Peroperative smear cytology of the CNS lesions

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What we need

• Good neurosurgeon
• Good radiologist
• Good bioptic sample

• Working knowledge of the imaging methods

• Clinico-radiological corelation
What we need

• Age
  – e.g. Choroid plexus carcinoma versus AT/RT versus MTS

• Clinical history

• Localisation and MRI findings
• **12-years-old girl** (SD-IAP 393, B. Rychlý)
Choroid plexus carcinoma
35-years-old woman
MTS of the papillary lung adenocarcinoma
What we need

• Age

• Clinical history
  – e.g. Giant cell GBM versus PXA

• Localisation and MRI findings
• 22-years-old men
• Short clinical history (months), without epilepsy
Giant cell glioblastoma
Pleomorphic xanthoastrocytoma, WHO grade 2

- Children and adolescents with history of refractory epilepsy
- Solid / solid-cystic, enhancing superficial tumor in the temporal lobe
- Involvement of the dura / calvarium
• Mitoses in the cytology, necrosis and vascular proliferation are incompatible with PXA

Pleomorphic xanthoastrocytoma
What we need

• Age

• Clinical history

• Localisation and MRI findings
  – e.g. **solid-cystic enhancing cerebellar lesion** in the child = MB versus PA
  – In an adult = MTS versus haemangioblastoma
What we need
Smear CNS cytology

- Advantages
  - Elimination of the freezing artifacts
  - Excellent cytological details
  - Method between cytology and biopsy
  - Background interpretation (e.g., glial lesions versus metastasis)
  - Better sampling of the bulky tissues
  - Saves the small tissue samples (stereotactic biopsies)
  - Speed
• **Rapid fixation!**
• We prefer spray to dipping
• Air drying artifacts after few seconds!
Smear CNS cytology

• **Disadvantages**
  
  – **Assessment of the cellularity and architectonics is not reliable**
    » Always combine with frozen section, if possible!
  
  – **Disruption of mitotic figures**
    » If we find 1 or 2 = there are many!
  
  – **Some diagnostic features are fixation artifacts**
    » Perinuclear halos in oligodendroglioma
  
  – **Cohesive lesions are not smear-friendly**
4 patterns

- Cohesive lesions
- Glial lesions
- Non-cohesive lesions
- Epithelial lesions
Cohesive lesions

- Tissues with abundant reticulin / collagen
- Sufficient physical force will frequently yield some diagnostic cells
- Crush artifacts and lumps of tissue can make the smear useless

- schwannoma, haemangioblastoma, some meningiomas, PXA, gliosarcoma ...
Cohesive lesions

In vivo growth

Smear low

Smear high

Useless lump

Diagnostic cells
• 62-year-old woman
• Tumor of the cerebellar hemisphere
Atypical nuclei, vacuolated cytoplasm
Atypical nuclei, vacuolated cytoplasm
Haemangioblastoma

Inhibin α
- 53-year-old man
- PC angle tumor
Schwannoma

„Frying rope“
• 48-year-old woman
• PC angle tumor
Meningioma
• Cell clusters bound to other clusters by eosinophilic glial processes - look like clusters of seeds embedded in a cotton fiber matrix
Glial lesions

- Reactive processes will give a hypocellular, eosinophilic fluffiness, long, delicate branches and benign nuclei
- Neoplastic tissues will be much bluer, have atypical nuclei and fewer shorter, broader processes
Pilocytic astrocytoma, WHO grade 1

• Most common glioma in the children
  » young adults and rarely elderly people
  » NF1 syndrome (bilateral glioma of the optical nerve)

• Cerebellum, brainstem, hypothalamus, n. opticus
  » Rare in spinal cord, supratentorial

• Expansive solid-cystic, enhancing tumor (cyst-mural nodule)
Biphasic growth pattern

Capillary proliferation

„ancient“ changes

ODG-like
• 43-year-old woman, NF1
• Tumor lobi frontalis. l.sin
• 10-months-old boy, suprasellar tumor
• Encased branches of carotid artery
Pilomyxoid astrocytoma, WHO grade 2

Indistinguishable from PA in the cytology
EGB and RF are missing
Pilocytic astrocytoma: DDx

• Piloid gliosis
  • Frequently around haemangioblastoma, craniopharyngioma, spinal ependymoma

• Low grade diffuse astrocytoma

• Oligodendroglioma
Infiltrating astrocytomas

- Diffuse astrocytoma, WHO grade 2
- Anaplastic astrocytoma, WHO grade 3 (+ mitoses)
- Glioblastoma, WHO grade 4 (+ necrosis and/or microvascular proliferation)

- Most common gliomas in adults, second most common in children (after PA)
- Most common is glioblastoma
Infiltrating astrocytomas

• May occur anywhere
  – Cerebellum, spinal cord, thalamus and brainstem are not frequent

• In children often „brainstem glioma“

• MRI: Hypodense in T1, hyperdense in T2
• G3 – variable focal enhancement
• G4 – „ring enhancement“
• Gliosarcoma and giant cell GBM often well demarcated
• 56-year-old woman
Diffuse astrocytoma, Grade 2
• 54-year-old men
• Tumor lobi occipitalis
Diffuse gemistocytic astrocytoma, G2
Glioblastoma
Glioblastoma: DDx

- Metastases
- Other high grade tumors
- PXA
LG gliomas: DDx 1

• Normal brain / gliosis
  – Most easily smearing tissue – smooth, pink „fluffy“ smear
  – Gliomas are somewhat firmer
  – Low cellularity, no clustering, delicate capillaries
  – **Cortex:** heterogeneous cell population: oligo, astro, neurons, neuropil
  – **White matter:** oligo+astrocytes
Do not make diagnosis of glioma if you are not sure!
LG glioma: DDx 2

- Reactive gliosis in acute inflammatory demyelinization

  - Lower cellularity (astrocytes), but inflammatory cells rise the overall cellularity: **Heterogeneous cell population**

  - Many long delicate astrocytic filaments, benign nuclei

  - Few atypical cells will not make diagnosis of glioma
• 21-year-old women
Macrophages

Lymphocytes / oligodendrocytes

Astrocytes
“Use this term only with very sophisticated audiences; misinterpreting the process as Creutzfeldt-Jacob disease can lead to completely unnecessary panic in the operating room“.

J.T. Joseph 😊
Acute inflammatory demyelination
• **Lymphoma**
  – If clinical history is missing, or corticosteroids were administered for several days *always put the lymphoma in the final differential diagnosis*

• High grade glioma with necrosis
• Infections
• Brain infarct
Oligodendrogliaoma

- Adult patients, younger than in HG astrocytomas (4th decade)
- **Rare in children** (less than 3%)
- **Cortical localisation** = epilepsy, focal deficits
- Well demarcated, hypo – isodense in T1
- Calcifications, cysts
- Hyperdense in T2 / FLAIR
- Variable contrast enhancement in ODG grade 3
• Monotonous and evenly distributed population of cells with smooth round nuclei + delicate capillaries
  » differentiation from astrocytoma could be difficult in G3 ODG
• Sparse glial matrix, cells are free, almost discohesive
• Minigemistocytes, naked nuclei
• Remnants of myxoid background (microcysts content)
• Calcifications
• Neurons (infiltrated cortex)
44-year-old man
Cortical frontal tumor
Oligodendroglioma: DDx

• ODG is **rare in children**
  – ODG-like proliferation in **DNT and PA**

• Lymphoma
• Small cell carcinoma
• Neurocytoma
Ependymoma

• 3rd most common tumor in children (90% are intracranial)
• Most common spinal tumor in adults

• In the vicinity of ventricles, rare extraventricular
• Well circumscribed (G2 typically non-infiltrative)
• Enhancing, variably cystic

• Extent of resection is prognostically important
  – Correct peroperative diagnosis is critical
• 31-year-old men
Anaplastic ependymoma, G3
31-year-old men
Temporo-parietal tumor
Non-cohesive lesions

- Cells minimally bind to either their neighbors or their matrix
- Cells separate easily during smearing
- Give an even gradient of cells, from their origin to the edge of the slide
• 43-years-old woman
• STH producing pituitary adenoma
Monotonous cell population = Adenoma
75-years-old woman
Periventricular tumor
Lymphoglandular bodies

CD20

DLBCL
• 5-year-old boy
Medulloblastoma - classical

Molding, salt and pepper chromatin
Medulloblastoma: DDx

- Normal cerebellum
Cerebellar cortex

Medulloblastoma
• 2-years-old boy
• Tumor of the 4th ventricle
Atypical teratoid/rhabdoid tumor
• 15-years-old boy
• Tumor of the corpus callosum and l. frontalis
Epithelioid granuloma
Seminoma / Dysgerminoma
Adeno-Ca
Epithelial lesions

- Manner in which epithelial tissues shed their cells depends on the growth pattern:
  - Papillary structures, globular balls, and sheets
  - Cells have some cytoplasm, typically have distinct borders

- In poorly differentiated carcinomas, cell-to-cell binding properties decrease
Epithelial lesions
• 2-years-old boy
Choroid plexus papilloma
19- years-old men with testicular seminoma
Supratentorial tumor
Embryonal carcinoma
Conclusions

• Smear cytology is useful addition to the frozen section, sometimes the only possibility
• Interpretation in the context of clinical history and imaging is imperative
• 4 typical patterns – cohesive, glial, non-cohesive, epithelial
• Be prepared for rare lesions / surprises
• Cytoplasm / background = origin of cells
• Nuclei = benign versus malignant lesion
• Rapid fixation gives best results
Thank you!

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