We analysed a retrospective series of patients (pts) treated with a multimodal approach including induction chemotherapy (CT).
Material and Methods: Between 2000 and 2008, 29 pts with stage III-IV malignant epithelial tumours of ethmoid and nasal cavity were treated. Adenocarcinoma and salivary gland-type carcinomas were excluded. Treatment consisted of induction CT platinum-based (with docetaxel, 5 fluorouracil or etoposide or vinorelbine) followed by concomitant chemo-radiotherapy (group A, 18 pts) or craniofacial resection (CFR) and postoperative radiotherapy (RT), with or without concomitant cisplatin (group B, 11 pts). Follow up ranged from 7 to 87 months (median 37 months).
Results: See the table.

Characteristics	Group A: CT+CT/RT n (%)	Group B: CT+CFR+RT(CT) n (%)
Stage III	4 (22)	3 (27)
Stage IV	14 (78)	8 (73)
T3	5 (28)	3 (28)
T4a	6 (33)	4 (36)
T4b	7 (39)	4 (36)
Squamous cell carcinoma	7 (39)	6 (54)
SNUC	9 (50)	1 (9)
SNEC	1 (5.5)	1 (9)
Small cell carcinoma	1 (5.5)	3 (28)
Neuroendocrine YES	4 (22)	4 (36)
Differentiation NO	14 (78)	7 (64)

SNUC = Sinonasal undifferentiated carcinoma; SNEC= Sinonasal neuroendocrine carcinoma

Only 3 pts showed neck nodal disease at diagnosis (1 N1, 2 N2), all in group A. Radiological response to induction CT showed partial response in all but 4 pts (1 complete remission and 3 stable disease). Globally, 3- and 5-year (yr) overall survival is 68% and 42%. Fifteen pts showed a local recurrence: 11 in group A (9 pts underwent a salvage CFR) and 4 in group B. Only one pt treated with salvage surgery at local site reached ultimate local control. Two pts with isolate node recurrence were treated with surgery. Distant metastasis developed in 4 pts (1 in group A and 3 in group B). Treatment strategy did not impact on DFS. Neurendocrine differentiation in tumours was associated with reduced disease free survival (DFS) ($p = 0.01$). All small cell carcinomas and SNECs recurred in 2 yrs time, while 3 yr DFS of squamous cell carcinoma and SNUC is about 65%.
Conclusions: Survival of advanced stage nasal cavity and ethmoid carcinomas is not satisfactory. Induction CT followed by concurrent CT/RT is able to reach disease control similar to multimodality treatments including CFR, at least in some histotypes. Efforts should be spent to improve treatment of bad prognosis histologies, in particular with neuroendocrine differentiation.

8536 POSTER

Immunohistochemical study to identify prognostic biomolecular markers for nasopharyngeal carcinoma

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Background: We performed immunohistochemical study with pre-treatment biopsy specimens to identify prognostic biomolecular markers for nasopharyngeal carcinoma (NPC).
Material and Methods: From January 1998 through December 2006, 68 patients were histologically diagnosed as non-metastatic NPC and treated with radiotherapy at Seoul National University Hospital. Only 38 patients had the paraffin block for the immunohistochemical study. Thirty-one patients had undifferentiated carcinoma and 7 patients had squamous cell carcinoma. Thirty-two patients (84%) had advanced stage NPC (2002 AJCC Stage III-IV). All patients, except for 6, were treated with induction chemotherapy with two or three cycles of cisplatin based regimen followed by either radiotherapy alone (19 patients) or concurrent chemoradiotherapy with cisplatin (13 patients). Immunohistochemical staining was done for Met, COX-2, EGFR, $nm^2$3-H1, p63, Cathepsin-D, p53, *C-erb*B2, CD138, STAT5, Egr1, CSE1L, STAT3 and LIN28 with the usual methods.
Results: The median follow-up time was 30 months (range, 11−83 months) for all patients and 39 months (range, 19−83 months) for surviving patients. Thirty-five patients were Met positive and 22 patients showed high expression (58%). Twenty-seven patients exhibited CD138 and 17 patients showed high grade (45%). Twenty-two patients showed Egr1 expression (58%). High Met and CD138 expression were statistically significant negative prognostic factors on survival. The expression of Egr1 had a positive prognostic effect on survival. The combined score (CS) of these three prognostic factors, Met (0, low; 1, high) plus CD138 (0, negative; 1, low; 2, high) minus Egr1 (0, negative; 1, positive), was a strong prognostic factor. The median survival curve was distinctly separated according to this combined score (median survival: CS −1 or 0, 76 mo; CS 1, 71 mo; CS 2, 42 mo; CS 3, 24 mo, $P = 0.001$). The patients with Egr1 expression also showed better progression-free survival (PFS) than those without Egr1 expression. No prognostic value was revealed in COX-2, EGFR, $nm^2$3-H1, p63, Cathepsin-D, p53, *C-erb*B2, STAT5, CSE1L, STAT3 and LIN28.
Conclusions: High Met and CD138 expression were evaluated as negative prognostic factors on OS in NPC. The expression of Egr1 was a positive predictive value for PFS as well as OS. The combined score of these markers could be used to stratify biomolecular risk groups.

8537 POSTER

Hemophagocytosis-related keratinization in squamous cell carcinoma and carcinoma in-situ of the oral mucosa

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Background: Round-shaped dyskeratosis (RSK), a kind of keratin pearl, is one of the histological features of carcinoma in-situ (CIS) of the oral mucosa. Our hypothesis for the histopathogenesis of this peculiar structure is that RSK foci are generated by keratinization of basal cells which are exposed to oxidative stress by hemoglobin derived from erythrocytes which are extravasated due to the collapse of blood vascular channels in the stroma.
Material and Methods: To stage the RSK formation process in oral CIS, a total of 50 surgical specimens of oral CIS and squamous cell carcinoma (SCC) containing RSK or keratin pearl foci were investigated by immunohistochemistry for various cytokeratin (CK) subtypes and vascular endothelium- and erythrocyte-related antigens. ZK-1, a human oral SCC-derived cell system, was exposed to erythrocytes or hemoglobin and examined for its CK phenotypes and heme oxygenase-1 (HO-1) expression levels by immunofluorescence and RT-PCR. In addition, the dynamics of protease activated receptor-2 (PAR-2), a candidate for regulating hemophagocytosis, were determined to confirm the molecular mechanisms underlying this phenomenon.
Results: RSK specifically immunopositive for CK10 and CK17, and CK10/CK17/HO-1 expressions were also confirmed in the basal cells facing collapsed blood vessels, around which erythrocytes were disseminated. ZK-1cells showed erythro-/hemo-phagocytosis when incubated with erythrocytes or hemoglobin, and phagocytotic ZK-1 cells showed enhanced immunofluorescence intensities for CK10, CK17, and HO-1. At the same time, mRNA expression levels were elevated for the three molecules. Those expression levels were also enhanced when ZK1 cells were stimulated with PAR-2 agonist peptides.
Conclusions: RSK and some of the keratin pearls in oral CIS and SCC, characterized by their particular expressions of CK17 and CK10, are obviously induced by hemophagocytosis-related oxidative stress. PAR-2 may be involved in the hemophagocytosis by CIS or SCC cells, which seems to be induced by hemolysis due to rupture of intraepithelial blood vessels, which are also characteristic of oral CIS. Based on the results, we propose a new concept of abnormal keratinization caused by hemophagocytosis. This 'hemophagocytosis-related dyskeratosis' starts from the basal end of the epithelial layer, which is in a reverse direction to that of normal keratinization.

8538 POSTER

Xerostomia and dysphagia related quality of life in patients treated with interstitial brachytherapy boost for head neck cancer

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Background: To study patients' perspective of xerostomia and dysphagia after treatment for head and neck cancer with external beam radiation (EBRT) and interstitial brachytherapy (BRT)
Methods: Patients with head and neck cancer previously treated with BRT either alone or in combination with EBRT who were controlled and attended the follow up clinic were considered suitable for the study. Xerostomia questionnaire (XQ) and dysphagia questionnaire (DQ) were served to consecutive eligible patients from Jan 2008 to Jan 2009 at a single head neck unit. XQ (Meirovitz 2006) consisting of 8 questions with scores from 0−10 and higher score indicating more xerostomia was selected. Each item score was added and the sum score transformed linearly to a final score ranging between 0−100. DQ (Murry 1998) was used in which each item was scored on 3 point scale and the final score for each patient was the mean score of the 10 items with higher score suggesting better outcome.