General Pathology

Histogenetic Classification of Neoplasms

Epithelial Neoplasms

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Epithelial Neoplasms – table of contents

- Terminology
- Behaviour
- Macroscopy
- Histopathology
  - architecture
  - cytology
- Symptoms & diagnosis
- Complications

Pathological diagnosis of epithelial neoplasms

- typing
  - grading
  - staging
  - prediction
  - prognostication
  - central registers
NEOPLASIA – classification

HISTOGENETIC
- mesenchymal
- epithelial
- neuroectodermal
- mixed,
- germ cell (& teratoma, choriocarcinoma)
- mesothelioma
Epithelial Tumours

- surface epithelium
  - papillomas
  - carcinomas / papillocarcinomas
- glandular epithelium
  - adenomas
  - adenocarcinomas
- double diff.
  - neuroendocrine
  - mucoepidermoid....
Surface Epithelium

- squamous
- transitional urothelium

papillomas

carcinomas / papillocarcinomas
NEOPLASIA – classification

BEHAVIORAL

- benign
- borderline
- malignant

histological vs. clinical behaviour
Borderline mucinous neoplasm of the ovary
NEOPLASIA – growth

benign

borderline - locally

destructive

malignant

METASTASES
Carcinoma – infiltrative growth
Metastases carcinomatosae
Inn. axillarium
ca mammae
M 8500/6
Metastases multiplices hepatis – ca pancreatis

M 8500/6
Carcinosis meningum et metastases cerebri - adenocarcinoma pulmonis
M 8140/6
Embolia carcinomatosa pulmonum
Pleuritis carcinomatosa
Lymph nodes in carcinoma

pN0
pN0 (i+) isolated cells or groups < 0,2 mm
pN1(mi) – micrometastases < 2 mm
pN1, pN2, pN3 – macrometastases > 2 mm
NEOPLASIA – macroscopy

- mass
- ulceration
- both
Ca basocellulare
Ca basocellulare

M 8090/3
Ulcus rodens
Ca spinocellulare (in cicatrice post lupum vulgarem)
Ca spinocellulare
Ca spinocellulare
Cornu cutaneum
Chondrodermatitis nodularis chronic hellicis

Ca spinocellulare
Ca spinocellulare
Ca vesicae urinariae pT3
NEOPLASIA – histological architecture

solid
glandular
papillary
cystopapillary
dissociated
Carcinoma urotheliale
Carcinoma urotheliale
NEOPLASIA – cytology

Benign

similar to nonneoplastic

Malignant

cellular pleomorphism

NUCLEAR FEATURES:

hyperchromasia

(polyploidy, aneuploidy)

rough chromatine structure

irregular nuclear outline

large and/or multiple nucleoli

or undifferentiated monotonous cellularity
Ca spinocellulare  M 8071/6
Normal urothelium
LG IUN – mild dysplasia
Papilloma

M 8120/0
Tumor Diagnostics

TYPING = diagnosis of the tumor as a nosology unit with a unique ICD-O code

(all tumours)
Papilloma ureteris invertum

ICD-O M 8120/0
Malignant Tumor

TYPING        ICD-O
and
GRADING       G1 - G4
STAGING       pT pN pM

Tumor - Noduli - Metastases
Metastasis carcinomatis spinocellularis medullae osseae

ICD-O
M 8071/6
Malignant Tumor

GRADING  G1 - G4  based on histopathology and cytopathology differentiation and mitotic activity – estimate of tumor aggressiveness or level of malignancy. (Grade of the tumor tends frequently to increase with recurrences.)

STAGING  pT  pN  pM  estimate of level of tumor advancement at the time of diagnosis. (After the therapy re-staging is performed.)
Papillary Urothelial Neoplasia of Low Malignant Potential (PUNLMP)
Papillary urothelial carcinoma
low grade
G2
Papillary urothelial carcinoma – M8130/23
high grade  HG
Papillary urothelial carcinoma – M8120/3  high grade  HG, pT1a
Carcinoma urotheliale

pT1a

lamina propria mucosae

lymphangiopathia carcinomatosa

muscularis mucosae

Ca urotheliale
Carcinoma urotheliale

pT1b

muscularis propria

lymphocytis

ca urotheliale

lamina propria mucosae
Carcinoma urotheliale

Papillary ca
high grade
G3

M8120/3
Precanceroses

- often in the vicinity of the neoplasm
- bearing the same mutations
- precursors of recurrences
- concept of Intraepithelial Neoplasia (CIN, VAIN, VIN, PIN, PAIN, IUN,...)
von Brunn’s nests
HG IUN – moderate dysplasia
Epithelial Tumours

- surface epithelium
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  - carcinomas / papillocarcinomas

- glandular epithelium
  - adenomas
  - adenocarcinomas

- double diff.
  - neuroendocrine
  - mucoepidermoid....
Adenoma villosum appendicis vermiformis
Adenoma villosum appendicis vermiformis

M 8263/0

LG dysplasia
Adenocarcinoma apicis vesicae urinariae
Adeno carcinoma

apicis vesicae urinariae
Microcystic carcinoma

M 8140/3
Adenomata polyposa et adenocarcinoma int. crassi
Polyposis intestini
Molecular Diagnostics of Neoplasms

- **confirmation** - e.g. Burkitt lymphoma \( t(14:18) \)
- **prognosis** – e.g. Her2/NEU breast cancer
- **hereditary predisposition** BRCA 1
- **therapy decision & targets**: EGFR, ALK mutations in pulmonary carcinoma
Carcinoma urotheliale

Probe:

p16 (INK4A, 9p21)

Homozygous and hemizygous deletions of 9p21 are the earliest and most common genetic alteration in bladder cancer. The p16 gene has been identified as tumor suppressor gene in this region which is commonly deleted in bladder cancer.
Adenoma polyposum tubulovilloseum recti

EGFR, Her-1 (7p11) / SE7
Epidermal growth factor receptor (EGFR) - a cell membrane protein, providing signal transduction and cell growth - a strong prognostic indicator
Increased EGFR expression associated with reduced recurrence-free or overall survival.

M 8263/0
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Adenoma hypophysis suprasellare
Adenoma hypophysis plurihormonale
Neuroendocrine tumours

- well differentiated NET (carcinoid)
- medium differentiated NEC (atypical carcinoid)
- poorly differentiated NEC
  - SCC
  - LCNEC

1. **NeuroEndocrine Tumour NET**
   1. NET G1 (carcinoid) - M8240/3
      1. if hormonally active – insulinoma, gastrinoma, glucagonoma, somatostatinoma, VIPoma… /Mitoses <2/10HPF, Ki67 <2%/  
   2. NET G2 - formerly well diff. neuroendocrine carcinoma - M 8249/3  
      /Mitoses >2/10HPF, Ki67 >20%/  

2. **NeuroEndocrine Carcinoma NEC**
   1. large cell NEC - M8013/3  
   2. small cell NEC - M8041/3  

3. **Mixed AdenoNeuroEndocrine Carcinoma MANEC** M8244/3  

Exceptions: Tubular appendical carcinoid M8245/1; L-cell NET PP/PYY M8152/1
Carcinogens

- chemical
- physical - radiation
- biological
  - infectious – oncogenic bacteria & viruses
  - hormonal
„Just go on smoking... it doesn't matter any more...“
Ca bronchogènes

Hyalinosis et métastases carcinomatosae pleurae parietalis
Epithelial neoplasms
– symptoms & complications

**BENIGN**
- no symptoms - „incidentalomas“ … dif. dg. task
- mass - pressure, blockade – content/secretion retention – infection
- ulceration - bleeding OCCULT/massive – anaemia
- hormonal activity – rare, but more frequent than in malignancies, sometimes life endangering

**MALIGNANT**
- no symptoms (!!) - may remain silent for a long time…..
- mass - pressure, blockade – content/secretion retention – infection
- ulceration - bleeding occult/massive – anaemia
- cachexia (TNF, cachectin…) 
- hormonal activity - rare
- METASTASES - GENERALISATION
Clear cell kidney carcinoma

10 mm
Papillo carcinoma ureteris obstruction…
Ca urotheliale ureteris
Ca pylori

Pyloric rigidity - partial ileus
...ulceration, bleeding, anaemia, weight loss.....
...ulceration, bleeding, anaemia, weight loss......pain

Ca coli
Carcinoma - Diagnosis

- PUBLIC EDUCATION
- clinical investigation, imaging, lab. tests
- screening
- cytopathology
- histopathology
- molecular methods
late diagnosis...

Mammography screening available...

needle biopsy

histopathology

EARLY diagnosis & treatment
EGFR signal transduction and its blockade by ERBITUX
Central register of mammary carcinoma patients
Ca papillare gl. thyreoideae - early diagnosis

FNAB & cytoblock M 8260/3
Epithelial Tumours (introduction) - summary

- surface epithelium
  - papillomas
  - carcinomas / papillocarcinomas

- glandular epithelium
  - adenomas
  - adenocarcinomas

- double diff.
  - neuroendocrine, mucoepidermoid....

- most frequent neoplasms
- some clinically silent or challenge for differential diagnosis
- nationwide screening programs (cervix, breast, colon in the Czech Republic)
- early diagnosis – early treatment – improving prognosis