

788

# **NASOPHARYNGEAL CANCER (NPC) IN NORTHERN ISRAEL.**

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We continue to update our data on NPC with its higher than world average incidence in Israel. During 1968-1991, we treated a total of 75 NPC patients, 91% of whom were Stage III or IV, with full dose photon/electron radiotherapy to the primary tumor, neck, and base of skull. 41% received platinum-based chemotherapy as well. Current overall survival at 10 years is 44%. Our pediatric patients, all late stage, had 69% survival. Lymphoepitheliomatous or undifferentiated histologies were associated with higher survivals (68%, 50%) than was SCC (32%). Arab or Sephardi Jewish patients had 48-49% survival while Ashkenazi Jews had 31%. Arabs and Sephardi Jews have a higher likelihood of contracting NPC but also tend to manifest its more benign histological variants. The significance of chemotherapy is unclear; it may be marginally advantageous to survival in Stage III-IV lymphoepithelioma or undifferentiated tumor. However, consistently favourable prognosticators of survival included: age under 20, lymphoepitheliomatous or undifferentiated histologies, and ethnicity.

790

# **Prad-1 GENE AMPLIFICATION IN HEAD AND NECK SQUAMOUS CELL CARCINOMA.**

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Biopsies of 51 head and neck primary squamous cell carcinoma were analyzed for Prad-1 oncogene amplification (in 11q13) by PCR. Dopamin receptor gene were used as a control of amplifications. Twenty-seven (53%) carcinomas were found to be amplified. The number of copies ranged from 4 to 12. These results were correlated with primary tumor localization, TNM staging, extracapsular extension in metastatic lymph-nodes, histological differentiation, DNA ploidy, S-phase fraction, mitotic index, tumor vascularization, Ki-67 and immunohistochemical expression of keratins 6, 13 and 19.

A trend of correlation was found between Prad-1 amplification and low T stage ( $p=0.03$ ). However, the amplified tumors expressed keratin 13 in 41% and keratin 19 in 44% of tumor histological surface respectively, while in the non amplified tumors, the expression was 21 and 25% ( $p=0.02$ ). No relationship was found between amplification of Prad-1 and others parameters. These data need further investigation including follow-up and survival.

792

# **POST-ABLATIVE RECONSTRUCTION FOLLOWING HEAD AND NECK CANCER SURGERY WITH MICROVASCULAR FREE FLAPS**

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Between 1985 and 1992 microvascular free flaps (MFF) were used for the reconstruction of extensive defects after ablative surgery of head and neck carcinomas in 42 patients, treated at the University Department of Otorhinolaryngology and Cervicofacial Surgery in Ljubljana. For the reconstruction of skin or mucosa, radial forearm flaps were used most frequently, but apart from this, free jejunum grafts, lateral arm and latissimus dorsi flaps were used as well. In 6 patients with carcinoma of the floor of the mouth, reconstruction of the front part of the mandible was performed after segmental mandibulectomy by means of an osseous iliac crest flap, radial forearm or scapular osteocutaneous flap.

789

# **FINE NEEDLE CYTOLOGY DIAGNOSIS AND HISTOLOGICAL CONFRONTATION OF 691 SALIVARY GLAND TUMORS.**

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In the past 40 years, 691 cases of salivary glands tumors were diagnosed cytologically. 681 (96%) were confronted by histology. Remaining 10 nonconfronted cases concerned mainly metastases of known tumors. All archival cytologic and histologic available slides were reviewed and histological diagnoses were adapted to new WHO 1992 classification. 493 lesions were benign and 198 malignant. Tumors were: 295 pleomorphic adenomas, 56 Whartons, 45 adenoid cystic carcinomas, 47 inflammations, 32 metastases of various origin, 26 benign hyperplasias, 23 mucoepidermoid carcinomas, 20 lymphomas, 16 cysts, 13 oncocytomas, and remaining 118 cases were epithelial or conjunctive tumors which included 33 varieties. From 493 benign, the cytodiagnosis was done in 453 (92%) cases, 19 (3.5%) was unsatisfactory, 17 (3.5%) suspicious, and 4 (0.08%) was false positive. From 198 malignant, the cytodiagnosis was done in 165 (83%), in 6 (3%) was unsatisfactory, in 17 (9%) was suspicious and in 10 (5%) was false negative. Excluding unsatisfactories and including suspicious as malignant, the sensitivity was 0.948, specificity 0.955 and predictive positive value 0.896. This review has shown that aspiration of salivary tumors is accurate. We recommend the performance of cytodiagnosis in patients with salivary masses.

791

# **RADIATION THERAPY AND CONCOMITANT CDDP-5 FU COMBINATION FOR ANAPLASTIC THYROID CARCINOMA.**

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Anaplastic carcinoma of the thyroid is a rare and highly aggressive malignancy (medial survival: 3 to 6 months) affecting primary elderly patients. We report the result of a pilot study using a combination of Cisplatin (100 mg/m<sup>2</sup> bolus D1) and 5 FU (1000 mg/m<sup>2</sup>/day D2-5 in continuous infusion) delivered concomitantly during the first and the fourth week of post-operative external irradiation (50 Gy in 5 weeks + boost of 15 to 20 Gy). From 01/1989 to 12/1992, 7 patients were included in this trial. The median age was 64 (44-73). The performance status was  $\leq 2$  in the WHO scale. 4 patients had a maximal initial surgical resection (infra-centimetric residuums) and 3 only a partial resection. All the patients but one had pulmonary nodules at the time of diagnosis. One patient (partial resection, pulmonary metastases) died in the 4<sup>th</sup> week of the treatment, due to severe thyrotoxicosis. The 6 other patients completed the scheduled combined protocol. No severe adverse reactions was noted. Of the 5 patients with initial pulmonary nodules, no objective pulmonary response was noted. 4 of them died 2, 2, 7 and 10 months after the diagnosis respectively, 1 is alive at the 7<sup>th</sup> month. The patient with no distant metastase at the time of diagnosis is alive with pulmonary metastases 25 months after the diagnosis. For the 4 patients who were first treated by maximal resection, no local recurrence in the fields were seen 7, 25, 10 and 7 months after the diagnosis respectively. The 3 other patients were partial responders and none of them died of cervical relapse. These dismal results suggest that concomitant chemoradiotherapy with CDDP-5 FU is possibly efficient in terms of loco-regional control. However, this chemotherapy protocol is poorly effective on the pulmonary distant metastases.

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793

# **IMPROVED SURVIVAL AFTER NEOADJUVANT CARBOPLATIN/5 FU IN RESECTABLE STAGE II AND III SQUAMOUS CELL CARCINOMAS OF THE ORAL CAVITY AND THE TONSIL.**

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Although induction or neoadjuvant chemotherapy given prior to surgery and/or radiotherapy produces encouraging initial response rates in head and neck cancer, randomized studies have failed to demonstrate an advantage in long term local-regional control or survival. All randomized studies included only patients with far advanced stage III and IV disease. Thus this is the main reason for the low rate of complete responses demonstrated in the randomized trials (max. 18%). Frei et al. estimate that 40-50% complete responders are necessary before improved survival benefit will occur. Until yet such complete response rates with induction chemotherapy are only attainable in stage II and III disease. Therefore we started a prospective randomized trial in patients with resectable stage II and III SCC of the head and neck in 1988. Patients (pts) were randomized to receive either induction chemotherapy with 3 cycles of Carboplatin/5 FU prior to surgery and radiotherapy (arm A, 38 pts.) or standard treatment with surgery and radiotherapy (arm B, 38 pts.). Oral cavity and tonsil (group I) were stratified versus base of the tongue and hypopharynx (group II). Most of the randomized patients belonged to group I (57 pts., 28 in arm A, 29 in arm B). 26 of 28 pts. in arm A are evaluable for chemotherapy response and survival while 28 of 29 pts. in arm B are evaluable for survival. Results in group I: 11 CR (42%), 12 PR (46%), 3 NR (12%). After a follow-up of 12-48 months overall survival is 85% in arm A and 41% in arm B ( $p<0.03$ ). Disease-free survival is 62% in arm A and 34% in arm B (n.s.). Identical results were found in Cologne and Kassel. As of today the number of pts. in group II (19 pts) are too small for a statement, but preliminary data indicate no difference in overall and disease-free survival between arm A and B.

Key word: SCC of the HN, Induction chemotherapy, Survival is standard therapy