S166 Tuesday 14 September 1999 Proffered Papers

vs greater than 6.4 U/gHb). These results indicated that G6PD-abnormal or -deficient individual may predispose NPC, and may be resulted in poor prognosis. The underlying mechanisms of low G6PD patients more susceptible to oxidative damage, and of the effects to radiotherapy will be further delineated.

621 POSTER

Temporal relationship between serologic Epstein-Barr (EB) viral antibodies and treatment outcome in nasopharyngeal carrinoma

S.G. Tang, T.J. Chang, S. Tsang, J.H. Hong, W.M. Liang. Department of Radiation Oncology, Chang Gung Memorial Hospital, Tao-Yuan County, Taiwan

Purpose: Literature has reported the importance of anti-EB viral capsid & early antigen (VCA&EA) antibodies as tumor markers of NPC. There are, however, controversial points with respect to clinical significance of anti-EB VCA immunoglobulin A, G (IgA, G) and anti-EBEA titers in the serum. In a prospective study the value of these antibodies in predicting the prognosis of NPC was evaluated.

Methods: One hundred and sixty two irradiated non-metastatic patients were recruited between 1994 & 1996. Indirect immunofluorescent assay of antibody was applied on serum samples collected before & after RT & every 3 months in the following 2 years.

Results: Patients with undifferentiated carcinoma or neck node of greater than 6 cm yield significantly higher level of mean pre-RT anti-EBEA antibody than patients with non-keratinizing carcinoma (P = 0.0386) or neck node of ≤ 3 cm (P = 0.0099) while post-RT serologic level of VCA IgA remained to be the only independent anti-EB factor in predicting complete remission rate (>160 VS ≤ 160 , odds ratio = 3.91, P = 0.008). Two year recurrence free survival rates were relatively high in patients with low (≤ 160) anti-EBEA titers measured at 3.6 and 12 months post-RT (p = 0.0002, 0.0337 & 0.0001 respectively).

Conclusion: Post-RT anti-EBVCA IgA level correlated well to treatment response while anti-EBEA antibodies before RT and during follow up period may help in predicting nodal status, pathogic types & 2 year recurrence free rates.

622 POSTER

Clinical relevance of urokinase-type plasminogen activator (uPA) and its inhibitor PAI-1 in oral squamous cell carcinoma (OSCC)

H.-F. Zeilhofer¹, K.P. Bock¹, P. Dettmar², B. Hundsdorfer¹, K. Ulm⁴, R. Sader¹, H.-H. Horch¹, H. Höfler², M. Schmitt³. ¹Dept. of Oral-Maxillofacial Surgery; ²Inst. of Pathology; ³Dept. of Gynecology; ⁴Inst. of Medical Statistics and Epidemiology, TU Munich, Germany

Purpose: Invasion and metastasis in solid, malignant tumors require tumor associated proteases to dissolve the surrounding tumor matrix and the basement membranes. The serine protease uPA and its inhibitor PAI-1 play a key role in these processes. Several inependent studies on different kinds of cancer (e. g. breast, ovary, kidney) prove the prognostic value of uPA and PAI-1. Elevated levels of uPA and/or PAI-1 predict poor outcome of cancer patients. For oral squamous cell carcinoma, however, the possible prognostic relevance of tumor-associated proteolytic factors to the malignant process has still to be evaluated.

Methods: In the present study we used enzyme-linked immunosorbend assays (ELISA) to determine uPA and PAI-1 antigen concentrations in primary tumor tissues of 47 patients afflicted by oral squamous cell carcinoma.

Results: Patients with either high PAI-1 (<27.61 ng/mg protein) or uPA (5.41 ng/mg protein) contents in their primary tumors have an increased risk of relapse (uPA: p = 0.02; PAI-1: p = 0.006). Patients whose primary tumors have lower levels of these antigens have a lower risk than patients with high uPAI-1 and PAI-1 concentrations. Statistical analysis revealed uPA and PAI-1 to be independent from classical morphohistological prognostic factors

Conclusion: In OSCC uPA and PAI-1 are strong and independent prognostic factors which allow us to identify high risk patients. Both uPA and PAI-1 might help us to improve the individual oncological therapy. uPA and PAI-1 could become new targets in cancer therapy.

POSTER POSTER

Causes of interruption of radiotherapy in nasopharyngeal carcinoma patients

Y.-P. Chen¹, N.-M. Tsang¹, T.-K. Tseng¹, J.-H. Hung¹. ¹Chang Gung Memorial Hospital, Radiation Oncology, Kwei-Shan, Taiwan

Purpose: In the past few decades, NPC researches have primarily focused on diagnosis and treatment while few studies have assessed why some patients fail to complete the recommended full-course radiotherapy. This study is to explore the factors involved in patient's decision to discontinue treatment and the outcome.

Materials and Methods: A total of 3,273 nasopharyngeal carcinoma patients were treated in a span of 18 years from 1979 to 1996. Of these, 276 did not complete the full-course treatment of radiation therapy. The medical records of these patients were studied to determine the contributing factors for treatment interruption.

Results: Of the 276 patients whose treatment were interrupted, 120 (43.5%) were unable to endure the acute side effects of radiation therapy and afraid of possible complications from the treatment; 57 (20.7%) had doubt on the diagnosis or had the subjective perception that the treatment will be ineffective in view of the severity of their disease; 50 (18.1%) resorted to folk prescriptions; 17 (6.2%) were due to the socioeconomic problems; 15 (5.4%) reverted to have treatment in other hospitals for transportation consideration. Five-year survival rate on these patients was 10%, with median survival of 1.2 years.

Conclusions: This finding suggests that more attention should be paid to providing care with regard to side effects of the procedure and to reinforcing pre-treatment education. Given the fact that poor prognosis in these patients, clinicians, working together with medical staff as a team, should provide patients with adequate support so that their pressures to cope with the social, economical, psychological and educational aspects of NPC will not be obstacles to the completion of radiotherapy.

624 POSTER

The role of definitive radiation therapy for larynx preservation in patients with advanced laryngeal cancer

K.C. Keum¹, G.E. Kim¹, C.G. Lee¹, C.O. Suh¹, J.K. Roh², K.M. Kim³, Y.H. Kim³, W.P. Hong³. ¹ Yonsei University College of Medicine, Radiation Oncology, Seoul; ² Yonsei University College of Medicine, Medical Oncology, Seoul; ³ Yonsei University College of Medicine, Otorhinolaryngology, Seoul, South Korea

Background and Purpose: Recently, neoadjuvant chemotherapy (CT) and radiation therapy (RT) have been advocated as a standard treatment for laryngeal preservation in patients with locally advanced laryngeal cancer. However, it is still being debated whether adding neoadjuvant CT to conventional RT makes an effective contribution to laryngeal preservation. The current study was designed to resolve this controversy.

Materials and Methods: Eighty patients (stages III, IV) with squamous cell carcinoma of the larynx were divided into two groups according to treatment modalities, which consisted of RT alone (N = 40, Group I) and neoadjuvant CT plus RT (N = 40, Group II). Comparative analysis was undertaken in order to investigate the differences in the organ preservation rate and treatment results between the two groups.

Results: There was no significant difference in the response rate and patterns of treatment failure between the two groups. The five-year survival rate was similar between Group I (24%) and Group II (31%) (P=0.1556). In addition, the larynx was almost equally preserved in Group I (62%) vs. Group II (63%).

Conclusion: RT without neoadjuvant CT seems to be a valid alternative treatment for the purpose of laryngeal preservation in locally advanced laryngeal cancer.

625 POSTER

Impact of radical or non-radical surgery combined with postoperative radiotherapy of the oral cavity cancer on treatment outcome

A. Maciejewski¹, A. Rembielak², K. Składowski³. ¹Department of Surgical Oncology; ²Radiotherapy Department; ³Radiotherapy Clinic I, Center of Oncology – MSC Institute, branch Gliwice, Poland

Purpose: To evaluate relationship between degree of macro – and/or microscopic radical or non-radical surgery and postoperative radiotherapy on treatment outcome of the patients with oral cavity cancer.

Head and neck Tuesday 14 September 1999 S167

Methods: 81 patients (pts) with oral cavity cancer were treated with combined surgery and radiotherapy in the MSC Institute, branch in Gliwice, Poland between 1990 and 1997. There were 15 pts (18%) in T_1 , 34 pts (43%) in T_2 , 17 pts (21%) in T_3 and 15 pts (18%) in T_4 stage. Forty four patients had positive neck lymph nodes, i.e. 22 (27%)-N₁, 21 (26%)-N₂ and 1 (1%)-Nx. The risk of loco-regional recurrences and distant metastases was scored using Peters scale including tumour grading and margins, number of positive nodes, extracapsular invasion, vessels embolia. Radiotherapy was given in daily fractions of 2 or 1.8 Gy to total dose of 60 \div 70 Gy depending on the risk score. Neck nodes were electively irradiated with a total dose of 50 Gy and it was increased up to 60 \div 70 Gy depending on the risk score.

Results: Median follow-up was 28 months ($2\div81$ months). Surgery was macroscopically radical in 74 pts (91%) and non-radical or uncertain in 7 pts (9%). Loco-regional control was observed in 73 pts (90%), uncomplete control in 4 (5%). In the remaining 4 pts (5%) it was impossible to determine the effect of irradiation at the end of the treatment because of very severe mucosal reaction. Loco-regional recurrence was observed in 19 pts (23%), distant metastases in 2 pts (2%), mainly in those with non-radical surgery.

Conclusion: It seems that the precise determination of surgical macroand microscopic margins and complete information concerning the risk of the loco-regional failure has an important impact on optimization of postoperative radiotherapy.

626 POSTER

Totally implantable venous access devices (TIVAD) and head and neck cancer. Results of a prospective and homogeneous series of 170 patients

Ph. Maillart, G. Lorimier, E. Gamelin, A. Lortholary, R. Delva, E. Fondrinier, F. Larra. Centre Paul Papin, 2 rue Moll, 49000 Angers, France

Introduction: Head and neck cancer is often observed in smoking and alcohol abuse patients. These particular patients with an important infectious risk (tracheotomy, dirty skin, bad hygiene) need a safe central venous access for chemotherapy and supportive care. TIVAD provide a good vascular access

Materials: We carried out a prospective and homogeneous series of 170 patients treated between 01/94 and 12/98: 166 males and 4 females with a median age of 51 years old (range 37–67). All patients have a sqamous cell carcinoma stage III or IV. (38% recurrent, metastases). We used a Districath® (Districtass®) TIVAD.

Methods: All patients received the same regimen consisting of cisplatin 25 mg/m² d 1–4, fluorouracil 1000 mg/m² as continuous perfusion over 96 hours d 1–4 every 21 days (3 cycles) for neoadjuvant (103 pts), concomitant (3 pts), recurrent or metastatic (64 pts) chemotherapy. Others uses are: blood transfusions, perfusions. TIVAD were implanted by percutaneous cannulation of the subclavian vein after local analgesia under sterile surgical procedure.

Results: TIVAD is a good vascular access (failure of implantation 0%) for chemotherapy (continuous perfusion, bolus). We observed 0 intolerance, 0 infection, 0 septicemia during the treatment. The percutaneous implantation is a reliable and rapid technique with a light morbidity (0 death due to the method).

Conclusion: TIVAD used in head and neck cancer patients provide a reliable and safe venous access for chemotherapy and supportive care. They reduce the infectious risk and improve the security and quality of life of patients.

627 POSTER

Nasopharyngeal carcinoma with cranial nerve palsy

Joseph Tung-chieh Chang, Li-Hui Chen, Ji-Hong Hong. Department of Radiation Oncology; Chang Gung Memorial Hospital, Linkou, Taiwan

Purpose: To evaluate various prognostic factors and the impact of imaging modalities on tumor control in patients with nasopharyngeal cancer (NPC) with cranial nerve (CN) palsy.

Methods: From Sep. 1979 to Dec. 1996, 313 NPC patients with CN palsy received radical radiotherapy (RT) in Chang Gung Memorial Hospital-Linkou. Imaging methods used varied over that period, and included conventional tomography (T) for 54 patients, computerized tomography (CT) for 228 patients magnetic resonance image (MRI) for 31 patients. Upper CN (II–VI) palsy was found in 249 patients, lower CN (IX–XII) in 13, and 51 patients had both. All patients had good performance status (WHO < 2). The RT was delivered by megavoltage or Co-60 X-ray. Therapeutic modalities did not change significantly over the 17-year study period. The median external RT dose was 70.2 Gy (63–74.6). Brachytherapy was also

given to 146 patients in addition to external RT. It was delivered by the remote after loading high dose rate technique. 121 patients received cisplatin based chemotherapy before or after radiotherapy. Recovered from CN palsy occurred in 169 patients during or after radiotherapy. All the patients had been followed more than 2 years.

Result: The 3 year-overall survival was 45.8% and 5-year 30.6%. Patients who had undergone MRI study had better survival than those studied with CT scan or T study. 5-yr survival was 49.3%, 30.7% and 22.2% respectively. Patients with both CN palsy had worse survival than those with only lower CN or upper CN involvement. Patients who recovered from CN palsy had better survival than those who did not. The addition of brachytherapy decreased survival while an external RT dose of more than 70 Gy may improve the survival. The use of chemotherapy did not improve survival or tumor control in this study.

Conclusion: The use of more modern image study was associated with improved survival of patients with NPC causing CN palsy. Patients recovering from CN palsy had better survival. Giving more radiation dose via external beam may a better way to achieve tumor control rather than brachytherapy.

628 POSTER

Radiochemotherapy in the treatment of locally advanced head and neck cancer: Results after five years of a randomized study

M. Santarelli, N. Raffetto, P. Torcia, V. De Santis, V. Donato, R. Maurizi Enrici. Radiology-"La Sapienza" Rome, Radiotherapy, Via Val Travaglia 6, 00100 Rome, Italy

Purpose: This study was undertaken to evaluate the efficacy of two regimens of chemoradiotherapy in the treatment of locally advanced head and neck cancer.

Methods: From 1992 to 1997, 127 patients with locally advanced head and neck cancer (stage III–IV) were randomized. Sixty-six patients (group a), 42 male and 24 female, with a median age of 48 years (range 40–7) received during radiotherapy two course (1_{th} – 6_{th} week) of chemotherapy with carboplatin (300 mg/m² day 1) and etoposide (60 mg/m² days 1 to 3). Sixty-one patients (group b) received two cycles of chemotherapy with 5 FU (750 mg/m² days 1 to 5) and MIT C (10 mg/m² day 1). The median dose of radiotherapy was 60 Gy (range 55–66 Gy) 180 cGy/d 5w.

Results: The actuarial five years survival rate (Kaplan-Meier) was 38% for group a (CBDCA + etoposide + RT) and 25% for group b (5FU + MIT C + RT). The difference was statistically significant (P = 0.036). Toxicity group a: mucositis G III in 41 patients and G IV in 16; disphagia G III in 46 patients and IV in 5; leukopenia in 24 patients.; 28 patients required nutritional therapy. Toxicity group b: mucositis G III in 38 patients and G IV in 17; disphagia G III in 48 patients and G IV in 3; leukopenia in 23 patients; 25 patients needed nutritional therapy.

Conclusions: The data of actuarial survival five years rate suggest that concomitant chemotherapy in group a (CBDCA + etoposide + RT) is better than concomitant chemotherapy in group b (5FU + MIT C + RT).

629 POSTER

Expression of p73 protein, a p53 homologue, in normal & malignant undifferentiated cells of head & neck malpigian epithelium

L. Faridoni, J. Bosq, F. Janot, M.L. Le Bihan, G. Riou, D. Caput, J.C. Ahomadegbe, <u>J. Bénard</u>. *Institut Gustave Roussy, 94805 Villejuif, France*

In about 50% head and neck squamous cell carcinoma (HNSCC), there are p53 mutations as well as occasional p53 nuclear accumulation (likely without mutations) in normal basal & parabasal cells of the peritumoral tissue (Ahomadegbe et~al.,~Oncogene 1995). P73 gene, with a high p53-homology in the DNA binding domain, encodes 2 isoforms differing by C-terminal splicing, $p73\alpha$ & β . In vitro, $p73\alpha$ induces p21 gene transactivation and apoptosis. To investigate putative p73 involvement in malpigian epithelium carcinogenesis, immunohistochemical studies using a polyclonal antibody raised against a C-terminus α isoform epitope (a gift of D Caput, Sanofi, France) were performed on normal mucosa adjacent to 29 HNSCC (11 undifferentiated and 18 well differentiated).

Results: In normal malpigian epithelium, an intense and conspiscuous nuclear staining restricted to basal and parabasal cells as opposed to a total lack of staining in keratinized differentiated layers were consistentely observed. In 11 undifferentiated cancers, there is a homogeneous and diffuse staining in all tumor cells; in contrast, in 18 well differentiated tumors, all dif-