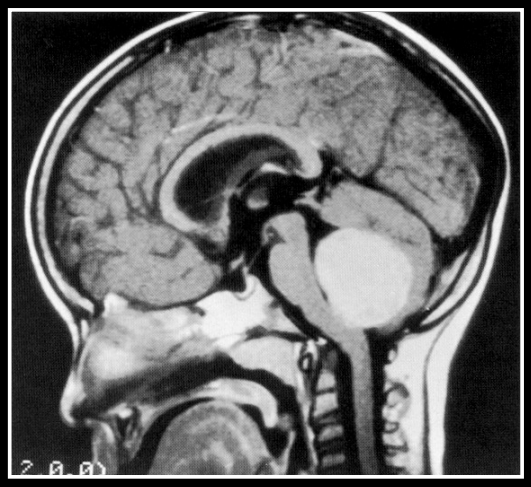
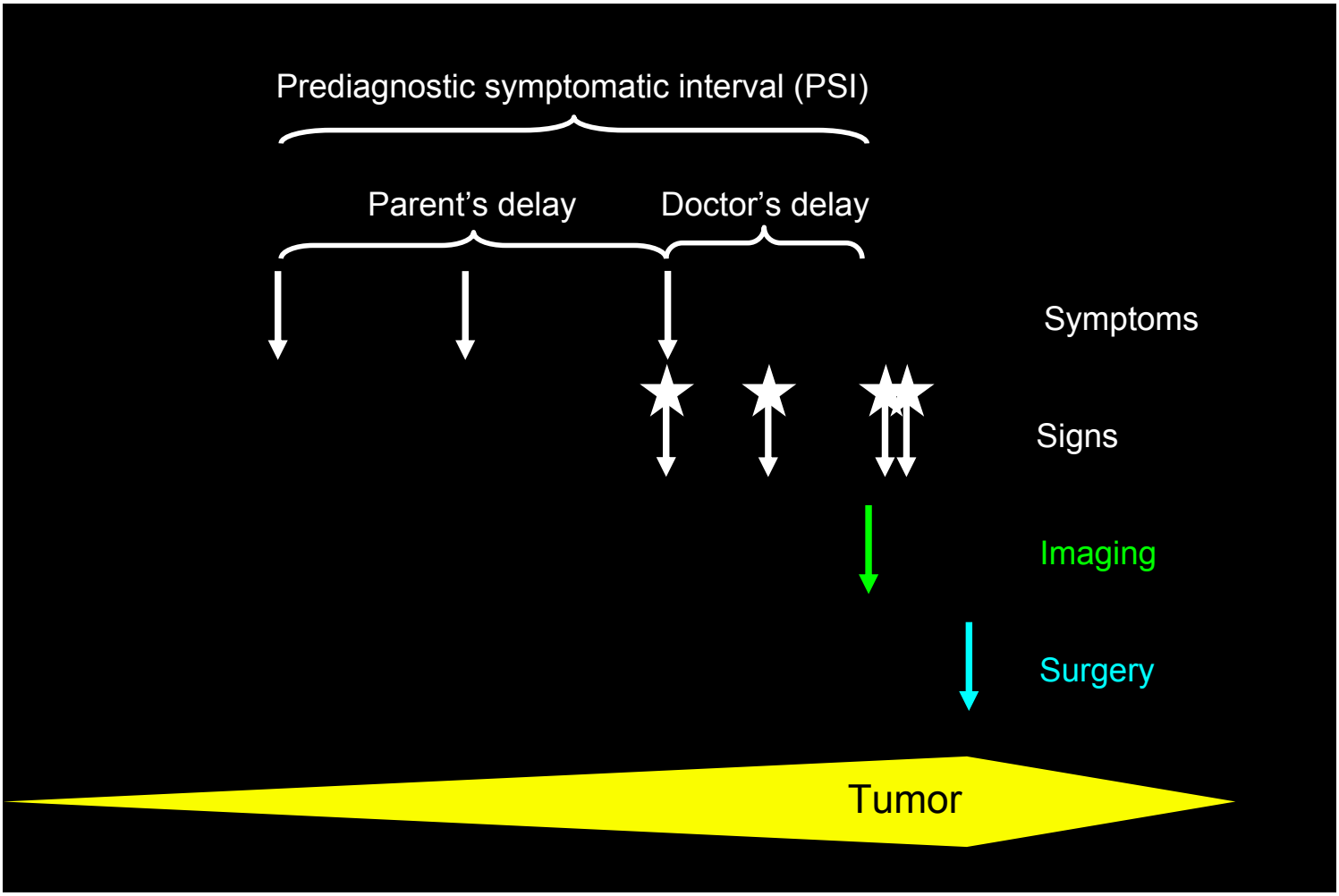
Initial Signs and Symptoms in Children with Brain Tumors



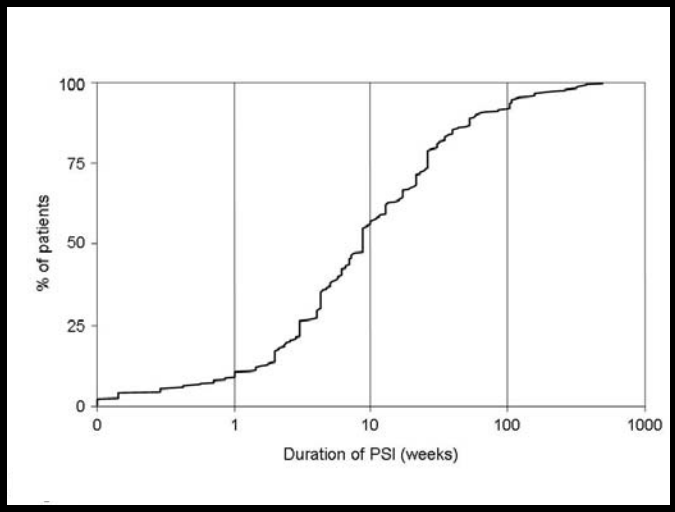
Dobrovoljac M, Hengartner H, Boltshauser E, Grotzer MA. Delay in the diagnosis of pediatric brain tumors. Eur J Pediatr 2002 (n=252)

Signs and symptoms	All	<2 yr	≥2 yr
Headache	35 %	2 %	43 %
Nausea / vomiting	26 %	18 %	28 %
Seizures	14 %	20 %	12 %
Behavioral changes (mood, character, school)	10 %	12 %	9 %
Ataxia	8 %	8 %	8 %
Squint / diplopia	8 %	6 %	8 %
Lethargy	5 %	4 %	5 %
Hemiparesis / quadriparesis	5 %	8 %	4 %
Head tilt	5 %	12 %	3 %
Anorexia	3 %	6 %	2 %
Growth failure	3 %	-	3 %
Sleep disturbance	2 %	2 %	2 %
Polyuria / polydipsia	2 %	-	3 %
Visual loss	2 %	2 %	2 %
Weight loss	2 %	4 %	1 %
Facial nerve palsy	2 %	4 %	1 %
Enlargement of the head	2 %	8 %	-
Sunset eyes, separation cranialsutures	1 %	4 %	-
Dizziness	1 %	-	1 %
Nystagmus	1 %	4 %	-

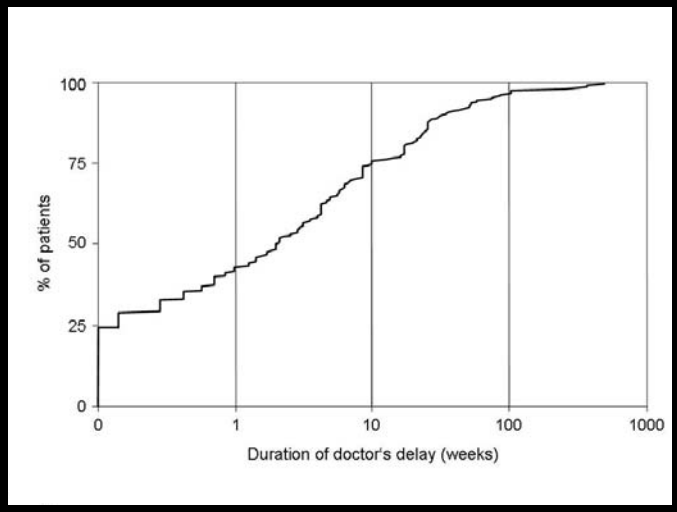


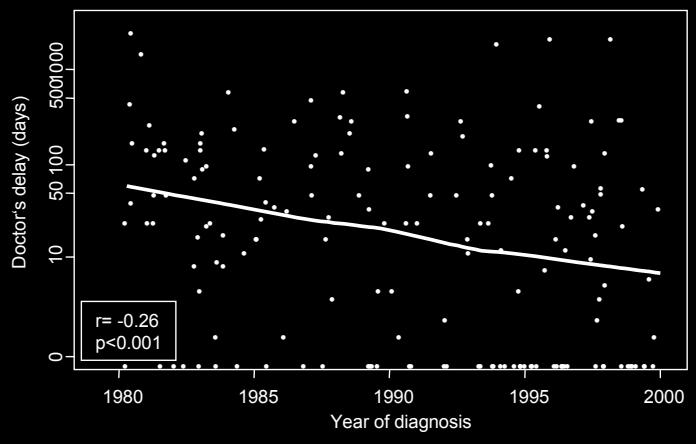
Cummulative Distribution of PSI and Doctor's Delay

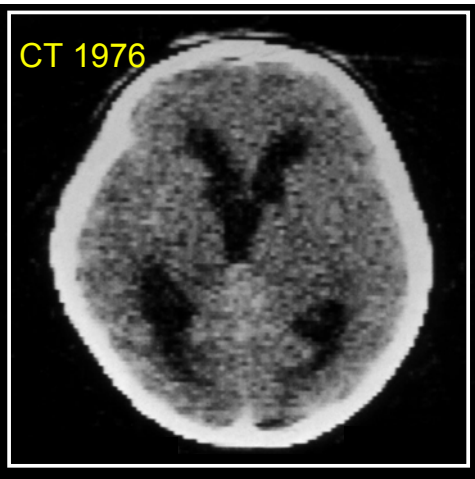
PSI (weeks)

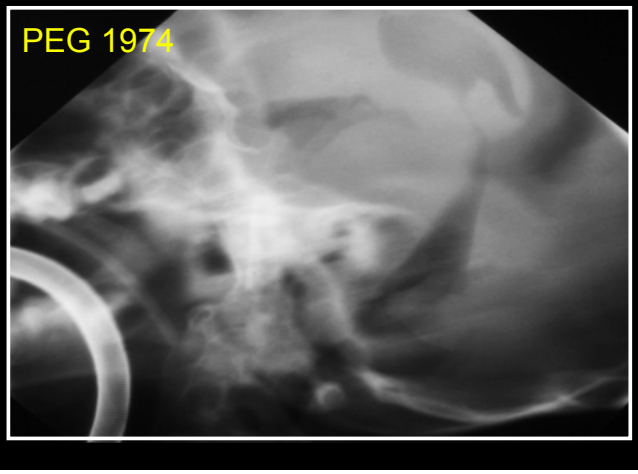


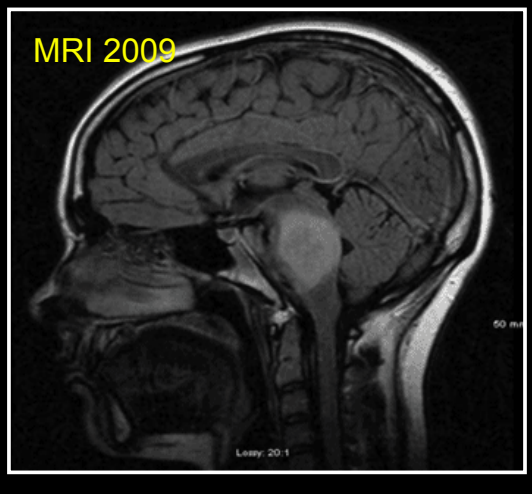
Doctors's Delay (weeks)



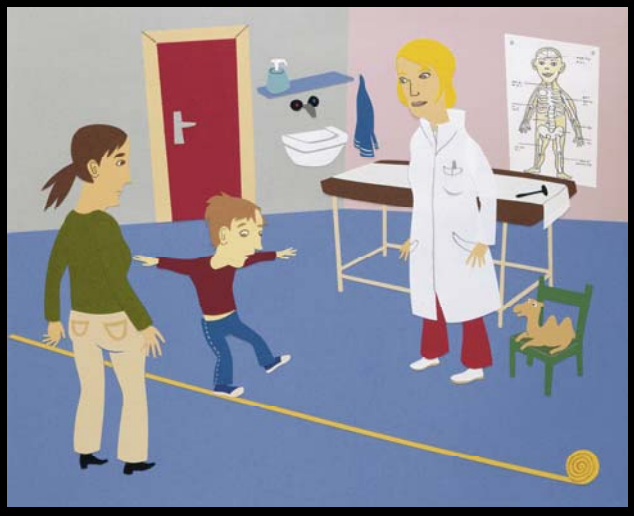








Frequency of Signs and Symptoms Noticed by Medical Doctors >30 Days Prior to Diagnosis

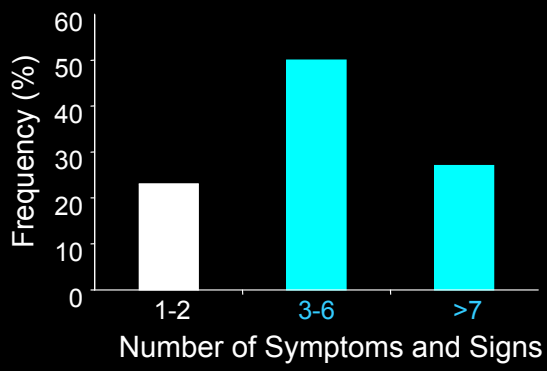


Signs and symptoms	No. patients	% patients with this sign
Headache	31	23 %
Nausea / vomiting	28	19 %
Seizures	18	35 %
Behavioral changes (mood, character, school)	15	29 %
Ataxia	11	9 %
Squint / diplopia	10	11 %
Head tilt	7	19 %
Weight loss	7	23 %
Hemiparesis / quadriparesis	6	7 %
Polyuria / polydipsia	6	75 %
Lethargy	5	15 %
Growth failure	4	44 %
Facial nerve palsy	3	8 %
Visual loss	6	3 %
Papilledema	2	8 %
Enlargement of the head	2	9 %
Cranial neuropathies other than III, IV, VI, VII	2	5 %
Sleep disturbance	2	13 %
Anorexia	2	22 %
Dizziness	2	33 %

Headache as Leading Symptom of a Brain Tumor?

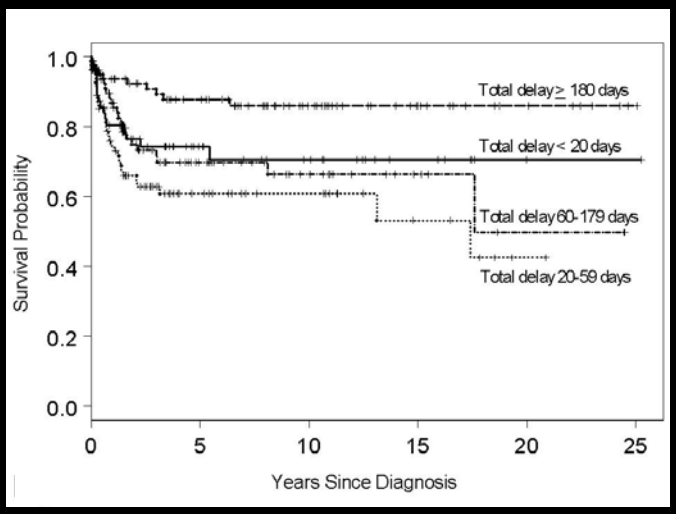
- Headache is suffered by 5-30% of elementary school children, whereas the annual incidence of brain tumors in this age group approximates only 0.003%
- However, analysing 3276 patients, only 3% of children with headache and a brain tumor had no abnormality on neuological examination (J Neurooncol 1991)

Number of Symptoms and Signs in Children with Brain Tumors at Diagnosis

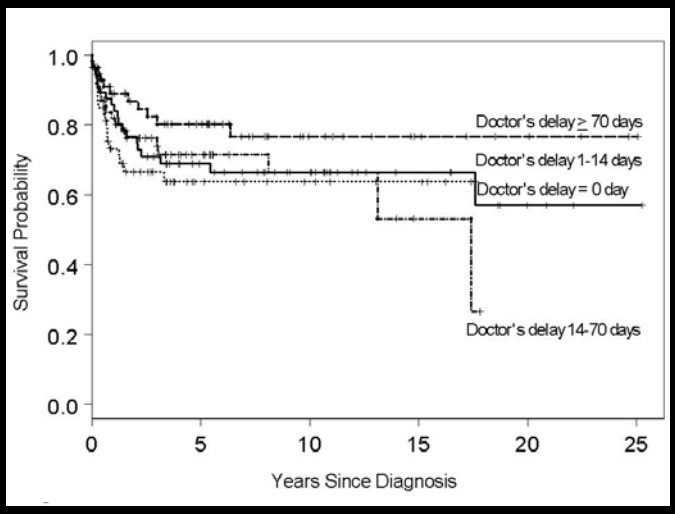


Duration of PSI and Survival Probability

Survival in Relation to PSI



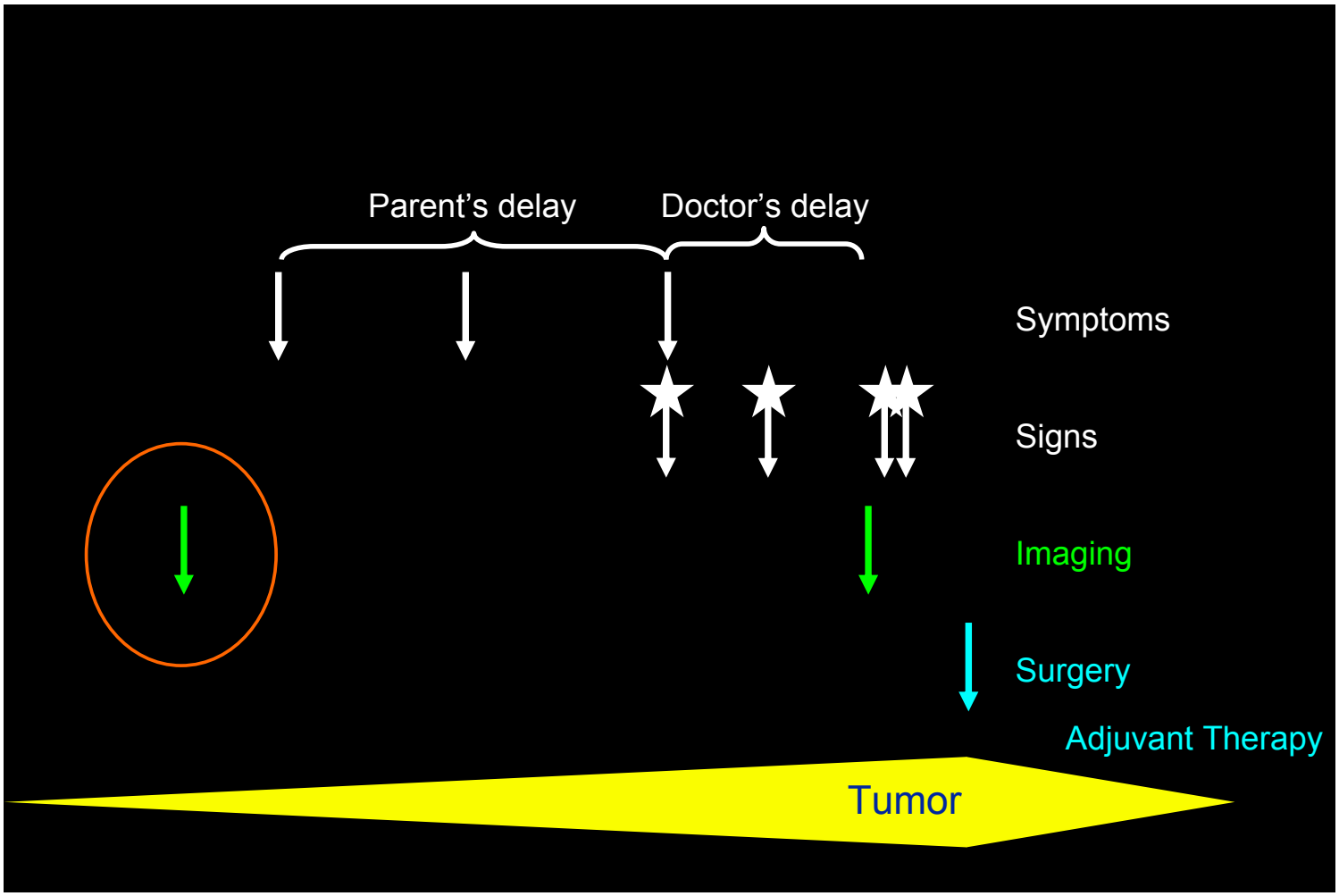
Survival in Relation to Doctor's Delay



Kukal K, Dobrovoljac M, Boltshauser E, Ammann RA, Grotzer MA Eur J Pediatr 2009 (n=315)

Conclusions

- The effect of tumor biology on survival seems to be dominant and overwhelms any possible opposing effect on survival of a delay in diagnosis
- Any delay after diagnosis should be omitted
- A high level of awareness, a detailed medical history and repeated correctly interpreted neurological examinations should lead to an earlier diagnosis



Incidental Findings of Mass Lesions on Neuroimaging of Children

Background and Study Aims

- Incidental findings are previously undetected abnormalities that are unrelated to the purpose of the examination.
- Meta-analysis by Morris et al. in adults (BMJ 2009):
  - 2.0 % prevalence of non-neoplastic incidental brain findings
  - 0.7% prevalence of neoplastic incidental brain findings
- The aims of this study are to describe incidental findings of CNS mass lesions and their evolution, as well as to discuss management options.

Perret C et al. Neurosurg Focus 2011

Methods

- Retrospective study on children under 18 years old with primary CNS tumors, admitted to the University Children's Hospital of Zurich, from January 1995 to December 2010.
- In the same time period: 24'047 neuroimaging studies (12'725 brain MRI, 9161 brain CT, 2161 spinal MRI) in ~15'000 patients

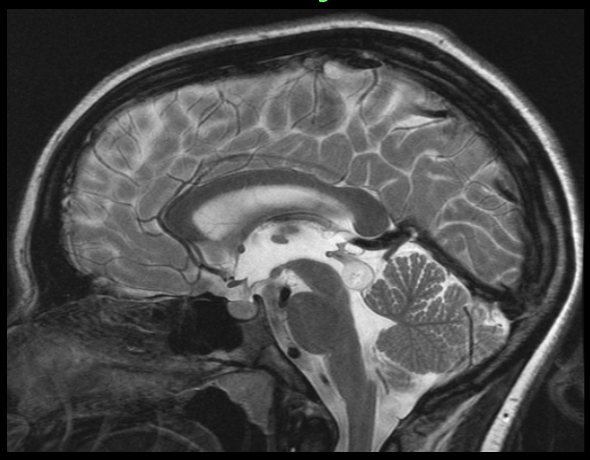
Perret C et al. Neurosurg Focus 2011

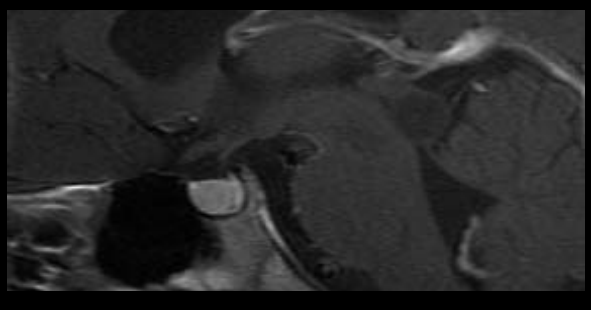
Results

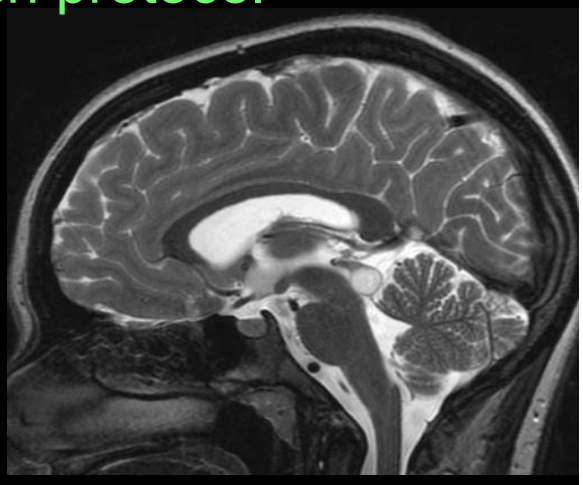
- In 19 (5.7%) of 335 patients with newly diagnosed CNS tumors, the diagnosis of CNS mass lesion was an incidental finding.
- Reasons for neuroimaging in these 19 patients were:
  - head trauma (n=6)
  - neurological evaluation (n=4)
  - research protocols (n=3)
  - malformations (n=2)
  - seizures (n=1)
  - endocrinological evaluation (n=1)
  - psychiatric evaluation (n=1)
  - orbital lymphangioma (n=1)

Perret C et al. Neurosurg Focus 2011

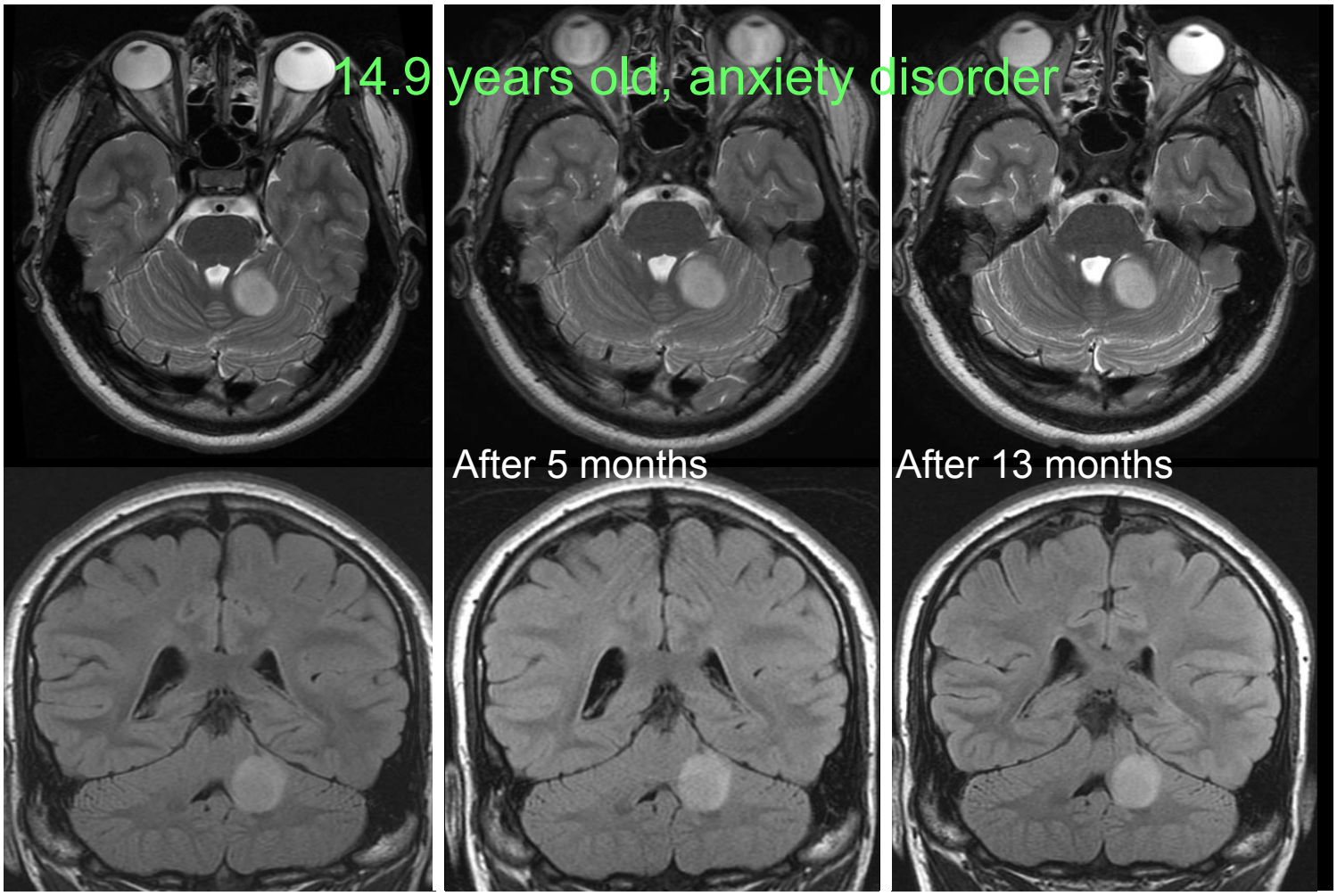
14.6 years old, research protocol

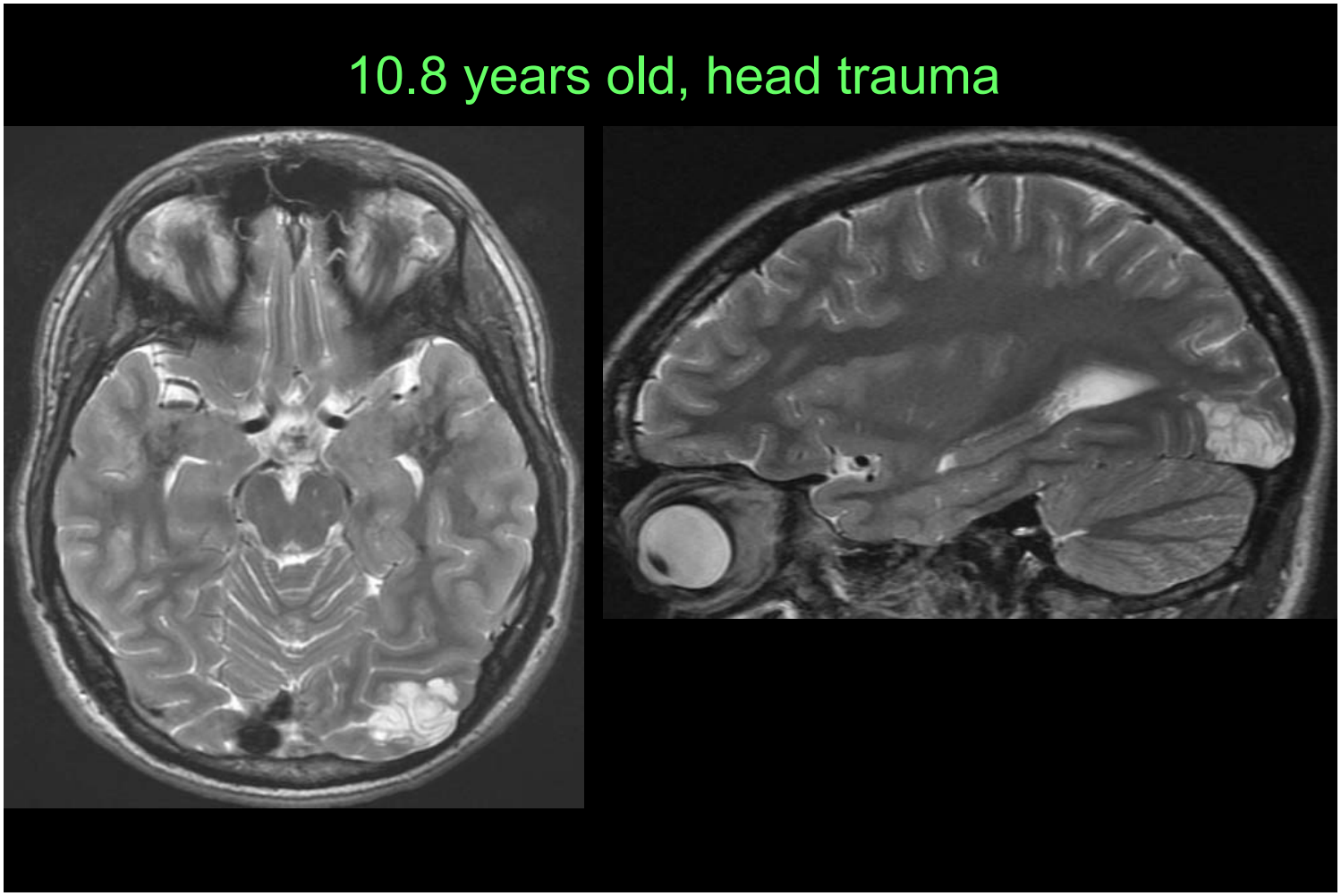


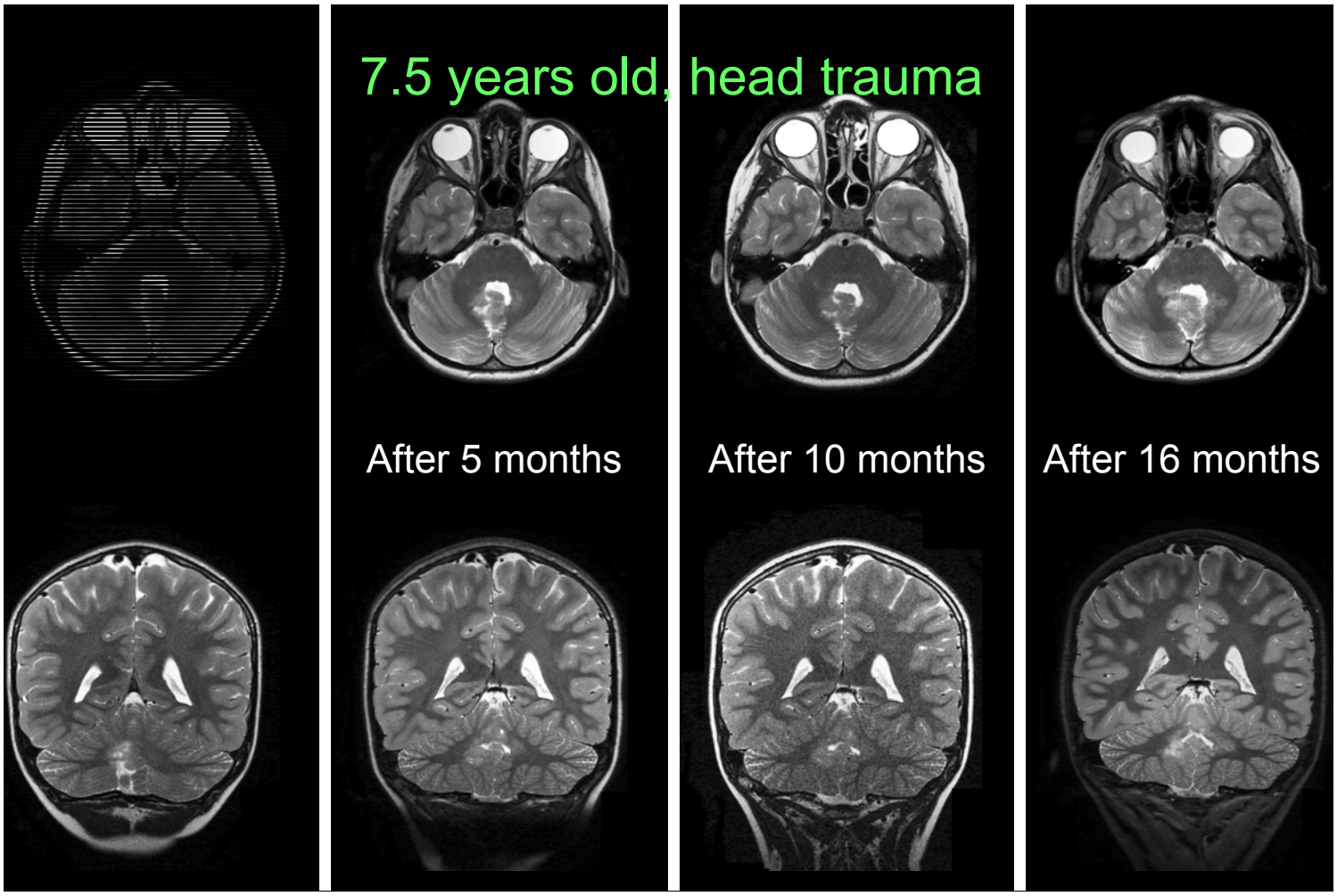




After 18 months


14.9 years old, anxiety disorder
After 5 months
After 13 months


10.8 years old, head trauma



Management

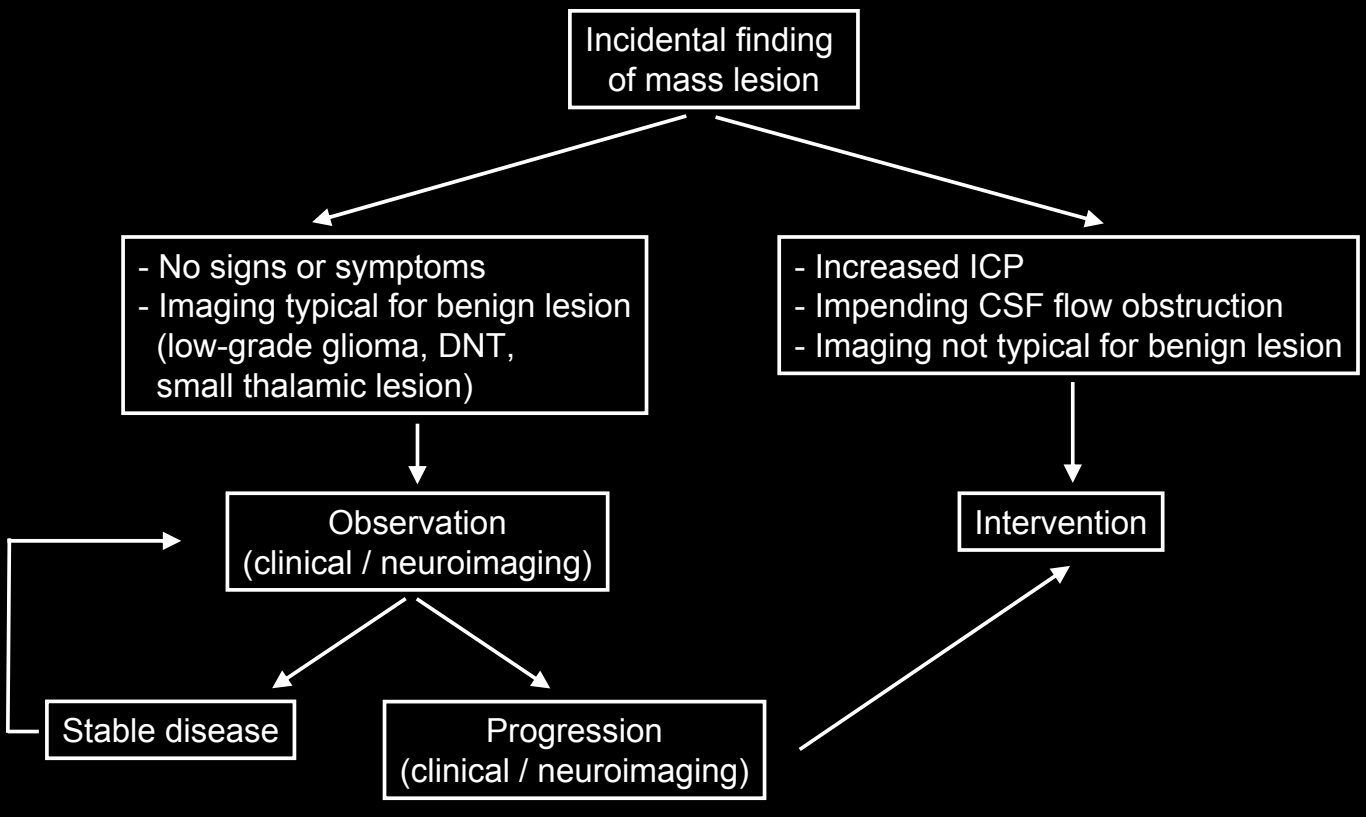
- 7 patients underwent immediate surgery:
  - low-grade glioma (n=4)
  - craniopharyngioma (n=1)
  - ependymoma (n=1)
  - choroid plexus papilloma (n=1)
- 12 were treated conservatively/observation
- 10/12 conservatively treated patients remained stable (median follow-up time: 2.3 years)
- 2/12 underwent delayed surgery because of tumor progression
  - medulloblastoma (n=1)
  - fibrillary astrocytoma (n=1)

Perret C et al. Neurosurg Focus 2011

Conclusions

- Clinicians are increasingly challenged by the discovery of incidental CNS mass lesions.
- At our institution, the prevalence of incidental CNS mass lesions is estimated to be approx. 0.1%.
- A subgroup of such lesions can be followed conservatively, clinically and radiographically.

Perret C et al. Neurosurg Focus 2011



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Pitfalls in the Diagnosis of Brain Tumors

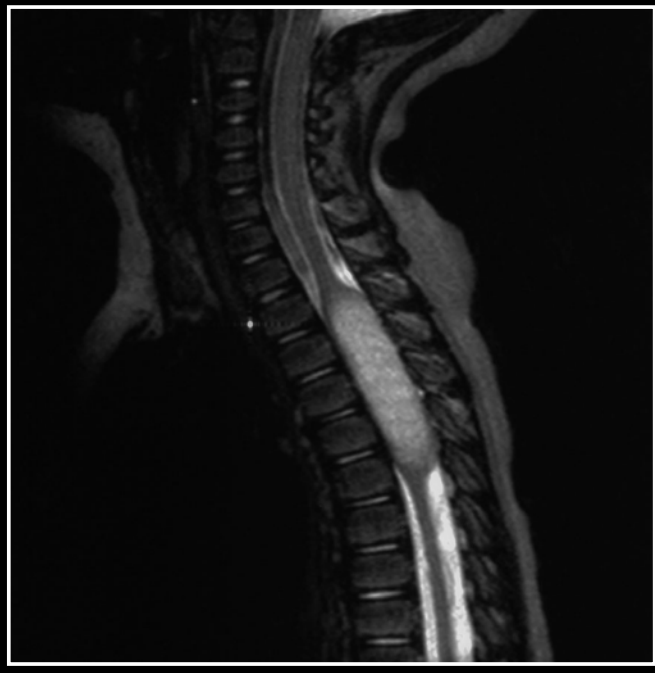
- Clinical findings
  - interpretation of history and examination
  - request for neuroimaging at false location
- Neuroimaging
- Histological findings

Omuro et al. Lancet Neurol 2006

Neuroimaging at False Location

20 months old boy
Intermittent crying – pain (?)
MRI head normal

Video → very suggestive of back pain
MRI spine

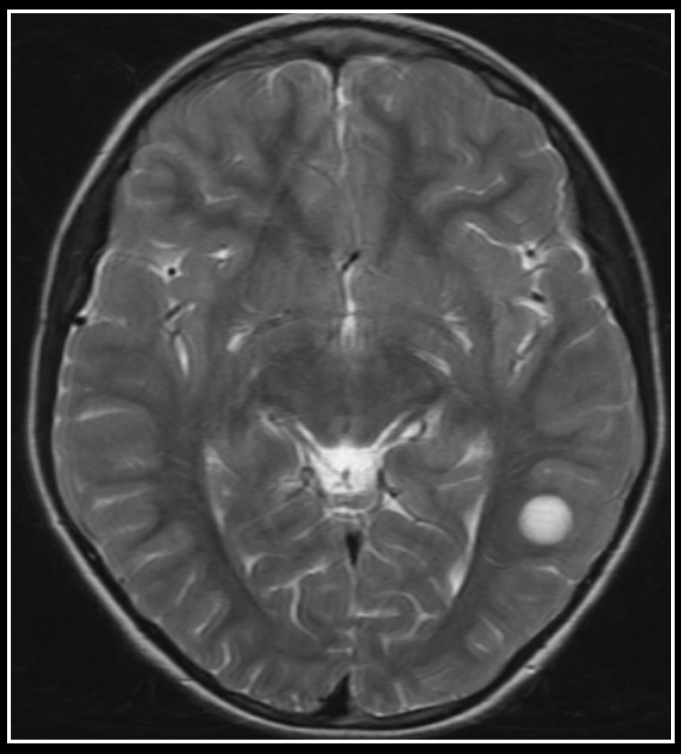


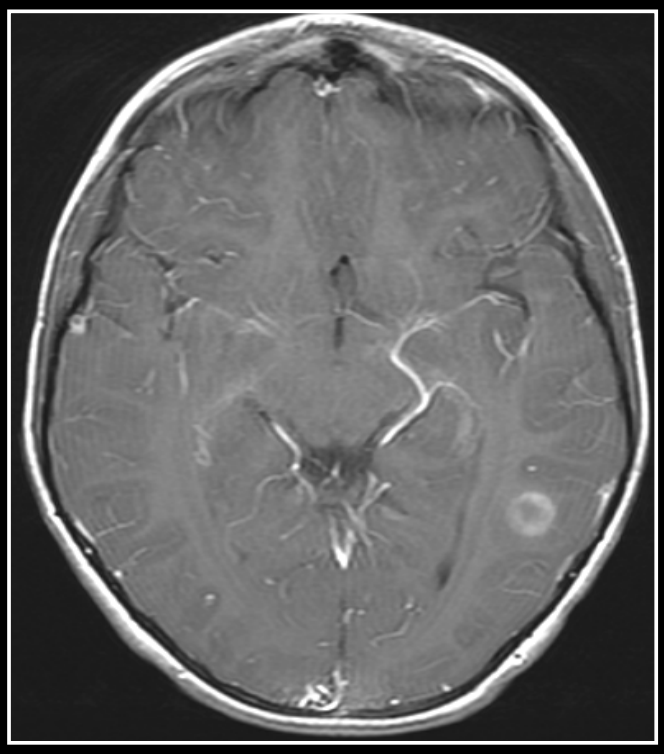
Neuroimaging

- Non-neoplastic diseases presenting as tumefactive enhancing brain lesions
  - MS and demyelinating diseases
  - Neurosarcoidosis
  - Pyogenic abscess
  - Toxoplasmosis in AIDS
  - Tuberculoma
  - Neurocysticercosis
  - Fungal infection
  - Subacute ischemic stroke
  - Cavernoma
  - Radiation necrosis

    ……
- Non-tumoral presentation of neoplastic lesions

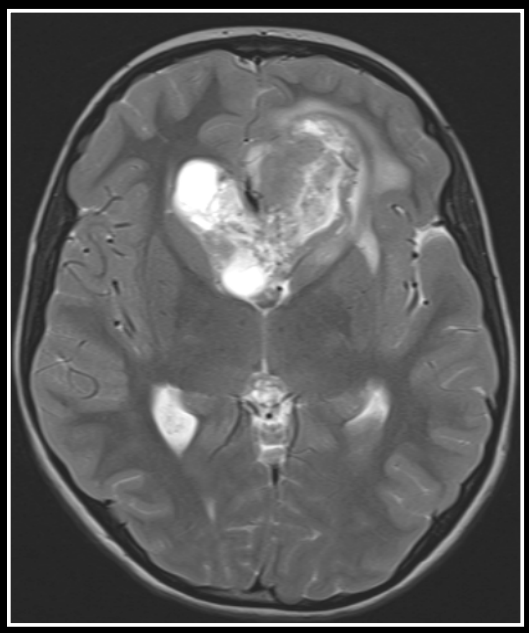
focal seizure in a 9-year old boy





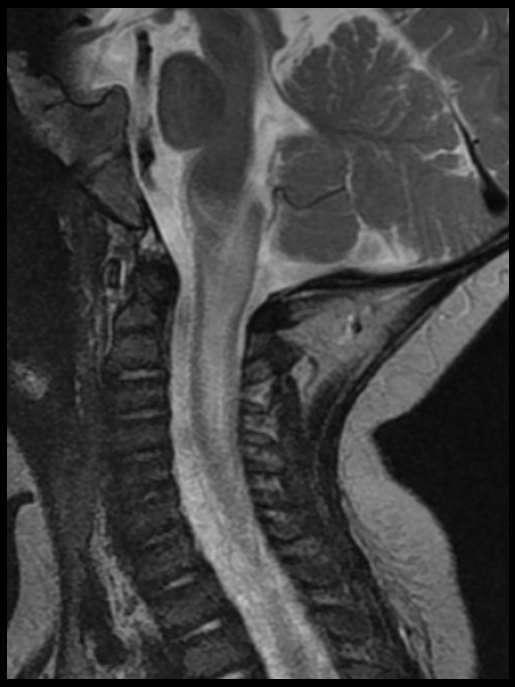
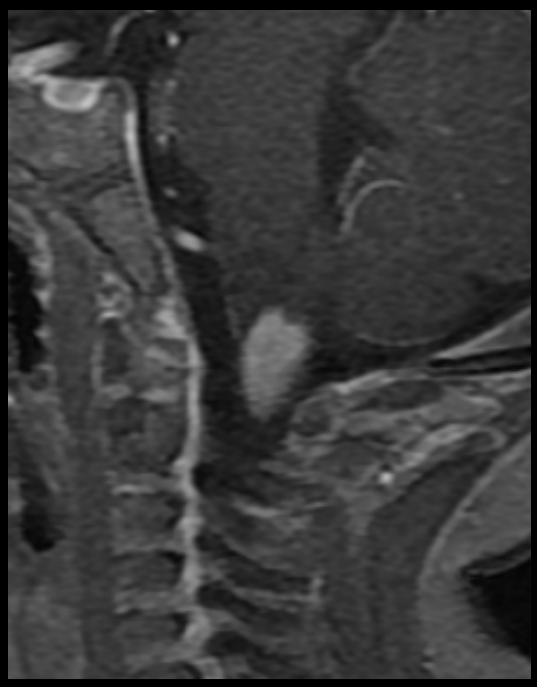
False Histological Finding

- Local Neuropathology:
  Anaplastic Ependymoma
- Reference Neuropathology
  Glioblastoma multiforme



No Histological Finding

- Acute onset of torticollis and right arm pain(?) and weakness in a 1-year old boy
- Conservative treatment for some days – no change
- MRI
  excentric (right-sided) enhancing lesion in medulla oblongata – widespread oedema in cervical cord
- Neurosurgical opinion
  preoperative: steroids

Preoperative MRI

- Operation: removal of lesion
- Intraoperative histology: PNET
- Final histology (by several institutes)
  - no CNS tumor
  - inflammatory infiltrate
  - no evodence for lymphoma
  - „ghost lymphoma“ following steroid treatment (?)
- Follow-up (8 years)
  normal MRI
  normal neurological examination

„To avoid masking a diagnosis of CNS lymphoma and other steroid-responsive diseases, steroids should be avoided until the diagnosis is established, unless severe or life-threatening mass effect is present.“ Omuro et al. Lancet Neurol 2006

Take home message

- Diagnosis of brain tumours is straightforward in the majority of patients
- Beware of pitfalls at various levels
- Re-consider examination - imaging - histology