2515 POSTER

Neuropsychology in the investigation of the nature of the brain function disorders after castration in breast cancer patients

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Goals: The cognitive dysfunctions and other brain functions disorders can be the consequences of the changes in emotional well-being induced with the decease and treatment experience as well as the result of the neuro-endocrine influence on the brain function. Treatment for the estrogen and/or progesterone receptor positive breast cancer in pre-menopausal women supposes the castration ovarian ablation or tamoxifen use. The aspects of post-castration syndrome in both varieties – medication and surgery – can lead to the decrease in the cognitive functioning. The most evident and early symptoms of post-castration syndrome are the psycho-emotional changes. There is the evidence of the cognitive problems in this group of the patients. The qualification of these problems should be the subject of neuropsychological investigation.
Method: In 64 breast cancer patients the complex neuropsychological investigations (Luria's method) and examination of the emotional well-being (standard questionnaire) were carried out before and after castration (in 18 weeks). The anxious and depressive disorders were psychologically treated in short course and then the third neuropsychological complex study was carried out.
Results: The results show the significant decrease in cognitive functions in 78% of the patients. In a half of these cases the deficit of programming and control is evident as the main factor of the neuropsychological syndrome. In 34% of the patients the deficit of the activation is evident as neuropsychological factor. In 31% of the patients the psychotherapy reduces the anxiety level and in 24% of the patients it leads to the better scores in memory and movement tests with additional motivation escalation.
Conclusions: In the structure of the mental disorders there is specific input of the programming and activation disorders as neuropsychological factors. The secondary emotionally induced changed can be reduced with the psychological help.

2516 POSTER

Primary central nervous system lymphoma in Japan: changes in clinical features, treatment and prognosis during 1985–2004

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Background: We have conducted nationwide surveys of primary central nervous system lymphoma (PCNSL) treated since 1985 in Japan. Results obtained for patients seen between 1985 and 1994 and between 1995 and 1999 were published. In the present study, we conducted further investigations of PCNSL patients treated between 2000 and 2004, and compared their clinical features, treatment details and outcome with those of patients seen in the preceding two periods.
Materials and Methods: A total of 739 patients with histologically-proven PCNSL were analyzed. Seventeen institutions were surveyed, and data on 131 patients treated between 2000 and 2004 were collected. These data were compared with updated data of previously obtained ones on 466 patients treated between 1985 and 1994 and 142 patients treated between 1995 and 1999.
Results: Recent trends towards decrease in the male/female ratio (approaching unity), increase in aged patients, and increase in patients with multiple lesions were seen. Regarding treatment, decrease of surgical tumor removal and increases of the use of intravenous chemotherapy and methotrexate-containing regimens were observed. The median survival time was 18, 29 and 24 months in patients treated between 1985 and 1994, those treated between 1995 and 1999, and those treated between 2000 and 2004, respectively, and the respective 5-year survival rate was 15%, 30%, and 30%. The survival data in the more recent two periods were significantly better than those in the oldest period. Higher age, poorer performance status, and high lactate dehydrogenase level were associated with poor prognosis in all the periods. In patients treated between 1995 and 1999 and those treated between 2000 and 2004, those who received systemic chemotherapy had better prognosis than those who did not. This was supported by multivariate analysis for patients in the most recent period. There was a trend towards improved survival in patients receiving methotrexate-containing chemotherapy in the recent decade.
Conclusions: This study revealed several notable changes in patient, tumor and treatment characteristics during recent years. The prognosis of PCNSL patients improved during recent 10 years.

2517 POSTER

Radiotherapy and concomitant Temozolomide, with or without adjuvant Temozolomide in the treatment of glioblastoma multiforme

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Introduction: For decades treatment of glioblastoma multiforme (GBM) has consisted in maximum surgical resection followed by possible radiation therapy (RT). In a recent study published by EORTC and NCIC, it was demonstrated that the combination of concomitant and adjuvant Temozolomide (TMZ) with RT improved survival against exclusive RT. Nevertheless, important questions are still raised about the optimum administration of TMZ.
Objectives: This retrospective study was carried out to detect possible differences in survival of patients between treatment with RT and concurrent TMZ, and the same treatment followed by adjuvant TMZ.
Materials and Methods: in January 2001, concurrent treatment with RT and TMZ was begun in patients with GMB in our centre. Following maximum possible surgical resection, the first 12 patients received 3D conformed RT, 60 Gy (2G/day) and 75 mg/m^2 TMZ, daily throughout the duration of RT. In January 2002, and up to December 2004, this approach was modified, associating systematically 6 cycles of adjuvant TMZ (150–200 mg/m^2/day) for 5 days (every 28) in the next 27 patients. The 39 patients included in the 2 successive periods were the object of this study, the main aim being to carry out a comparative analysis of survival.
Results: The median survival time for the whole series was 9 months, with significant differences amongst those treated with combined RT and concomitant TMZ: 6m (5−7); and RT with concomitant and adjuvant TMZ: 14 m (6−22m), $p = 0.01$. When considering other variables (age, type of surgery, and adherence to TMZ), multivariate analysis of survival with Cox regression models showed that adjuvant TMZ and compliance of $\geqslant$75% to TMZ treatment were the only significantly independent variables.
Conclusion: Our findings suggest that the administration of combined RT with concomitant and adjuvant TMZ in treating GMB results in higher survival rates than RT and concomitant TMZ, though it is necessary to carry out a prospective randomised trial to demonstrate this hypothesis.

2518 POSTER

Prolonged maintenance chemotherapy with Temozolomide (TMZ) after concomitant treatment in newly diagnosed GBM: safety profile

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Background: TMZ concomitant to RT followed by 6 cycles of adjuvant TMZ has become standard of care in the treatment of newly diagnosed GBM, obtaining a statistical significant survival benefit over radiotherapy alone. In this study concomitant and adjuvant part, demonstrated grade 3−4 hematological toxicity in 7% and 14% of patients respectively.
Methods: Adult GBM patients were treated with TMZ (75 mg/m^2/day) concomitant to RT (60 Gy/30F) followed by adjuvant TMZ (150–200 mg/m^2 days 1−5, q28). Adjuvant TMZ was continued for a maximum of 12 cycles in patients with no evidence of disease and until progression in patients with evidence of disease. Prophylactic trimetoprim-sulphamethoxazole 3 times weekly was administered.
Results: 104 patients (67 males), median age 53 (range 20−73), median KPS 90 were enrolled. A median of 6 cycles of adjuvant TMZ were delivered (range 0−30). During the concomitant phase, grade 4 neutropenia occurred in 1 patient (0.9%), and grade 3−4 thrombocytopenia in 4 patients (3.8%). Grade 1 to 2 lymphocytopenia occurred in 10 patients (9.6%). One patient reported pneumonia with normal white blood cells. Five patients (4.8%) discontinued treatment in the concomitant part: 2 for grade 3 dermatological rash, 2 for haematological toxicity (one for prolonged grade 4 thrombocytopenia resolved in 6 weeks, and 1 patient for grade 4 neutropenia and thrombocytopenia, still unresolved after more than 15 months). One patient died after concomitant treatment for pulmonary embolism. During the adjuvant phase, grade 3 to 4 neutropenia and thrombocytopenia occurred in 2% and 5% of patients, respectively. Two

patients discontinued treatment in the adjuvant part, one at third cycle for prolonged grade 4 thrombocytopenia, and one after fifth cycle for prolonged grade 2 thrombocytopenia.
Conclusions: A prolonged maintenance TMZ chemotherapy doesn't impact negatively on toxicity profile.

2519 POSTER

A prospective study of cognition, mood and quality of life in patients receiving parasellar radiotherapy

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Background: Pituitary adenomas, craniopharyngiomas and parasellar meningiomas are located adjacent to the mesial temporal lobes, orbital frontal lobes and the hypothalamus, which are areas important for the control of mood and cognitive functions such as problem solving, memory, attention, concentration and verbal expression. To date, no prospective studies have explored the cognitive and quality of life sequelae of radiotherapy primarily limited to the parasellar region.
Materials and Methods: 30 adult patients who were planned to receive fractionated stereotactic radiotherapy for the treatment of parasellar tumors were recruited from the Vancouver Cancer Centre between November 2001 and September 2003. Patients participated in serial neurobehavioural assessments on three occasions, within the week prior to radiotherapy, six months following the completion of radiotherapy and one year following the completion of radiotherapy. Assessments included self-reported measure of mood states; self-reported measures of quality of life (EORTC QLQ-C30 and the associated brain tumour module BCM 20); caregiver ratings of behaviour and activities of daily living and standardized clinical neuropsychological measures (attention/concentration, psychomotor speed, executive function and memory). A further assessment 3 years post treatment is currently underway.
Results: 29 patients were available for analysis. There were no significant differences in cognitive function, mood or quality of life at 6 months or 1 year compared to baseline testing ($p > 0.01$). Results will be available for the 3 year assessment when this is completed in May 2007.
Conclusion: This prospective study has demonstrated that fractionated stereotactic radiotherapy to tumours in the parasellar region does not result in any serious decline in cognition function, mood or quality of life within the first year post treatment.

2520 POSTER

Oral Temozolamide concurrent with radical radiotherapy for patients with glioblastoma multiforme: The University Hospitals of Leicester Experience

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Purpose: To monitor outcome amongst patients with glioblastoma multiforme (GBM) receiving radiotherapy (RT) with concurrent Temozolamide and compare the results with data from published randomized control trial (by Stupp et al).
Materials and Methods: The results of the randomized controlled trial by Stupp et al presented at ASCO in 2004 and published in 2005 showed that patients with GBM treated with RT and concurrent and adjuvant Temozolamide have a better survival than those treated with RT alone. Due to lack of funding in our centre, we treated these patients with RT (60 Gy in 30 fractions over 6 weeks) and concurrent Temozolamide only (75 mg/m^2 daily for 42 days). A retrospective audit was carried out to monitor the outcome of patients with GBM treated in our centre with this regimen until June 2006. Data was collected from patient case notes, chemotherapy and radiotherapy prescriptions and computer database in our centre. Statistical analysis was carried out using SPSS package.
Results: 35 patients were identified (25 males, 10 females). Mean age was 58 years. 72% underwent craniotomy and debulking, whereas 29% had biopsy only. 33 patients received concurrent chemoradiation, of whom 27 patients (82%) completed the treatment. Significant toxicity due to chemotherapy was reported in only 15% of cases (mostly haematological) with one patient requiring dose reduction and 3 patients discontinuing the treatment. 70% of patients showed symptomatic improvement at six weeks following treatment. Although the mean time to progression was 4.3 months, the median survival was 9.5 months and 27% of patients were still alive at 20 months following diagnosis.
Conclusion: Even outside of clinical trials, the addition of Temozolamide concurrently to radiotherapy seems to be well tolerated with good compliance and acceptable toxicity similar to published data. Furthermore, long term survival can be achieved in a significant proportion of cases.
For patients with GBM radiotherapy with concurrent Temozolamide only appears to be a feasible and promising option with long term outcome comparable to published data and warrants further evaluation within clinical trials
However due to small sample size, the results need to be interpreted with caution.

2521 POSTER

Quality Assurance in the EORTC Low Grade Glioma Trial 22033–26033: the dummy run

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Purpose: To early detect deviations of radiotherapy (RT) in the ongoing EORTC22033–26033 trial on primary temozolomide (TMZ) vs RT in low grade gliomas after stratification for genetic 1p loss.
Materials and Methods: Performance of the dummy run (DR) is required once the first patients are randomized. A case of incomplete resected left frontal astrocytoma WHO II was proposed. DICOM-datasets (pre-, post-surgery MRI scans; planning CT-scan in treatment position) were made available online. DR consists of two parts: (1) Definition of the tumour, clinical and planning volume. Volumes were 3D reconstructed and evaluated; (2) After acceptance centres performed the RT plan. Target volumes were defined by 5 experts from 5 countries. Dmax to the organ at risk (OAR) should not exceed 10 Gy for retina and lens, 55 Gy for optic chiasm, optic nerves and the brainstem. Normal brain should receive less than 60% of dose. We analysed: target volumes, plan characteristics, PTV coverage, conformity index (CI)=PTV95%/PTV, PTV inhomogeneity (U) and Dmax to OAR by using DVH and isodose chart.
Results: 22 centres entered 77% of currently randomised patients and have finished most parts of the DR. We report on 20 case solution plans. Investigators volumes (size and anatomy) were compared against expert volumes. Two centres were requested to repeat GTV-PTV delineations due to major deviations. The majority of OAR were systematically contoured except the internal ear, lens, lacrimal gland and normal brain. All plans were 3D-conformal, used a commercial treatment planning system and isocentric technique according to ICRU50−62. For 5 plans dose was not prescribed at isocenter and not reported at the axe intersection in another 5 plans. Tissue heterogeneity corrections were not applied in 2 institutions. The majority used a 4(2−5) field set-up. Hot spots ranged:102%-109%. Conformity was good with CImean = 0.99(0.95−1) and Umean = 6%(4%-11%). Two sites had a major deviation in dose homogeneity and another two had a significant PTV under-dosage. Dmean to the normal brain was 18.6 Gy (12.5−28.4 Gy).
Conclusion: The majority of the centres planned RT in compliance with protocol requirements. Two centres needed to restart PTV delineation and a majority needed to add specific OAR. The advantage of DR at the beginning of trial is to give recommendations. The learning effect is expected to improve consistency between centres, improve radiation planning and volume definition and as such the reliability of the trial results.

2522 POSTER

Adult medulloblastoma: McGill experience

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Background: Medulloblastoma comprises about 15% of childhood neurologic malignancies but only accounts for 1−3% of such tumors in adults. Given that adult medulloblastoma is rare and an internationally recognized standard of care does not exist, we decided to review the demographics, management and survival data of patients treated and followed at the McGill University teaching hospitals over the past 18 years.
Methods: Medical records were investigated to identify eligible patients diagnosed with medulloblastoma over the age of 18. Retrospective clinical chart review was undertaken to gather data on patient demographics, presenting symptoms, tumor characteristics, treatment modalities and morbidity, relapse and survival.