General Pathology

Histogenetic Classification of Neoplasms

Neuroectodermal, Mixed, Germ Cell Neoplasms, and Mesothelioma

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Neuroectodermal, Mixed, Germ Cell Neoplasms, and Mesothelioma – table of contents

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- Pathological diagnosis of these neoplasms
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    - staging
    - prediction
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NEOPLASIA – classification

HISTOGENETIC

- mesenchymal
- epithelial
- neuroectodermal
- mixed
- germ cell (teratoma, choriocarcinoma)
- mesothelioma
Neuroectodermal Tumours - derived from:

- ganglion cells: gangliocytoma, neuroblastoma
- glial & Schwann cells: gliomas, neurilemmoma, glioblastoma, neurog. sarcoma, ganglioglioma, ganglioneuroma
- melanocytes: pigmented nevi, melanoma

CNS & PNS located
WHO – CNS - 2007

134 nosology units

no more new....
Gliomas

astrocytic – diffuse astrocytoma G2, anaplastic a. G3, glioblastoma G4

oligodendroglial – oligodendroglial G2, anaplastic o. G3

oligoastrocytic - oligoastrocytoma G2, anaplastic o. G3

ependymal – myxopapillary G1, subependymoma G1, anaplastic e. G3

tumours of the choroidal plexus – papilloma G1, atypical p. G2, papillocarcinoma G3

astroblastoma G3

(cont.)
Neuronal and mixed glioneuronal (epilepsy associated)

- ganglioglioma G1

Dysembryoplastic NeuroEpithelial Tumour – DNET G1

Tumours of the pineal gland

- pinealocytoma G1
- pinealoblastoma G3

(cont.)
Embryonal tumours (G4)

- meduloblastoma
- atypical teratoid tumour
- CNS Primitive Neuroectodermal Tumour – PNET
- neuroblastoma
- ganglioneuroblastoma

Tumours of the cranial and paraspinal nerves

- schwannoma, neurofibroma, perineurioma, G1
- MPNST G3

(cont.)
Meningeal tumours

- meningioma G1, atypical G2, anaplastic G3
- mezenchymal tumours - *arachnothelium derived*
- primary melanocytic lesions

Tumours of the hemopoetic system

- malignant lymphomas – mostly DLBCL
- histiocytic – namely H-S-CH dis.

(cont.)

*Differential diagnosis! Different histogenesis!*
Germinal tumours

germinoma
embryonal carcinoma
embryonal yolk sac tumour
choriocarcinoma
teratoma mature, immature

Tumours of the sellar region (except pituitary)

craniopharyngeoma
granular cell tumour of the neurohypophysis

(cont.)
Metastatic tumours of the CNS

Heterogenous histogenesis!
Differential diagnosis!
Neuroectodermal Tumours - 
derived from:

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- mixed (ganglion and glial cells): ganglioglioma, ganglioneuroma
- melanocytes: pigmented nevi, melanoma

CNS & PNS located
Gangliocytoma

**Def.:**
well differentiated slowly growing neuroepithelial tumour composed of neoplastic mature ganglion cells

**Age /sex** – no special predisposition (diagnosed mostly in childhood – young adults)

**Incidence:** RARE

**Histogenesis:** most probably highly differentiated remnants of embryonal neuroblasts
Neuroectodermal Tumours -

- derived from:
  - ganglion cells
    - gangliocytoma, neuroblastoma
  - glial & Schwann cells
    - gliomas, neurilemmoma
  - mixed (ganglion and glial cells)
    - ganglioglioma, ganglioneuroma
  - melanocytes
    - pigmented nevi
    - melanoma

CNS & PNS located
Neuroblastoma
(WHO: Neuroblastic tumours of adrenal gland and sympathetic nervous system)

Def.: childhood embryonal tumours of migrating neuroectodermal cells derived from the neural crest and destined for the adrenal medulla and sympathetic nervous system

Age /sex – 96% in the 1st decade, no sex predilection

Incidence: most common solid extracranial malignant tumours during the first two years of life

Histogenesis: see definition

Clinic: palpable mass (retroperit, abd., cervical), X-ray - thoracic

Macro: soft gray-tan mass, regressive changes

Micro: undiff. + differentiating neuroblasts (NSE, synaptophysin…)

Variants: neuroblastoma (undiff.), ganglioneuroblastoma intermixed, ganglioneuroblastoma nodular, ganglioneuroma

Behaviour: malignant, dependent on age and histology variant
Neuroectodermal Tumours

derived from:

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- melanocytes: pigmented nevi, melanoma

CNS & PNS located
Ganglioneuroma
Paraganglioma

Def.: benign neuroendocrine neoplasm arising in specialised neural crest cells associated with autonomic ganglia

Macro: encapsulated, solid

Micro: uniform cells forming compact nests (Zellballen)

Biology: benign
Carotid Body Tumour

Chief cells: chromogranin A+
Sustentacular cells: GFAP +
WHO Classification of Tumours of the Adrenal Gland (WHO 2004)

- Adrenal cortical tumours
  - Adrenal cortical carcinoma
  - Adrenal cortical adenoma

- Adrenal medullary tumours
  - Malignant phaeochromocytoma
  - Benign phaeochromocytoma
  - Composite phaeochromocytoma/paraganglioma

- Extra-adrenal paraganglioma
  - Carotid body
  - Jugulotympanic
  - Vagal
  - Laryngeal
  - Aorticopulmonary
  - Cauda equina
Phaeochromocytoma

**Def.:**
benign tumour of chromaffin cells
(intraadrenal paraganglioma)

**Macro:** whittish, solid, regressive changes

**Micro:** solid alveolar (Zellballen)

**Behaviour:** benign (15% bilateral, 10% in children, 10% malignant)

PASS score – Phaeochromocytoma of the Adrenal Gland Scoring Scale

*MEN II* and von Hippel-Lindau disease component
Phaeochromocytoma

640 g, PASS score 6
M 8700/1     D 441
Pheochromocytoma
Embryonal tumours (G4)

- medulloblastoma
- atypical teratoid tumour
- CNS Primitive Neuroectodermal Tumour – PNET
- neuroblastoma
- ganglioneuroblastoma

Tumours of the cranial and paraspinal nerves

- schwannoma, neurofibroma, perineurioma, G1
- MPNST G3

(cont.)
Neurilemmoma (WHO Schwannoma)

**Def.:** a usually encapsulated benign tumour composed of differentiated neoplastic Schwann cells

**Age/sex:** all ages, peak 4-6th decade, no sex predilection

**Incidence:** common solid head, neck, extremities, INTRACRANIAL intramedullary

**Histogenesis:** see definition

**Clinic:** periph. - palpable asymptomatic mass, intraspinal – pain, **intracranial** – cerebellopontine lesion symptoms – hearing, tinnitus, facial paresthesias

**Macro:** white, soft – firm, encapsulated, (+nerve)

**Micro:** elongated Schwann cells, palisading, Verocay bodies

**Variants:** Antoni A, B, biphasic, cellular, pigmented, plexiform

**Behaviour:** slowly growing, benign, malignant transformation rare
Neurilemmoma
Neurilemmoma subcutaneum  S100+
Embryonal tumours (G4)
- meduloblastoma
- atypical teratoid tumour
- CNS Primitive Neuroectodermal Tumour – PNET
- neuroblastoma
- ganglioneuroblastoma

Tumours of the cranial and paraspinal nerves
- schwannoma, 
- neurofibroma
- perineurioma, G1

MPNST G3

MIXED

(cont.)
Neuroectodermal Tumours - derived from:

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- mixed (ganglion and glial cells): ganglioglioma, ganglioneuroma
- melanocytes: pigmented nevi, melanoma

CNS & PNS located
Meningeal tumours

- meningioma G1, atypical G2, anaplastic G3
- mezenchymal tumours - arachnothelium derived

primary melanocytic lesions

- rare on the meninges or in the eye, common on the SKIN

WHO Classification of Skin Tumours (WHO 2006)
Melanocytes – Melanophores - Melanophages
Melanocytic Skin Lesions - 1/3

- **Freckle** – *ephelis* – a hyperpigmented macule due to increased melanin amount in a normal density of melanocytes

- **Lentigo simplex** - small well circumscribed hyperpigmentation due to increased frequency of basal melanocytes

- **Café-au-lait spots** – hyperpigmented keratinocytes. In neurofibromatosis present at birth.

- **Naevus spilus (congenital)** – up to 10cm in diam.

- **Dermal melanocytoses** – blue spots (mongolian, n. Ito, n. Ota, melanocytic hamartomas)

*naevus*: Latin for birthmark
Melanocytic Skin Lesions - 2/3

- Acquired melanocytic nevi
  - junctional
  - dermal
  - compound (dysplastic)
  - deep dermal (blue) nevus

- Congenital melanocytic nevus
Naevus intradermalis naevocellularis
Naevus intradermalis naevocellularis
Naevus intradermalis naevocellularis
Naevus junctionalis
<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
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<tbody>
<tr>
<td>Malignant melanoma</td>
<td></td>
</tr>
<tr>
<td>- Superficially spreading</td>
<td>M 8743/3</td>
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<tr>
<td>- Nodular</td>
<td>M 8721/3</td>
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<tr>
<td>- Lentigo maligna</td>
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<td>- Acral-lentiginous</td>
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<td>- Desmoplastic</td>
<td>M 8745/3</td>
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<td>- Melanoma arising from blue naevus</td>
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<td>- Melanoma arising in a giant congenital naevus</td>
<td>M 8761/3</td>
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<td>- Melanoma of childhood</td>
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<tr>
<td>- Naevoid melanoma</td>
<td>M 8720/3</td>
</tr>
<tr>
<td>- Persistent melanoma</td>
<td>M 8720/3</td>
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</tbody>
</table>
Malignant Melanoma

World incidence:
2000   133000
2008   197000  *increase by 5% / year*
11th position worldwide
Melanoma malignum
Metastases melanomatis maligni ad cerebrum

47% of patients have mutation BRAF and half of these are stage IV.
metastases melanomatis ad hepar
Man 56 yrs

- progressive neurological symptoms
- brain CT negative
- CSF
  - no signs of inflammation
  - scattered atypical cells
  - neoplasm?
  - systemic degeneration?
Liquor cerebrospinalis
Metastases myocardii auriculae dx. cordis
Micrometastasis cerebri
Metastasis renis
Metastasis myocardii
Metastasis myocardii

HMB45
Diagnosis

Morbus principalis:
Melanoma malignum originis ignotae generalisatum.

Complicationes:
Metastases tumorosae multiplices cerebri, medullae spinalis, myocardii et renum.
Haemorrhagia lobi frontalis hemisphaerii sin. cerebri.
Endocardiosis marantica valvae mitralis.
Infarctus recentes aliquot lienis, renum et cerebri.
Diagnosis

Causa mortis: Generalisatio tumorosa. Oedema cerebri.

Histogenetic Classification of tumors continued...

- mixed tumours
- germ cell tumours
- mesothelioma
Mixed Tumours

Def.: Tumours (benign or malignant) composed of two or more different cell lines that are normally present in the place of tumour origin.
Neurofibroma

*Def.*: a well demarcated intraneural or diffusely infiltrative extraneural tumour consisting of a mixture of cell types including Schwann cells, perineurial-like cells, and fibroblasts. Multiple in Neurofibromatosis 1.

*Age /sex* – all ages, no sex predilection

*Incidence:* common

*Clinic:* palpable asymptomatic mass, mostly cutaneous nodule (s) ass. with café-au-lait spots

*Macro:* white, firm, circumscribed

*Micro:* elongated Schwann cells, fibroblasts, Wagner-Meissner-like tactile corpuscles

*Variants:* atypical, cellular, plexiform, may be pigmented

*Behaviour:* slowly growing, benign, malignant transformation rare – mostly in plexiform variants
Neurofibroma
Histogenetic Classification of tumors continued...

- mixed tumours
- germ cell tumours
- mesothelioma
Germ cell tumours
- pluripotent germ cell differentiates into variable structures

- **germinoma** (seminoma/dysgerminoma)
- embryonal carcinoma
- yolk sac tumour
- choriocarcinoma
- teratoma (mature, immature)
Seminoma testis

PLAP

38 yo
Mesoblastoma vitellinum – yolk sac tumour
Choriocarcinoma
Teratomas

Def.: Tumours (benign or malignant) composed of two or more different cell lines that are **NOT** normally present in the place of tumour origin.
Teratoma

- Coetaneous - differentiated - cystic
- Embryonal - nondifferentiated - solid
Teratoma maturum ovarii
„Other“ Tumours

- mixed tumours
- germ cell tumours
- mesothelioma
Mesothelioma

*Def.*: a neoplasm derived from the coelom cavity epithelium – mesothelium

- benign - circumscribed (papillary, adenomatoid)
- malignant – circumscribed, diffuse
Asbestosis
Ca bronchogenes

Hyalinosis et metastases carcinomatosa pleurae parietalis