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Abstracts

OFP-13-011

Multi-stage pathological and immunohistochemical characterisation of N-butyl-N-(4-hydroxybutyl)-nitrosamine-induced murine bladder cancer

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Background & Objective: N-butyl-N-(4-hydroxybutyl)-nitrosamine (BBN)-induced bladder tumours in mice represent an attractive model of muscle-invasive bladder cancer (MIBC), which mimicks the basal-like transcriptomic subgroup. Lineage tracing studies in mice suggested that MIBC, including basal tumours, arise from carcinoma in situ (CIS) lesions. However, in routine pathology practice, the majority of human CIS express a luminal immunohistochemical (IHC) phenotype CK20+. In this context, we sought to characterize early stage lesions occurring in BBN-exposed mice, using IHC markers of basal and luminal subtypes
Method: To study multiple stages of tumour progression, 35 mice bladders were obtained at different time points following oral BBN exposure of a maximum of 14 weeks. Morphological and IHC analysis of basal (CK5, CK6, CK14), luminal (CK20, GATA3, FOXA1) and proliferation (Ki67) markers were performed.
Results: Morphological analysis identified a spectrum of lesions during BBN exposure, including isolated early lesions -hyperplasia (n=1), dysplasia (n=3) or CIS (n=4)- pTa (n=13), pT1 tumours (n=10) and MIBCs (pT2 and pT3, n= 6). Squamous differentiation was observed in 79% of pTa-pT3 tumours. A basal IHC pattern was identified in 2 of 3 dysplasia lesions and in all CIS lesions, which were associated with high proliferation (Ki67≥20%). pTa to pT3 cases displayed a basal-like phenotype in 86% of cases.
Conclusion: Our study shows that BBN-induced bladder tumours at both CIS and invasive stages are of basal-like IHC phenotype, suggesting that BBN-treated mice may represent a model of basal CIS. Further genomic and transcriptomic analyses of stage-specific lesions following laser-capture microdissection are ongoing.

OFP-13-012

Osteonectin overexpression in the case of prostate cancer with intraluminal inclusions

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Background & Objective: Osteonectin (OSN) is secreted by osteoblasts during bone formation, initiating mineralization and promoting mineral crystal formation at sites of ectopic calcification. Also OSN was found in many types of human malignant tumours. The aim is to study the OSN expression in patients with prostate cancer (PC) and the presence of intraluminal inclusions (prostatolithes and amyloid cells).
Method: OSN expression was investigated in tumours and in the adjacent prostatic tissue of 30 PCs with intraluminal inclusions and 30 PCs without them by immunohistochemistry. In each group 15 samples refer to moderately differentiated G2 and low-differentiated G3 tumours. Samples were fixed, embedded in paraffin, and analized for OSN accumulation using the anti-OSN antibody, followed by DAB detection substrate and counterstained with Mayer's haematoxylin.
Results: OSN expression was increased in PC tissues with pathological inclusions in comparison to those without them ($p<0.001$, Student test). Osteonectin was mostly localized in tumour cells cytoplasm, its expression was not observed in tumour microangiourea cells and in stroma. It was found that the OSN expression by tumour cells reduced during reduction of the malignant tumour differentiation (comparison of subgroups G2 and G3) ($p<0.001$ and $p<0.01$ respectively for groups I and II).
Conclusion: OSN overexpression in tumours and in the adjacent prostatic tissue of PCs with intraluminal inclusions may be regarded as a prospective role for the osteosteogenic phenotype development of tumour cells and for the bone metastasis promotion.

Tuesday, 11 September 2018, 17:15 - 19:15, Room B1
OFP-14 | Joint Session: Endocrine Pathology / Head and Neck Pathology

OFP-14-001

Differentiated thyroid carcinoma of the paediatric age: genetic and clinical scenario

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Background & Objective: Follicular-derived differentiated thyroid carcinoma is the most common endocrine malignancy in children. The different clinical and pathological features between paediatric and adult thyroid carcinomas could be related to a different genetic profile. However, few studies are currently available and most of them involved a limited number of patients and mostly focused on radiation-exposed population. A greater knowledge of the genetics might improve the diagnostic frame and lead to an individualized therapy.
Method: We studied 57 paediatric patients who underwent surgery for diagnosis of differentiated thyroid carcinoma between 2000 and 2017. The presence of mutations in BRAF, NRAS, PTEN, PIK3CA genes, and in TERT promoter, were analyzed through sequencing. RET/PTC rearrangement has been investigated with Fluorescent in situ hybridization. Clinical-molecular features of paediatric patients were compared with those of 165 adult patients.
Results: In paediatric age, male gender and subjects < 15 years have a more extensive disease and more frequent lymph nodes and distant metastasis. Compared to adults, in paediatric patients there is a more frequency of lymph nodes and distant metastasis ($p=0,01$); moreover, paediatric patients are more prone to have a second treatment ($p<0,01$). The frequency of BRAFV600E mutation is lower in paediatric DTCs ($p<0,01$). NRASQ61R, NRASQ61K and TERTC250T are rare in children and adolescents; no mutations were found in PTEN and in PIK3CA.
Conclusion: Paediatric differentiated-thyroid cancer has a greater aggressiveness at diagnosis and a greater risk of recurrence than adult's one. Differently from adult, point mutations have not a genetic key role.

OFP-14-002

Specific molecular mechanisms of tumour progression from well differentiated to poorly differentiated thyroid carcinomas identified by next generation sequencing analysis

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Background & Objective: The molecular background of thyroid cancer histotypes, including poorly differentiated carcinoma, has been investigated in recent years using high throughput technologies. However, molecular studies specifically designed to explore the mechanism of tumour progression from well-to-poorly differentiated forms are still missing
Method: Fifteen cases of poorly differentiated carcinomas with associated well-differentiated papillary or follicular components have been micro-dissected to isolate and characterize at the molecular level the two tumour populations using the Oncomine Focus Assay (IonTorrent platform, ThermoFisher Scientific) covering somatic CNA and fusions in 52 cancer relevant genes
Results: Eleven cases yielded adequate DNA and RNA for next generation sequencing analysis. A high prevalence of alterations in the RAS (5/