Initial Signs and Symptoms in Children with Brain Tumors

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


Prediagnostic symptomatic interval (PSI)

Parent’s delay → Doctor’s delay → Symptoms → Signs → Imaging → Surgery → Tumor
Cummulative Distribution of PSI and Doctor’s Delay

PSI (weeks) vs. Doctors’s Delay (weeks)

- PSI (weeks)
  - Duration of PSI (weeks)
  - % of patients vs. Duration of PSI (weeks)

- Doctors’s Delay (weeks)
  - Duration of doctor's delay (weeks)
  - % of patients vs. Duration of doctor's delay (weeks)

- Year of diagnosis vs. Doctors delay (days)
  - p = -0.26
  - p < 0.001

Medical Imaging:
- CT 1976
- MRI 2009
- PEG 1974
Frequency of Signs and Symptoms Noticed by Medical Doctors >30 Days Prior to Diagnosis

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

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 neurological examination (J Neurooncol 1991)
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.

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

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
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
14.9 years old, anxiety disorder

After 5 months

After 13 months

10.8 years old, head trauma
After 5 months
After 10 months
After 16 months

7.5 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
Pitfalls in the Diagnosis of Brain Tumors

Clinical findings
– interpretation of history and examination
– request for neuroimaging at false location

Neuroimaging

Histological findings

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
- Neurosarcoïdosis
- 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
Operation: removal of lesion

Intraoperative histology: PNET

Final histology (by several institutes)
- no CNS tumor
- inflammatory infiltrate
- no evidence 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