Tumor treatment related changes in the CNS

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consequences of treatment on CNS

(sub) acute
- infarction
- posterior fossa syndrome
- radiation reaction
- sinus/venous thrombosis by L-Asparaginase
- reversible posterior encephalopathy (PRES)
- tacrolimus/cyclosporine

chronic
- leukoencephalopathy (radiation/MTX)
- degeneration of nuclei
- radiation necrosis
- intelligence defects
- bleeds/cavernomas
- growth problems
- obesity
- second tumors
infarction after surgery

• hazards of resection of chiasmatic gliomas:
• 17% infarcts (n=102 children)
• the younger the worse (3 y vs. 5 y)
• no infarcts after biopsies of whatever technique
• Conclusion: if material is needed prefer biopsies and avoid resections
hypertrophic olivary degeneration

- disturbance of the connection: nucleus ruber – nucleus dentatus – nucleus olivaris inferior (Guillain-Mollaret-triangle)
- scarce literature and rare acc. to literature
- etiology:
  - trauma
  - idiopathic
  - surgery in the posterior fossa
HOD
Wernicke disease

- 16 y old girl with a DIPG after irradiation and under TMZ
- sudden loss of consciousness
- artificial ventilation
- tumor progression suspected

- B1 level was reduced, however, on substitution no complete recovery was achieved
Wernicke disease
Wernicke disease
leukoencephalopathy

• after irradiation especially whole brain irradiation
• after MTX i.v. oder i.th., especially if after irradiation
• importance for brain function?
• classification acc. to Fazekas:
  grade 0    normal
  grade I    punctated
  grade II   confluent
  grade III  largely confluent

  *Fazekas et al. Europ Neurol 1989; 33: 169*
LEP grade I
LEP grade II
LEP grade III
MTX LEP in MB

- 36 children below 3 y at the time of diagnosis:
  - 35 i.v. MTX (10-165 g/m² cum. dose)
  - 21 i.ventr. MTX (20-102 mg cum. dose)
  - 17 CNS irradia. (18-35 gy)

- sign. correlation of intraventr. MTX dose and LEP (p<0.01)
- no correlation to IQ
- maximum after about 1 year
- reduction in 50% within 2-3 years

acute MTX-toxicity

- restricted diffusion is diagnostic
- reversible
- strokelike event
- 6-11 d nach MTX (intrathecal)

Rollins et al. AJNR 2004
acute MTX-leukoencephalopathy
acute MTX-leukoencephalopathy
necrotising LEP (MTX after irrad.)
MB 3 months after irradiation
MB 6 months after irradiation
MB 9 and 12 months after irradiation
simple rule

• MB (and probably other embryonal tumors) and ependymomas recur not in another place within the brain parenchyma but either as local recurrence and/or meningeal dissemination

                      Warmuth-Metz et al: Neuro Oncol  2011

therefore

• a new lesion within the brain at another place can only be treatment related (radiation reaction or second tumor even if histology is eg PNET)
nomenclature of a radiation reaction

• immediate reaction: edema during irradiation

• early delayed reaction: weeks to months after termination of irradiation

• late delayed reaction: 3 months or later (up to many years) nach treatment, usually within 2 years

Rabin BM et al: Radiation induced changes in the CNS Radiographics 1996
time course of temporary radiation reaction

- typical development of WML after a median of 7.8 months after the start of irradiation (1.9-13 months)
- reduction after a median of 6.2 months (1.7-23.5 months)

  *Fouladi M et al: J Clin Oncol 2004; 22: 4551*

- T2-lesions and contrast enhancement after an average of 6 months after IMRT (4-9 months)
- reduction within 6 months (3-25 months)

suspicion of a radiation reaction after accelerated irradiation and carboplatin

- incidence 13.5%
- enhancement within or surrounding a previously non-enhancing tumor
- enhancement with a distance to the tumor but within the treatment field
- enhancement in the periventricular white matter especially caplike around the ventricular borders or enhancement in the corpus callosum
- soap bubble- or swiss cheese pattern of enhancement

**suspicion of radiation necrosis**

- **enhancement**
  - cortical enhancement: 61%
  - only cortical enhancement: 2%
  - white matter: 98%
  - only white matter: 39%
- **enhancement in corpus callosum**: 27%
- **spreading wave front**: 98% (vs. nod.)
- **swiss cheese/soap bubble**: 90% (vs. solid)
- n=52

Rogers et al: J Neurooncol 2011; 101
perfusion imaging
MRS
chronic radiation necrosis
cavernous hemangioma

- after irradiation in children
  - after 1-26 years (mean 5-16 y)
  - 3.4% incidence after irradiation at age 7 y?
  - possible precursor capillary teleangiectasie
  - dose >30 Gy, dose related
  - risk of bleeds higher than in inborn cavernomas
  - no true incidence, as the demonstration is dependant on the MR-sequences used and has not been systematically evaluated

Burn et al.: J Neurosurg 2007
Jain et al: AJNR 2005
cavernous hemangioma
cavernous hemangioma
secondary tumors

• main cause irradiation
  – meningiomas, often high grades
  – typical interval 10 y and more

  Müller H et al. Strahlenther Onkol 2012

• combined treatment
  – meningiomas, high grade gliomas, PNETs
  – typical intervall 9 y

• only after chemotherapy?
• extremely bad prognosis
secondary tumors
hypothalamic obesity

T1-signal of nuclei
bright T1 in nuclei

- myelin degradation? myelin repair (NF1)
- treatment consequence? dent. nucl. after irradiation  
  Kasahara S et al: Radiology 2011; 258
- storage of Gadolinium
  - linear vs. cyclic Gd-chelates
  - patients with normal renal function!
  - correlation to the amount of Gadolinium  
    Kanda T et al: Radiology 2015; epub
    Errante Y et al: Invest Radiol 2014; 49
    Radbruch A et al: Radiology 2015; 275
Danke - thank you