

## Keynote Lectures

Wednesday, 1 September 2010, 11.45–12.30, Aula Duza

### KL-01 New trends in breast pathology

Chairperson: T. Tot, Sweden

#### 001

##### New trends in breast pathology

*M. van der Vijver\**

\*The Netherlands

Thursday, 2 September 2010, 11.45–12.30, Aula Duza

### KL-02 Emerging mechanisms of tumor initiation and progression: lessons from the bladder cancer model

Chairperson: H. van Krieken, The Netherlands

#### 001

##### Emerging mechanisms of tumor initiation and progression: lessons from the bladder cancer model

*B. Czerniak\**

\*The University of Texas, M D Anderson Cancer Center, Houston, USA

Bladder cancer has served as one of the most important sources of information about the events that underlie the development of human solid malignancies. Although “field effects” that alter the entire bladder mucosa appear to initiate disease, tumors develop along two distinct biological “tracks” referred to as papillary and non-papillary that present different challenges for clinical management. More recently, whole organ mapping combined with genomic platforms have identified a novel class of candidate tumor suppressors (forerunner genes) that localize near more familiar tumor suppressors but are disrupted at an earlier stage of cancer development. These studies suggested three steps for the involvement of the model tumor suppressor locus, RB1, in tumor development. In the first step, one allele of forerunner (FR) gene and RB1 is inactivated by deletions. In the second step, homozygous inactivation of the FR genes is accomplished by hypermethylation or mutations. The inactivation of FR genes is associated with the initial clonal

expansion of preneoplastic urothelial cells. In the third step, the contiguous tumor suppressor, RB1, is inactivated by a mutation, which is associated with clonal evolution into carcinoma in situ progressing to invasive cancer. Furthermore, we have discovered that aggressive muscle-invasive tumors express molecular markers characteristic of a developmental process known as “epithelial-to-mesenchymal transition.” Emerging evidence indicates that urothelial cancers contain subpopulations of tumor-initiating cells (cancer stem cells), but the phenotypes of these cells in different tumors may be heterogeneous, raising questions about whether or not the two major subtypes of cancer share a common precursor.

Friday, 3 September 2010, 11.45–12.30, Aula Duza

### KL-03 Predictive pathology: fact or fancy?

Chairperson: F. Carneiro, Portugal

#### 001

##### Predictive pathology: fact or fancy?

*F. Bosman\**

\*University Hospital Maastricht, Dept. of Pathology, The Netherlands

Pathology as a medical specialty has been around for about a century and a half, even though the interest in understanding disease, the focus of pathology as an academic discipline, has inspired physicians since the dawn of mankind. Understanding disease remains the primary focus of pathology. In the practice of diagnostic pathology, this knowledge, notably through its morphological expression, is applied to the diagnosis of disease through the examination of cells and tissues. Relatively new in this field is the notion of pathology as ‘the science behind the cure’. This phrase, coined by the Pathological Society of Great Britain and Ireland, refers to a widening of the scope of pathology: ‘Understanding disease’ continues to be applied to diagnosis and classification, but now also to conceiving of new ways to treat and of new diagnostic tools assisting the physician in choosing the appropriate treatment. Targeted therapy, the target being a molecular pathway involved in the pathogenesis of the lesion, along with biomarkers that are predictive for response to treatment, are in the forefront of pathology. Targeted drugs that require ‘companion’ diagnostics, a combination also called ‘theragnostics’, are reshaping the practice of pathology. It is this

Five years later, a new ulcer appeared. The patient neglected the tumour during a period of 10 years. The BCC progressively invaded with a buttock, the upper third of posterior left thigh and the left gluteus maximus muscle, inducing severely altered general status and anemia. We performed a wide excision (including the muscle) and we reconstructed with a fascio-cutaneous flap and skin grafts (2010).

**Conclusion:** BCC can be a cancer with a high local aggressivity if the patient or the surgeon underestimates it.

#### 0107

##### Basal cell carcinoma of the eyelids and periorbital region

*S. Dumitriu\*, C. Costea, D. Radulescu, S. Stolnicu, A. Dumitriu, C. Ungureanu, E. Morosanu, D. Butcovan*  
\*UMF Gr T Popa Iasi, Dept. of Pathology, Romania

**Objective:** Eyelids represent a special location of the basal cell carcinoma (BCC) due to the proximity of the eyeball. The aim of this study was to review the clinical and histopathologic features and outcomes of eyelid basal cell carcinomas.

**Method:** The clinical records and histopathologic specimens of 426 patients with eyelid basal cell carcinomas were reviewed and analyzed retrospectively. The main outcome measures are clinical characteristics, lesion size, histologic subtypes, severity of peritumorous inflammation, recurrence rate and prognostic features.

**Results:** The most common histologic subtypes were infiltrative, nodular, and basosquamous basal cell carcinomas. Of the patients, 31.5% were previously recurrent. Recurrent basal cell carcinomas were larger, with longer duration of lesion. Basosquamous basal cell carcinomas were more likely to have prior recurrences, larger lesion size, and the highest rate of orbital invasion. Perineural invasion was most frequent in morpheaform and basosquamous subtypes. Peritumorous inflammation differed between subtypes and was highest in the superficial subtype. The recurrence rate was 6.2%.

**Conclusion:** The outcomes were worse than previously reported due to the delay in treatment. The prognostic factors associated with secondary orbital invasion are previous recurrences, aggressive histologic subtypes, longer duration of lesion and larger lesion size.

#### 0108

##### Histological assessment of small bowel hypoperfusion lesions in the pig

*A. L. Oliveira\*, D. Ferreira, H. Vala*  
\*Agrarian Superior School, Viseu, Portugal

**Objective:** Authors propose the use of a quantitative morphological assessment for helping in studies concerning intestinal hypoperfusion. The method was applied to small intestine mucosa stained with standard hematoxylin and eosin in pigs that underwent severe hypotension due to acute hemorrhage.

**Method:** Six large white pigs underwent total intravenous anesthesia with propofol and remifentanyl. Arterial blood (25 ml/kg) was passively removed from the femoral artery over 20 min. Volume was replaced using Ringer lactate in group 1 and hydroxyethyl starch 130/0.4 in group 2, with a delay of 20 min after bleeding. One hour after the volume replacement, pigs were euthanized and small intestine samples were taken for histopathological examination. Parameters were classified using two specific scales (Chiu 1970; Çetin 1995; Kaplan 2007). Mucosal loss (ML) percentage and crypt/interstitium ratio were obtained (Faleiros 2001).

**Results:** Inflammatory infiltrate was present in all animals, varying from grade 2 to grade 3. Hydropic cellular degeneration and epithelial detachment were more pronounced in duodenum and more noticeable in group 1. In group 1, ML percentage was  $2.18 \pm 0.46\%$  in duodenum,  $0.62 \pm 1.07\%$  in jejunum and  $0.45 \pm 0.77\%$  in ileum. In group 2, ML percentage was  $0.75 \pm 1.30$  in duodenum and  $0 \pm 0\%$  in the other intestinal segments. In the whole small intestine was  $1.08 \pm 0.78\%$  in group 1 and  $0.25 \pm 0.35\%$  in group 2. Crypt/interstitium ratio did not present significant differences between the groups.

**Conclusion:** Quantitative morphological assessment may be useful in quantifying the degree of mucosal lost in small intestine stained with hematoxylin and eosin from pigs submitted to acute severe bleeding.

#### 0110

##### Vasculitides associated with malignancies

*M. Otani\*, H. Hayashi, A. Nakazawa, M. Yoshida, S. Yoshida, H. Serizawa*

\*Tokyo Medical University, Dept. of Pathology, Hachioji, Japan

**Objective:** Vasculitis shows various kinds of physical symptoms. ANCA-related vasculitis and autoimmune disease are famous for its cause. Malignancies are also related to vasculitides. In this paper, we present two rare malignancies causing vasculitides.

**Method:** Case1: The patient was a 78-year-old male who had vasculitis syndrome. Computed tomography revealed aortic thrombus and narrowing of the renal arteries, suggesting polyarteritis nodosa. Case2: An 86-year-old male was diagnosed as malignant lymphoma. Acute renal failure with gross hematuria developed. MPO-ANCA was positive.

**Results:** Case1: The tumor in the thoracic aorta was found at autopsy. Histologically, the tumor consisted of isolated atypical cells, suggesting sarcoma. Immunohistochemically, tumor cells were positive for CD31. The same atypical cells were seen in the intrarenal arteries as emboli accompanied with vasculitides. Case2: Autopsy revealed lymphoplasmacytic lymphoma (LPL) involving kidneys. And more, amyloid deposition in the lungs and MPO-ANCA-associated crescentic glomerulonephritis, i.e. MPA, were noted.

**Conclusion:** Aortic angiosarcoma is an extremely rare lesion, and it is known that the tumor often causes distal emboli and presents vasculitis syndrome. The second case was diagnosed as LPL, MPA and amyloidosis. MPA is known to occur in some patients with malignancy. It has been reported that some malignancies produce vasculitides-inducing factors. In our cases, such factors produced by malignant cells might induce vasculitides.

### 0113

#### Monoclonal antibodies in the diagnostic of spinal metastases

G. Kropczyński\*

\*Zabrze, Poland

The skeletal system is the third most frequent seat of metastases, and metastatic tumours are the most common bone malignancies. The diagnostic workup of spinal metastases begins with the identification of the primary neoplastic site. The aim of the study was to determine the utility of monoclonal antibodies in the diagnostic workup of spinal metastases.

**Materials and methods:** This is a retrospective analysis of 203 patients whose histopathologic examination confirmed the presence of neoplastic foci in the spine. Samples of metastatic tumours of 57 patients whose primary tumour sites had not been identified were subjected to an immunohistochemical analysis based on monoclonal antibodies and assays for antigens associated with tumours most often producing bony metastases.

**Results:** The monoclonal antibodies and assays were shown to be useful aids for the identification of the histology and location of the primary tumour in patients in whom routine histological assessments had failed to determine the histological type of tumour.

**Conclusions:** The length of survival of patients with malignant spinal metastases is influenced by the type of neoplasm and locally radical surgery combined with palliative radiation therapy. In many cases, effective immunohistochemical workup can contribute to halting the progression of the tumour by enabling qualification for appropriate surgical and oncological treatment.

### 0114

#### Origine and frequency of pulmonary bone fragment embolism: an autopsy study

N. Willi\*, T. Thiesler, P. Ochsner, G. Cathomas

\*Kantonsspital Liestal, Institute of Pathology, Switzerland

**Objective:** Pulmonary bone fragment embolism (PBFE) is a rare event observed at autopsy. Pulmonary bone marrow embolism (BME) is more common, but both types of embolisms are considered to have little clinical relevance. The aim of this study was to analyze the frequency of PBFE and BME and correlate these events with clinical findings.

**Method:** In an autopsy cohort, the frequency of embolic particles of PBME and BME was evaluated by reanalyzing all pulmonary H&E- and Elastin-stained (EvG) sections.

**Results:** In a total of 1,002 autopsies, 5 (0.5%) PBFE and 29 (2.9%) BMEs were detected. Compared to BME, PBFE were significantly more common in patients with osteomyelitis [2 of 8 (25%) versus 0 of 29,  $p < 0.05$ ]. In contrast, BME was more common in patients with costal fractures (16 of 29 versus 1 of 8,  $p < 0.05$ ), but no patient showed both types of embolism. In addition, PBFE and BME were observed in patients with bone metastasis and orthopaedic devices. The highest density (30.5 particles per square centimeter) was observed in a patient who died immediately following femoral medullary nailing, presenting with the clinical picture of pulmonary thromboembolism.

**Conclusion:** In the autopsy cohort analyzed, an incidence of 5‰ for PBFE was considerably higher as previously reported and PBFE showed a strong correlation with osteomyelitis, and the application of orthopaedic devices and extensive PBFE may lead to death. BME are correlated with rib fracture, but no association between PBFE and BME was observed, suggesting a different pathogenetic mechanism.

### 0115

#### Local flaps used for post-tumoral facial defects

C. Tamas\*, S. Shaukat, L. Popa, C. Stanescu,

S. Stolnicu, D. Radulescu

\*University of Medicine, Dept. of Plastic Surgery, Iasi, Romania

**Objective:** The reconstruction of facial soft tissue defects can be difficult because we should regain the shape and the function of the region. The facial esthetic units should be respected too, and we cannot neglect the oncological limits of excision.

**Method:** We are reporting 63 patients with facial tumors operated in the last 5 years (2005–2010), 71.4% (45) aged over 50 years and 66.7% (42) males. They needed excision