was to evaluate the usefulness of FNAC and IFSE in patients with NSTN undergoing surgery.

Patients and Methods: We retrospectively analyzed a series of 606 patients with a SNTN who underwent both preoperative FNAC and IFSE prior to partial or total thyroidectomy. There were 118 (19.5%) men and 488 (80.5%) women, with an overall median age of 44 years (range 16-81 years). Final pathologic examination showed 500 (82.5%) benign nodules, including 239 (39.4%) follicular adenomas, and 106 (17.5%) thyroid carcinomas, of which 80 (75.5%) papillary, 18 (17.0%) follicular, 5 (4.7%) undifferentiated, and 3 (2.8%) medullary carcinomas. Patients with benign tumors were significantly ($p<0.05$) younger

Results: In the preoperative differential diagnosis between hyperplastic thyroid nodules and thyroid tumors, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of FNAC was 93.6%, 98.9%, 92.1%, 99.4%, and 95.9%, respectively. In the detection of malignancy sensitivity, specificity, PPV, NPV, and accuracy were 94.3%, 99.8%, 98.8%, 99.0%, and 98.8% for FNAC, and 95.3%, 100%, 99.0%, 100%, and 99.2% for IFSE (p=NS, chi-squared test). The combination of FNAC and IFSE did not improve significantly (p=NS) the results. In fact, IFSE suggested a thyroid cancer in only one of the 6 patients with false negative FNAC, and failed to detect malignancy in 5 of 18 (27.8%) follicular carcinomas.

Conclusions: In patients with NSTN and an adequate FNAC suggesting malignancy IFSE may be unnecessary, and in those with follicular tumors the results of both FNAC and IFSE should not affect the final intraoperative decision-making.

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Results of Interferon alpha 2b (Introna) treatment in 22 patients with metastatic progressive differentiated endocrine tumors

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Digestive endocrine tumors (ET) are uncommon tumors; treatment of metastatic disease is not well established. Oberg and Collegues first described the potential role of Interferon alpha 2-b in the treatment of non curable progressive disease. We report here the results in 22 consecutive patients (pts) with progressive histologically proven ET treated with interferon alpha 2b (Introna): 14 men - 8 women, median age 57,8 years (40 - 75). Eleven were enterochromaffin ET (1 bronchial, 1 rectal, 8 ileal); 8/11 patients had carcinoid syndrom and 11 high serotonin levels. Eleven were pancreatic ET, 5/11 with clinical functional syndrome and high hormonal blood levels (1 vipoma, 1 glucagonoma, 1 insulinoma, 2 gastrinomas). All had documented progressive disease in the past six months before Interferon treatment. They all had been pretreated: surgery (20) including liver transplantation (2), octreotide (13), chemotherapy (10) and hepatic chemoembolisation (7). The median time beetween first diagnosis and interferon treatment was 3.9 years (1 month - 17.4 years). Interferon was given subcutaneouly three times a week first at 1.5 MU per injection and escalated to 5 MU until progression.

Results: Median follow -up was 23 months (6 - 80). Among 12 patients with secretory syndromes, 10 (83%) had objective responses (OR): 3 complete (CR) and 7 partial (PR), including 7/8 carcinoid syndromes (2 CR) and 3 pancreatic ET (1 CR). Hormonal responses were evaluated in 13 patients, with 8 OR (3 CR). Effects on tumeur burden could be assessed in 20 patients. These were 2 OR (9%), 11 stable disease (SD, 50%), 7 progressive disease (PD, 41%), with similar profiles in enterochromaffin and pancreatic ETs. Eleven patients are still on treatment. As regards toxicity, 2 patients discontinued Interferon at 2 and 6 weeks, respectively. Other effects included neutropenia, anemia, elevated transaminases, dysthyroidism, sexual dysfunction and flux-like syndrome, each in 4 patients at most.

Conclusion: were observed 59% stabilisation with 9% OR in patients with progressive endocrine tumors after previous therapy. Tolerance was fair. Interferon in useful in a substantial proportion of patients with ETs, and should be prospectively evaluated against other treatment modalities.

Tumour biology/Human genetics

400 POSTER

Isolation of human leukocyte antigen (HLA)-associated peptide(s) in the absence of HLA-restricted specific cytolytic T lymphocytes (CTL)

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The human leukocyte antigens (HLA) class I and class II are critical molecules for T cell recognition of endogenous and exogenous non-self antigens and hence are the major players in immune surveillance. As bladder cancer is one of the most immune sensitive tumours, based on their response to BCG, a unique combination of an in-housed established bladder tumour cell lines Fen (the original class I negative and class I positive Fen cells after the restoration of the missing class I antigen by β2-m gene transfection) were used for detail biochemical analysis of the nature of the corrected class I antigens and the associated peptides using various approaches. These included: immuno-precipitation, dot blot, immunocytochemical staining, SDS PAGE and high performance liquid chromatography (HPLC).

The results showed that.

(1) Trasfection of Fen cell line with normal β2-m gene resulted in restoration of missing class I antigens as assessed by HPLC and dot blot assay.
(2) Both interferon alpha (IFNα and IFNγ stimulation of cells led to an up-regulation of class I antigens, more so in the case of IFNγ.
(3) The intact class I antigens could be isolated from lysate of the β2-m gene transfected cells using sepharose CNBr-W6/32 beads and DEA as a dissociation reagent.
(4) Dissociation of class I antigens from heads by DEA and analysis by the SDS PAGE showed the presence of both free heavy and light chains of class I antigens.
(5) More than 20 class I-associated peptides with molecular weight of 700 to 3000 Daltons could be isolated from W6/32-loaded beads but only from lysate of HLA positive Fen cell line. The data also showed that 1×10^6 of positive Fen cells contained about 200 ug total protein of which about 0.10ug was class I of which about 2 ng was class I-associated peptides.

These findings demonstrated that gene transfection approach could be used to restore missing class I antigens on otherwise a class I negative bladder tumour cell line. The results also showed the feasibility of using various immuno-biochemical techniques to isolated HLA-associated peptides form lysate of a class I positive tumour cell line in the absence of specific cytolytic T lymphocyte (CTL). These approaches may provide a realistic possibility for extraction and identification of putative tumour specific peptide(s) from tumour specimens with the aim to use such peptide(s) for immunotherapy in cancer patients.

401 POSTER

Profile of p53 expressions in human tissue biopsies of bladder and head and neck tumours: Effects of various in vitro manipulations of p53 on tumour cell behaviour in vitro

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In this investigation the profile of p53 expression in tumour tissue biopsies from bladder and from oro-phamgeal tumours was investigated using immunocytochemical staining method. In addition, various techniques including SDS page gel electrophoresis, colorimetric assay and gene transfection were used to investigate the influence of p53 on the behaviour of established human tumour cell lines in vitro. The results showed that:

(a) positive p53 expression was present in more than 40% of cases from both regions, although their profile of the expression differed.

(b) both gamma radiation and cisplatin treatment of tumour cell lines showed induction of p53.

(c) the susceptibility of two cell lines, one with constitutive expression of p53 and one with no p53 expression, showed that the expressing cells were more sensitive to the gamma radiation.

(d) the insertion of wild type and therefore non-mutated p53 into a bladder tumour cell line showed that the inserted cells apoptosed very rapidly whereas the cells inserted with the mutated p53 survived.

If these data could be translated to an in vivo setting, it would be possible that the introduction of wild type p53 gene by gene transfection into tumour cells independent of their p53 gene mutational status, would prove to be beneficial in that if the cellular p53 gene is mutated, the introduction of the