

HEAD AND NECK SURGERY

HN001 SURGICAL MANAGEMENT OF T1 – T2 CANCER OF THE OROPHARYNX

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Purpose Early stage oral cavity cancer may be treated by surgery, radiotherapy, or a combination of therapies. Radiotherapy is probably most widely used, but we have had a preference for surgical management in selected cases. The aim of this study is to analyse the outcome from this approach.

Methods A retrospective cohort study of cases identified from the computer files of the Sydney Head and Neck cancer Institute at Royal Prince Alfred Hospital was undertaken. Eligible patients were those with T1 or T2 squamous cell carcinoma of the oropharynx, treated with definitive surgery with or without radiotherapy. All neck stages were included. Previously treated patients were excluded.

Results A total of 108 patients were identified. M:F ratio was 3:1, median age 60, number of T1 and T2 stages were 32 and 76, while 57 patients were N0, and 51 patients had clinical neck disease. 68 patients underwent post operative radiotherapy. Median follow up was 43 months. At the time of follow up 70 patients were alive with no evidence of disease, 11 were alive with disease, 15 had died with disease, and 11 had died from other causes than the cancer. There was 1 with disease status unknown.

Conclusion Surgery provides effective treatment for selective patients with early stage cancer of the oropharynx. It also offers the chance of decreasing or avoiding radiotherapy toxicity. A randomized trial comparing surgery with or without radiotherapy, with radiotherapy with or without chemotherapy is recommended.

HN002 SKULL BASE SURGERY – HOW MAY THE RESULT BE IMPROVED?

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Background Craniofacial resection as a preferred treatment option for patients with benign and malignant tumours of the skull base.

Aim To review the results of skull base surgery in our multidisciplinary programme and to compare these against international benchmarks, as well as identifying factors that may improve the outcome of treatment.

Method 62 consecutive patients who underwent skull base resection and reconstruction were culled from our database.

Results Follow up averaged 52 months. Various reconstructive techniques were used including immediate facial reanimation ($n = 5$) and free tissue transfer ($n = 18$). There was no peri-operative death. 3 patients developed a surgical complication requiring return to theatre including CSF leak and tension pneumocephalocele with infection in one patient. General medical complications prolonged admission in 5 patients.

33 patients were treated for malignant disease. 13 of these had a delay in definitive surgical treatment of more than 3 months. This included inadequate initial surgery in 11 cases, most of whom also had radiotherapy prior to referral. 8 of these 13 cases developed a recurrence (6 local, 1 neck, 1 distant) post-operatively despite clear surgical margins in 7. At an average follow-up of 46.5 months 7 of these cases had died (5 related to and 2 unrelated to) their disease at an average of 16.5 months post-operatively.

Conclusions Meticulous reconstruction to seal the cranial base reduces surgical complications. Inadequate initial treatment and delay in definitive surgical treatment makes clear margins more difficult to achieve and reduces the potential for cure in the group of patients with cancers.

HN003 PROPHYLACTIC LYMPHADENECTOMY REDUCES POSTOPERATIVE THYROGLOBULIN LEVELS IN PAPILLARY THYROID CANCER

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Purpose The aim of this study is to determine whether the use of prophylactic ipsilateral level 6 lymphadenectomy (LND6) in patients with papillary thyroid cancer (PTC) and clinically node negative neck offers an advantage over total thyroidectomy (TT) alone.

Methodology A cohort study of patients undergoing surgery for PTC was performed. Patients with PTC and no clinical evidence of lymphadenopathy at presentation were included. Patients were stratified on the basis of extent of surgery. A protocol of TT and routine LND6 for PTC was introduced into the unit in 2002. Group A patients had TT and LND6. Group B patients had TT alone. The number of radioiodine treatments (6GBq) was recorded. Serum thyroglobulin (TG) levels following the first dose of ablative radioiodine were compared.

Results From December 1995 to April 2005, 447 patients with PTC and no clinical evidence of lymphadenopathy underwent surgical treatment. Group A ($n = 56$) had TT and LND6. Group B ($n = 391$) patients had TT alone. MACIS scores were equivalent Group A, 4.70 and Group B 4.3. The number of ablative doses of radioiodine used following surgery was similar Group A 1.0, Group B 1.2, ($P = 0.5$). The first post ablative TG levels measured were significantly lower in Group A ($0.4 \mu\text{g/L}$) compared with Group B ($9.3 \mu\text{g/L}$), $P = 0.016$. The proportion of patients with undetectable serum TG at 6 months post surgery was greater in Group A (72%) compared with Group B (43%), ($P < 0.001$). Long term postoperative complications were the same.

Conclusion In PTC the addition of routine LND6 is associated with lower postoperative levels of thyroglobulin compared with TT alone.

HN004 CYCLIN A1 EXPRESSION IN LARYNGEAL CANCERS CORRELATES WITH DIAGNOSIS OF NEW PRIMARY MALIGNANCIES OF AERODIGESTIVE TRACT

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Field cancerisation due to widespread genomic insult secondary to alcohol and tobacco abuse is a well known feature of HNSCCs. In patients with HNSCC there is a 1% per annum risk of developing new primary malignancies of the aero-digestive tract. To date no biological marker has been discovered that would herald this development. Cyclin A1 is a cell cycle regulator involved in G1/S cell transition. High levels of Cyclin A1 expression have been noted in human testes and myeloid leukaemias. Its expression appears to be prompted by elevated levels p53 expression.

The aim of this study was to establish the role of CyclinA1 and mutant p53 in HNSCCs.

Using standard peroxidase immunohistochemistry 115 patients treated for laryngeal squamous cell carcinoma were investigated for protein expression of Cyclin A1 and Mut-p53.

Positive expression of Cyclin A1 and Mut-p53 expression were noted in (83/115); (25/115) patients respectively. There were no statistically significant correlations between Cyclin A1, Mut-p53, clinicopathologic parameters, local recurrence, disease free or overall survival. Ten patients were diagnosed with new primaries during the follow up period. A statistically significant correlation was noted between Cyclin A1 expression and diagnosis of new malignancies of the aero-digestive tract $P = 0.002$.

There is growing evidence that over expression of Cyclin A1 favours entry of cells into the S phase and thus favour cell proliferation. Positive expression of Cyclin A1 may represent an irreversible wide spread genomic change that favours further cell proliferation and future malignancies. A closer surveillance of these patients maybe warranted.

HN005 ELECTIVE THYROIDECTOMY: DEVELOPMENTS IN CLINICAL PRACTICE

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Elective hemithyroidectomy is a common operation with a low complication rate. In a review of 200 cases performed at our centre, the rate of recurrent laryngeal nerve palsy was low (permanent: 1.0%, transient: 1.5%); post-operative hypocalcaemia was uncommon (persistent 1.0%; transient: 1.5%); haematoma in the immediate post-operative period occurred in 1 isolated case. 90% of patients whose operations were scheduled as day surgery cases were discharged on the day of surgery. Amongst patients who were inpatients, 75% were discharged on the first post operative day. Our initial experience suggest that it is safe and feasible to perform hemithyroidectomy as day surgery procedure in the majority of patients using defined selection criteria. Other alternatives in technique such as the lateral approach, identification of the superior laryngeal nerve and the selective use of surgical drains should be evaluated further to guide clinical practice.

HN006 IMMUNOTHERAPY FOR NPC – THE PRESENT AND THE FUTURE

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Purpose To study Epstein Barr Virus (EBV) specific cytotoxic lymphocyte (CTL) responses in patients with nasopharyngeal carcinoma (NPC) to develop the framework for immunotherapy as a treatment for NPC.

Methods NPC patients were recruited from PAH Head and Neck Clinic. Testing was performed to determine if a patient's tumour contained EBV using EBV encoded RNA staining (EBER). Optimisation of cell culture techniques was performed and subsequently T cell bulk cultures were expanded in the laboratory at QIMR from peripheral blood mononuclear cells separated from a sample of the patient's blood. The T cell bulk cultures were stimulated with irradiated lymphoblastoid cell lines coated with peptides from LMP 1 and 2 (the proteins from EBV expressed on NPC tumours) as deemed appropriate by the patients HLA type. These cell cultures were expanded for 3 to 4 weeks and assessed in vitro.

Results 27 patients have been recruited to the study through PAH. Of these 70% have EBER positive tumours. 60% of patients recruited have a HLA type making them suitable for generation of specific CTL. Optimal culture conditions including stimulation frequency and peptide and interleukin concentration have been established. Of the patients with a HLA appropriate for further study bulk cultures have been successfully generated for 93% of patients.

Conclusions The above results together with the optimisation of culture conditions support the development of immunotherapy for NPC. To this end a protocol for a phase I trial for adoptive immunotherapy for stage III and IV NPC has been developed.

HN007 REGULATORY T CELLS LOCALISE IN NASOPHARYNGEAL CARCINOMA (NPC) TUMOURS

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Objectives To analyse peripheral blood mononuclear cells (PBMCs), normal mucosa and tumour samples from nasopharyngeal carcinoma (NPC) patients with newly diagnosed disease.

Methods Meshed tissue samples and PBMCs were collected from newly diagnosed NPC patients with control samples collected from patients undergoing sinus surgery or septoplasty. These samples were compared by flow cytometric analysis staining with the monoclonal antibodies specific for CD19, CD3, CD4, CD8, CD25, and CD56. The function of the tumour-infiltrating lymphocytes was tested using latent membrane protein (LMP) 1 and 2-specific peptides to stimulate IFN γ production. Real-time PCR was employed to assess EBV DNA levels, amplifying the BALF5 gene.

Results 29 NPC patients were recruited into the study, comprising of both Caucasian and Asian ethnicities. Eleven tumours were analysed, demonstrating a mean 11-fold increase of CD4+CD25hi cells compared with circulating PBMCs and/or normal mucosa either from patients with NPC or controls.

Conclusions The increased incidence of regulatory T cells at the NPC tumour site may contribute to down regulation of function of LMP-specific CTL. This may partly explain the weak immunological response at tumour sites and potentially has implications for adoptive immunotherapy for the treatment of NPC.

HN008P PROLONGED HOSPITALIZATION FOLLOWING TONSILLECTOMY IN HEALTHY CHILDREN

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Objective To determine the incidence and factors that influence prolonged hospitalization in healthy children following tonsillectomy.

Method A retrospective analysis was performed of all the children who underwent tonsillectomy with or without other otolaryngological procedures in a tertiary care centre. Analyses were carried out on otherwise healthy children who were unexpectedly hospitalized for 2 nights or more to identify factors that influenced their length of stay as well as readmission to hospital.

Results Out of a total of 1229 children who underwent tonsillectomy within the study period, there were 1130 children who were otherwise healthy. Within this group a total of 73 (6.5%) children were unexpectedly hospitalized for 2 nights or more. There were 45 (62%) males and 28 (38%) females with a mean age of 5.3 years and mean length of stay of 2.7 days. The most common reasons for prolonged hospitalization were poor oral intake and fever. Nine children (12%) in the unexpected group required readmission with delayed hemorrhage being the primary cause. While gender was not a risk factor, the unexpected group was younger compared to those discharged within 24 hours (5.3 years versus 6.2 years, P -value of 0.046).

Conclusion A significant proportion of otherwise healthy children require prolonged hospitalization following overnight-stay tonsillectomy. It is unclear whether planned discharge on day of surgery would be beneficial in lowering this rate.