

significantly associated with shorter recurrence-free survival in non muscle-invasive urothelial cell cancers. Claudin-10 protein was not detected in the samples and only scattered expression of claudin-3 and -5 proteins was found in a few tumour cases.

Conclusions: Claudins and Ki-67 might be used as potential markers to differentiate low grade and high grade urothelial cell cancers, thereby they might enhance the accuracy of pathological diagnosis and might add further information to clinical outcome.

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POSTER

Expression of Claudins and Their Prognostic Significance in Non-invasive Urothelial Neoplasms of the Human Urinary Bladder

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Background: The members of claudin family are major integral transmembrane protein constituents of tight junctions. Normal and neoplastic tissues can be characterized by unique qualitative and quantitative distribution of claudin subtypes which may be related to clinicopathological features. Differential diagnosis and prognosis of non-muscle invasive tumour entities of urinary bladder epithelium are often challenging.

Objective: To investigate expression profile of claudins in inverted urothelial papillomas (IUP), urothelial papillomas (UP), papillary urothelial neoplasms of low malignant potential (PUNLMP) and intraepithelial (Ta), low grade urothelial cell carcinomas (LG-UCC) in order to reveal potential prognostic and differential diagnostic values of certain claudins.

Patients and Methods: Claudin-1, -2, -4 and -7 protein expressions detected by immunohistochemistry and clinical data were analyzed in 15 IUPs, 20 UPs, 20 PUNLMPs and 20 LG-UCCs.

Results: UPs, PUNLMPs and LG-UCCs showed significantly decreased claudin-1 expression in comparison to IUPs. LG-UCCs expressing claudin-4 over median were associated with significantly shorter recurrence-free survival. PUNLMPs expressing claudin-1 over the median revealed significantly longer recurrence-free survival.

Conclusion: High claudin-1 protein expression might help to differentiate IUP from UPs, PUNLMPs and LG-UCCs. High claudin-4 expression may determine unfavorable clinical course of LG-UCCs, while high claudin-1 expression in PUNLMP was associated with markedly better clinical outcome.

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POSTER

NAT1 as a Genetic Predisposing Factor for Urinary Bladder Cancer in Lebanese

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Background: Urinary bladder cancer is the fifth most common cancer in Europe and ranks five in the United States. Historically, the majority of studies investigating bladder cancer focused on oncogenes, tumour suppressor genes, and subsequent cellular events. In the last few years, the role of drug-metabolizing enzymes in bladder cancer has come into focus. Genetic variants of metabolic enzymes are thought to result in critical changes in the metabolism of environmental carcinogens, subsequently altering individual bladder cancer risk. Arylamines, the main carcinogens implicated in bladder cancer, are metabolized by N-Acetyl-Transferases 1 & 2 (NAT1 & NAT2) isoenzymes. The reported NAT1 polymorphism suggests that the NAT1 acetylase genotype may be associated with bladder cancer susceptibility. In Lebanon, the rising incidence of urinary bladder cancer in the past few years is alarming. According to the latest National Cancer Registry report, bladder cancer is currently the second most common malignancy in males (15.1%), almost equal to lung cancer (15.2%). The purpose of this study is to investigate a possible association between NAT1 genotype and bladder cancer risk in a group of Lebanese males.

Materials and Methods: 54 cases and 105 hospital controls were randomly selected for the study from two major medical centers in the city of Beirut. Polymerase Chain Reaction-Restriction-Fragment-Length-Polymorphism (PCR-RFLP) was performed on peripheral blood DNA samples to determine NAT1 genotypes, and an interview-based questionnaire was completed to assess suspected risk factors. The association between bladder cancer and putative risk factors was measured using adjusted odds ratios (ORs) and their 95% confidence intervals (CIs) were derived using a logistic regression analysis. Finally, a gene-environment interaction analysis was applied.

Results: A statistically significant 7 fold increased bladder cancer risk (OR= 7.86, 95% CI: 1.53- 40.39) was observed for individuals carrying at

least one NAT1*14A allele. An interaction resulted between occupational exposure to fossil fuel emissions and alleles NAT1*14A and NAT1*10.

Conclusions: Our study provides strong evidence that NAT1*14A allele is a genetic predisposing factor for bladder cancer in Lebanese, and suggests a potential gene-environment interaction. Larger studies are needed to confirm these findings to further investigate the role of NAT1 genotype in bladder cancer etiology.

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POSTER

Recurrent Testicular Cancer in a Family With MYH-associated Polyposis

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Background: MYH-associated polyposis (MAP) is an autosomal recessive inherited syndrome with similar phenotype to attenuated familial adenomatous polyposis. Biallelic germline mutations in MYH predispose individuals to multiple adenoma or polyposis coli. Extraintestinal findings are also noted on occasion; breast, gastric, thyroid and haematological neoplasias as well as sebaceous adenomas and hypertrophy of the retinal pigment epithelium have been described. We report on a family with genetic diagnosis of MAP showing a -previously unreported- recurrent extraintestinal cancer.

Material and Methods: Clinical, pathological and genetic characterization of a family with suspected hereditary colorectal cancer. Lynch syndrome screening analysis was performed by tumour tissue analysis of microsatellite instability (MSI) and immunohistochemical expression (IHC) of MLH1, MSH2, MSH6 and PMS2 proteins. Germline mutation analysis of the MYH gene was performed by sequencing of the entire coding region and the intron-exon boundaries. Co-segregation analysis of the genetic findings in the family was also approached.

Results: The index subject was diagnosed of rectal cancer and multiple adenomatous polyps (n=8) in right colon at age of 44 yrs. Twelve years before was also diagnosed of testicular embryonal carcinoma. Familial history of cancer revealed a brother diagnosed of testicular embryonal carcinoma at age of 28 yrs and a total of 16 adenomatous polyps at age of 44 yrs. Their father has been diagnosed of few polyps at age of 79 yrs. At least, two different syndromes might be suspected: Lynch syndrome and MAP. The rectal cancer showed normal expression of the proteins analyzed by IHC, and not MSI was detected. Consequently, Lynch syndrome genetic analysis was disregarded. Therefore, MYH gene was tested to confirm the alternative suspicion of MAP and founding two heterozygous variants: [c.317G > A]+[c.1227_1228dup]. Both brothers showed the same genotype, and the genetic analysis of their parents demonstrated that those variants were located *in trans*.

Conclusions: Testicular cancer might be a new extraintestinal manifestation of MAP syndrome. Further analysis to establish the causal relation between MYH genetic variants and testicular cancer is underway. A better knowledge of the clinical phenotype of individuals with MAP will make possible the identification and the proper management of mutation carriers in the population at risk.

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POSTER

Bladder Preservation a Valid Option for Patients With Muscle Invasive Bladder Cancer – Single Centre Experience

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Introduction: Cystectomy is considered the standard of care for patients with muscle invasive bladder cancer, despite the fact that no randomized studies between cystectomy and radiotherapy or chemoradiotherapy exist (to show superiority of cystectomy). Patients however are often either not fit for cystectomy or do not wish to undergo cystectomy, and hence enter bladder preservation protocols. Here we report our experience in Cyprus with our bladder preservation protocol with all patients treated in the last 10 years.

Methods: 38 consecutive patients with muscle invasive transitional cell cancer were treated with bladder preservation in the last 10 years. Neoadjuvant chemotherapy with 3 cycles of Gemcitabine and Cisplatin, was offered to 20 patients with adequate renal function and performance status. After completion of chemotherapy, there was reassessment with cystoscopy