to ascertain the value of FDG-PET/CT in the staging of patients of pediatric solid tumors in comparing with the results of CT and MRI.
Method: Fifty-three patients with pediatric solid tumors (rhabdomyosarcoma in 16, Ewing's sarcoma in 11, osteosarcoma in 10, neuroblastoma in 8, germ cell tumor in 5, synovial sarcoma in 2, and Wilms tumor in one) had an FDG-PET/CT during staging or restaging evaluation. FDG-PET/CT scans were acquired with a PET/CT device (Aquiduo; Toshiba Medical Systems, Tokyo Japan) 60 min after tracer injection. The FDG-PET/CT was considered positive if uptake greater than the background activity was noted and could not be explained by normal physiology.
Results: One hundred and fifteen sites were evaluated. Fifty-two patients had positive PET scans at the primary sites. Mean standardized uptake values of each type of tumor at diagnosis were 6.2 in rhabdomyosarcoma,