

recommended, either scans to seek metastases or iodine-131 for ablation. There was one death, 12 years after diagnosis with metastatic disease. 5 patients chose not to be followed by any of our physicians and sought follow up elsewhere.

Conclusion: This approach has allowed for more efficient pre and post-operative management, especially in the advance planning of radioiodine ablation. During the first half of this new program the average delay between deciding to offer radioiodine ablation and the actual treatment date was 3.5 months. During the second half this was reduced to 1.2 months, despite using no new resources. Patients have expressed a high degree of satisfaction with this team and its' recommendations, especially that controversies were explained to them. The resulting database is now being used to develop an outline of management based on our own outcomes and available recommendations in the literature.

1089

PUBLICATION

Unknown primary with metastatic neck node: A tertiary health institution experience

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Background: Unknown primary with secondary neck node (UPSN) accounts of 2–4% of all head and neck cancers. We conducted a retrospective analysis for our patients with UPSN. We also analysed the possible prognostic variables.

Material and methods: Between January 1997 and January 2003, a retrospective study of 135 cases of UPSN were done. The inclusion criteria were presence of metastatic neck node and primary not detected in the clinical examination or the investigative work up. The patients planned for radical RT (29 patients) were treated with a dose of 70 Gray/35fractions/7 weeks. Patients planned for pre op RT (5 patients) received a RT dose of 50 Gray/25fractions/5 weeks followed by modified radical neck dissection. For palliative RT, patients were given either 20 Gray/5fractions/1week or 8Gray as a single fraction (74 patients). 27 patients were advised symptomatic care only in view of gross disease. The following variables were tested for impact on locoregional disease free survival: Duration of complaints, histology, nodal size, sex, predisposing risk factor, duration of complaints, neck node side, level of the neck node involved and the number of neck nodes

Results: Only 25.3% of the patients were suitable for any kind of radical treatment. The mean duration of initial symptoms was 6.23 months (1–48 months). The median follow up was 3 months (1–52 months). Nodal size was the only significant variable ($p=0.001$). The overall local control rate in our study was 20% (27/135). The overall survival was 23.7% (32/135 patients).

Conclusion: Nodal size is a significant variable in the overall prognosis of UPSN. The overall prognosis of such patients in our analysis was poor due to the locally advanced disease in majority of patients at presentation.

1090

PUBLICATION

Low energy photon radiation boost combined with surgery and external beam radiotherapy (EBRT) in early oral cancer. Preliminary results on treatment tolerance

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Background: Photon Radiosurgery System (PRS) is an X-ray delivery system designed to provide a high dose of low energy photon radiation. Clinical application of PRS for boost delivery is easy and cheap because background radiation exposure is minimal and no special shielding of the patient, personnel or operating room is required. We report preliminary results on tolerance of intraoperative PRS application combined with EBRT in 7 patients treated for early oral cancer.

Material and Methods: Seven patients with early squamous cell cancer of mobile tongue (4) and floor of the mouth (3) were evaluated for intraoperative PRS application combined with EBRT in Center of Oncology MSC Memorial Institute in Gliwice, Poland between December 2003 and July 2004. During tumor resection microscopic margin of normal tissue were obtained in all patients and target volume (TV), including tumor bed with 0.5 cm margin, was determined. Intraoperative PRS application was performed. The appropriate applicator was manually positioned. Retractors or 1 mm-thick lead shield was used when needed. The diameter of applicator varied from 3 to 4 cm. Mean delivered dose was 6.35 Gy (range 5–7.5 Gy) and was prescribed at 0.5 cm distance from the applicator surface. For each dose adequate time of exposition was calculated. Mean exposition time was 15.5 min (range 12.4–18.5 min). EBRT was started

after mean time of 44 days. In all cases 6 MV, 3D conformal irradiation was applied. Clinical Target Volume (CTV) consisted of tumor bed (CTV1) and lymph nodes at risk (CTV2). Radiotherapy was given conventionally up to elective dose level. Median time of EBRT was 32 days (range 6–39 days). Mucosal reaction of TV acc. to EORTC was assessed.

Results: Acute mucosal grade 3 reaction revealed in TV in all patients just after intraoperative PRS application. Significant additional increasing of mucosa reaction in TV has not appeared after EBRT. Lengthening of healing time to over 3 months (median time of 108 days) after EBRT with no consequential late effects has been observed in all patients. There were no local recurrences with local disease free survival median time of 312 days (range 187–365 days).

Conclusions: Intraoperative application of PRS is an easy method of boost delivery in oral cancer treatment. It seems to be well tolerated although extended mucosal recovery time is observed. Further study is needed to confirm these results.

1091

PUBLICATION

Combined Modality for Treatment of Buccal Cancer

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Introduction: To evaluate the combined modalities treatment result of buccal cancer and find the prognostic factors.

Patients and Method: There were 211 buccal cancer patients who received combined modalities treatment in Chang Gung Memorial Hospital – Linkou Medical Center under service of Taipei Chang Gung Oncology Group from January 1994 to December 2003. There were 203 (96.2%) patients were male and the median age was 46 ranging 23 to 79. The majority (84.5%) patients had habit of smoking, 69.1% had betel quid chewing and 58.4% had alcohol drinking. The stage distribution was stage I: 16 (7.6%) patients, II: 28 (13.3%) patients; III: 41 (19.4%) patients and IV: 126 (59.7%) patients. All the patients received radical surgery first then adjuvant radiotherapy was given due to stage III or IV disease or close margin (lt;5 mm) in resection margins. The median radiation dose was 60.8 Gy (ranging from 6 Gy to 72 Gy). The Cisplatin based concomitant chemoradiotherapy was given in neck lymph node with extracapsular spreading (ECS) patients after 1997.

Result: The 5 year disease specific survival (DSS) for stage I patients was 72%, stage II: 74%, stage III: 59% and stage IV: 52.1%. There were no survival difference in different T stage and regional extension factors such soft tissue extension, lymphatics and/or vessel permeation, nerve and/or bone invasion, however, N stage is significant in survival. The 5-year DSS for N0 was 64%, N1: 59% and N2 49% ($p=0.02$). Patients with ECS had worse survival (64.2% vs. 38.9%; $p=0.016$). The worst survival was in patients with N2 and ECS disease, the 5-year survival only 38% and other group is around 63% ($p=0.009$).

Conclusion: Patients with ECS and more than 2 lymph node metastasis are the highest risk for metastasis need more aggressive treatment.

1092

PUBLICATION

Prognostic significance of clinical-pathological features in high-risk head and neck squamous cell carcinoma (HNSCC) patients (pts) treated with postoperative concurrent chemoradiation (CRT)

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Background: Postoperative CRT can improve the disease-free survival (DFS) in high-risk HNSCC pts, but selection criteria need to be better assessed considering the acute and late toxicities and the benefits.

Patients and methods: This is a retrospective study of 32 consecutive pts with HNSCC of oral cavity (14), hypopharynx (9), larynx (8) or oropharynx (1), treated by surgery with curative intent and postoperative CRT (66 Gy, 2 Gy/d, combined with cisplatin 100 mg/m² on days 1, 22, 43), accrued between Mar/02-Dec/04. Eligible pts were considered as high-risk when presented: T3/T4 tumors (27), positive/close surgical margins (6), pN+ (26), lymphatic and/or vascular invasion (LVI, 10), perineural involvement (NI, 20), or extracapsular spread of nodal disease (ECS, 3). According to N status, pts were classified as N0 (6), N1 (12), N2 (13) or N3 (1); 18 pts had 2 or more positive nodes. Tumor grade was 1 (8), 2 (20) or 3 (4).

p53 expression, proliferation rate (Ki-67) and angiogenesis (CD34) were evaluated by immunohistochemistry. DFS was estimated by the Kaplan-Meier method and comparisons by the log-rank test.

Results: After a median follow-up of 17.2 months (mo), 6 pts relapsed and there were 6 deaths (2 in relapsed pts). Two distant relapses were observed. The median DFS (mDFS) of the 32 pts was not reached. The 2-year DFS rate was 54%. In the group of 29 pts without ECS (mDFS not reached), 8 relapsed, as compared to the 3 pts with ECS, in which 2 relapsed (mDFS 12.8 mo, HR 4.46; 95%CI 1.26–362.34, $p=0.034$). Due to the acute toxicity of CRT, only 20 pts received the 3 planned cycles of chemotherapy (CT), and 2 relapses occurred among these 20 pts (mDFS not reached). On the contrary, among the 12 pts that received 1 or 2 cycles, 8 relapsed (mDFS 14.3 mo, HR 7.75; 95%CI 2.11–29.06, $p=0.002$). Unexpectedly, considering the tumor grade, 6 pts relapsed among the 24 with grade 2/3 tumors (mDFS not reached), as compared to 4 pts among the 8 with grade 1 tumor (mDFS 20.8 mo, HR 2.76; 95%CI 0.78–18.36, $p=0.098$). No differences in DFS were observed according to primary site, tumor size, number of involved nodes, margin status, LVI, NI, duration of RT, p53-status, proliferation rate or angiogenesis.

Conclusions: Less than 3 cycles of CT and ECS could be identified as risk factors for relapsing after adjuvant CRT. Our data support the essential role of CT in this setting, but local and distant failures remain a problem in high-risk HNSCC pts submitted to adjuvant CRT.

1093

PUBLICATION

Concomitant radiochemotherapy with Mitomycin C and Cisplatin in inoperable carcinoma of the head and neck: preliminary results of phase II study

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Background: Phase II study on concomitant radiotherapy (RT) and chemotherapy with Mitomycin C (MMC) and Cisplatin (CP) in inoperable squamous cell carcinoma of the head and neck.

Material and methods: Treatment consisted of: (1) conventional RT (35X2 Gy/day in 7 weeks); (2) MMC 15 mg/m² IV, applied after delivery of 10 Gy (bioreductive agent, selectively toxic for hypoxic cells); (3) CP 14 mg/m²/day IV, applied during the last 10 fractions of RT (to counteract the effect of accelerated repopulation of surviving clonogens in tumor). Daily dose of CP was chosen after determination of dose limiting toxicity and maximum-tolerated dose in escalation part of the protocol [*Radiother Oncol* 2004; 73 (Suppl 1): S302]. Side-effects of the therapy were graded according to NCI and RTOG toxicity scales.

Results: Between 3/02 and 10/04, 24 male pts, 39–69 yrs old (median 57), entered the study. Sites of origin were oropharynx 12; hypopharynx 8; larynx 2; oral cavity 1; unknown 1. All tumors were UICC TNM stage IV (T4 19 [79%]; N3 7 [29%]).

Twenty pts (83%) were treated according to the protocol: all pts were irradiated to 70 Gy and received MMC. Four pts had <10 applications of CP.

The incidence of grade 3 acute systemic toxicity was 14 events that occurred in 10 pts (42%): leukopenia 5; hypokalemia 3; thrombocytopenia 2; hypocalcemia 2; increased creatinine and GGT in 1 pt each. Weight loss during therapy was 0–19% (median 9%); nasogastric-feeding tube was inserted in 7 pts (29%). Grade ≥3 radiomucositis was recorded in 21 pts (86%) and dermatitis in 8 pts (33%). In 10 out of 16 complete responders (63%), 16 severe (grade ≥3) late adverse events were recorded: skin fibrosis 5; xerostomia 3; impaired function of the larynx 3; hypothyroidism 2; pain, ototoxicity, and neurotoxicity in 1 pt each.

Radiologically, locoregional complete response rate at 3 mos was 54% (local, 74%; regional 67%). After successful surgery of residual neck disease in 3 pts, it was 87% regionally and 67% locoregionally. Two pts developed systemic mets. For pts alive on April 30, 2005, a median follow-up time was 19 mos (range 7–25 mos). The disease-free, disease-specific and overall survival rates at 18 mos were 53% (95% CI, 32–74%), 74% (95% CI, 56–92%), and 68% (95% CI, 49–87%), respectively.

Conclusions: Tested regimen was not associated with unacceptable toxicity. Considering prognostically extremely unfavorable profile of our pts, presented results justify additional recruitment of pts.

1094

PUBLICATION

In vivo optical coherence tomography monitoring of radiation mucositis in patients with head and neck cancer

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There are several systems for mucosal toxicity scoring in and after radio- and chemotherapy (WHO 1979, RTOG/EORTC 1984, LENT/SOMA 1995, CTCAE 2003). All of them are based on the visual estimation of mucosal changes (oral erythema, oedema, patches, ulceration) and on the patient's complaints (pain, xerostomia, swallowing and chewing dysfunction). There are no methods in the current practice to assess microscopic changes of mucosal structure during and after irradiation in various tissue components. Optical coherence tomography (OCT) has been actively developed since 1991. It creates real time cross-sectional images of subsurface tissues at a depth of up to 2 mm with spatial resolution close to that of the cellular level (10 to 15 µm). Clinical OCT applications include detection of early cancer and precancer, biopsy guidance, assessment of the lateral extent of neoplastic processes, differential diagnosis of diseases with similar clinical manifestation, and treatment follow up.

This study objective was to estimate changes of oral mucosa during and after radio- and chemotherapy using OCT imaging.

Materials and methods: From June 2004 to March 2005, 11 patients with stage II-IV of oropharyngeal squamous cell cancer were included into a prospective study. Patients were performed conventional radiation or chemoradiation (5FU+cisplatin) therapy up to total doses 66–70 Gy. OCT imaging was performed daily starting from the first day of irradiation in four points of oral mucosa: right and left cheek, right and left anterior pillar. After treatment, patients were monitored in 1.5, 3, 6, 9 and 12 months. Mucosal toxicity was scored according to CTCAE 2003.

Results: OCT imaging visualized mucosal changes, corresponding to different stages of acute mucositis development (Sonis, 1998). Normal mucosa has a high-contrast stratified structure. Its OCT images began to lose contrast after a total dose 2–6 Gy when no clinical manifestations were observed. Inflammatory phase appears in OCT images as reduced contrast between epithelium and connective tissue. Further reduction of epithelial thickness and contrast were observed in epithelial phase. Ulceration phase had completely unstructured OCT images. The recovery of normal mucosal structure lasted more than 100 days after end of the treatment, when no visual changes of mucosa were observed.

Conclusion: Mucosal changes, associated with acute reaction, can be visualized by OCT before any visual signs of mucositis development and can be seen when visual signs already disappeared. Further studies, combined with image processing, can lead to quantification of mucositis development in OCT images.

1095

PUBLICATION

Clinical experience of using docetaxel, cisplatin and 5-fluorouracil as induction chemotherapy in Bangladesh patients with non-resectable head and neck cancer

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Background: Significant activity has been shown with the combination of docetaxel, cisplatin and 5-fluorouracil (TPF) in the treatment of squamous cell carcinoma of the head and neck. We conducted a phase study to examine the response rate and toxicity of the TPF regimen in Bangladeshi patients.

Materials and Methods: Patients with non-resectable locally advanced cancers in head and neck region were treated with docetaxel 75 mg/m² (day 1), cisplatin 75 mg/m² (day 1) and 5-FU 750 mg/m² (day 1 to day 4) for every 21 days. Eligibility criteria of patients were over 35 years age, histologically confirmed squamous cell carcinoma (SCCHN), adequate hematological, renal and hepatic functions and no prior treatment