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INTERSTITIAL BRAIN BRACHYTHERAPY

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Thirty-two patients with malignant brain tumors received 33 brachytherapy applications. Of these, 20 were permanent and 13 were removable implants delivering a median dose of 6000 cGy. All patients except 1 received external radiation for a median dose of 6000 cGy and 17 patients received chemotherapy.

Complication rates were minimal and acceptable. Karnofsky scores improved in 10 patients, remained stable in 17 patients and worsened in 5 patients. Nineteen patients died with local disease, 3 died with local disease and distant metastases, 8 remain alive with local disease and two alive NED.

Glioblastoma multiforme patients survived 9 months after implant compared to 14 months for recurrent astrocytoma patients. Boost patients survived a mean 37 months from diagnosis compared to 42 months for patients with recurrent disease. Additional radiation by implants for brain tumors can improve survival and performance for selected patients; however, it remains palliative.

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INTRACRANIAL EPENDYMOMAS

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Forty-nine patients,26 male,23 female, with the diagnosis of intracranial ependymomas were treated at our department with postoperative radiotherapy between 1976 and 1989.Their age ranged between 1.5 and 27 (Median 10).Tumors were infratentorial in 31 (% 63) and supratentorial in 18 (% 37) patients.The surgical intervention was in the form of total excision in 18, subtotal excision in 27 and only biopsy in 4 patients. The histopathological diagnosis was low grade malignant ependymoma in 33 and high grade malignancy in 16 patients.All patients were treated with either craniospinal, cranial or wide local irradiation and total tumor doses were 5000 cGy in 23,5500 cGy in 22 patients.All peadiatric patients except 3 and 2 adult patients were treated with "Vincristine, CCNu +/- Procarbazine" combined chemotherapy regimen beside radiotherapy. The 3,5 and 10 year actuarial overall and disease free survival rates were % 70, % 57, % 57 and % 68, % 57, % 57, respectively. This study revealed significantly better survival rates in favour of adult patients (p=0.012).A trend is observed in favour of male patients and patients with low grade malignant tumors.

INTRACRANIAL EPENDYMOMAS, RADIOTHERAPY.

Oncogenes and Suppressor Genes

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CHROMOSOME 17q LINKAGE STUDIES OF 20 FRENCH BREAST AND/OR OVARIAN CANCER FAMILIES.

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A gene for early onset familial breast cancer (BRCA-1) has recently been mapped to the chromosome 17q12q-21 region (Hall et al 1990). A same locus was assigned for the breast and ovarian cancer syndrome (Narod et al 1991). In order to confirm the gene location and to test for possible genetic heterogeneity, we have conducted linkage analyses in 20 French gynecological cancer families : 14 breast cancer families, 5 breast and ovarian cancer families and 1 site specific ovarian carcinoma family, with five chromosome 17q markers (from centromere to telomere : D17S250; D17S579, 42D6, NM23 and D17S74). The five breast ovarian cancer syndrome families as a group give positive evidence for linkage (Lod score = 2.29 at θ = 0.00 with D17S579, the most closely linked marker to breast cancer gene) whereas the 14 breast cancer families do not. A lod score = 1.13 at θ = 0.00 from D17S579 was obtained for the site specific ovarian cancer family. This kindred contributes towards the hypothesis that site specific ovarian carcinoma syndrome is linked to chromosome 17q region shown to contain BRCA-1 gene. In the other hand heterogeneity of linkage of breast cancer is significant in France and support the existence of more than one susceptibility gene. Testing of additional families will tell us wether DNA linkage approch is a useful method to screen individual at high risk of inherited gynecological cancer.

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GENETIC ALTERATIONS IN CHILDREN WITH NEUROBLASTOMA (NBL) - RELEVANCE TO PROGNOSIS

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NBL is one of the most common heterogenous childhood cancers. The evidence that cancer develops as a result of the accumulation of genetic changes, led us to analyse the comparison of constitutional and tumor genotypes of 37 NBL tumors - loss of allels (LOH) for chromosomes 1p36, 11q, 14q, comparing to other clinical and biological features. 37 cases at diagnosis (10 under the age of 1 year) were analysed; 21 in stage IV, 8 stage III, 7 stage I-II and one IVS. MYCN amplification was found in 5 stage IV and 1 - III, LOH was observed in 35% of cases in Chr. 1p36 of whom 44% infants less than 1 year old. Chr. 11q23 in 11% and none in chromosome 14q. Allelic gain in tumor DNA was observed in 6 cases, 5 stage IV and one stage III unresponsive to therapy. No additional alterations were observed in 5 children during tumor progression. It is suggested that somatic imbalance consistent with deletions of Chr. 1p36 and 11q23 are involved in the tumorigenesis of NBL, while allelic gain, may be associated with advanced stage of the disease.

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FREQUENT MUTATIONS, DELETIONS AND NUCLEAR OVEREXPRESSION OF p53 GENE IN NODE METASTASES FROM HEAD AND NECK CARCINOMA

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In certain types of human cancer it has been reported that p53 mutation was associated with poor prognosis. In this study we have analysed 15 specimens of head and neck squamous cell carcinomas (HNSCC), all of which were lymph node metastases with extracapsular rupture, for the presence of p53 gene mutation and loss of heterozygosity (LOH) for S5 and p53 loci on the short arm of chromosome 17. The p53 protein was also analysed by immunohistochemistry of frozen tumour sections using anti-p53 antibodies. 10/15 (67%) specimens contained mutated p53 gene as shown by direct sequencing and/or single strand conformation polymorphism. Positive nuclear staining for p53 protein and LOH were observed in 100% and 56% of HNSCC exhibiting p53 mutation, respectively. These data show that p53 gene alterations are associated with HNSCC of poor prognosis and that this gene plays an important role in tumour progression of HNSCC.

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p53 EXPRESSION CORRELATES WITH DIFFERENTIATION BUT NOT SURVIVAL IN HUMAN OVARIAN CANCER.

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A series of 105 ovarian cancer biopsies was assessed by the immunoperoxidase technique supplying the CMI antibody. Sections were assessed relative to a positive control for intensity (control = 2) on a 3 point scale, and distribution was quantitated in a similar manner. The two scores were added (max = 6) for each patient: 55% of cases were negative, 19% scored 1-3 and 26% scored 4-6. There was no correlation with FIGO stage, bulk, residual disease or survival, but a higher score was found to correlate with poor differentiation (p=0.03). Serum autoantibodies to p53 were detected in one third of 220 sera tested by an ELISA technique, but there was no correlation with any clinical prognostic factors or serum CA125 level. The degree of differentiation was significantly correlated with the detection of positive serum tumour overexpression of p53 or the occurrence of both abnormalities (Kruskall-Wallis test p=0.01). Serum autoantibodies were only detected in 1 out of 73 control women. Our hypothesis is that a proportion of ovarian cancers produce a mutant p53 which is antigenic, and our conclusion from the preliminary data is that detectable p53 expression in ovarian cancer is associated with histology of poor differentiation, but not survival or other clinical prognostic factors.