Multimodal Differentiation of Posterior Fossa Masses of Children

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Radiology Core Clerkship
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Outline

- Anatomy of the Posterior Fossa

- Menu of Tests

- Index Patient
  - Presentation
  - Differential Diagnosis
  - Multimodal Evaluation of Posterior Fossa Mass

- Companion Patients

- Future Directions
Posterior fossa anatomy

Transverse Section: Base of Skull (upper surface)

rostral  caudal
posterior cranial fossa
cervical spinal cord
foramen magnum

sagittal section

"Neuroanatomy." EHSL - Spencer S. Eccles Health Sciences Library Home Page.

Rizzo, D.C. Fundamentals of anatomy & physiology
Menu of tests for posterior fossa masses

- **Magnetic Resonance Imaging (MRI): the clinical gold standard**
- **Plain Radiography**
  - In general, poor choice for imaging posterior fossa structures
  - Sometimes used to examine foramina at skull base

- **Computed Tomography (CT)**
  - Speed of acquisition is an advantage
  - Initial test without contrast to consider subarachnoid bleeding
  - Does give superior detail regarding tumor histology

- **Vascular Tests**
  - Often used to examine proximity to blood supply

- **Functional Tests:**
  - Occasionally, PET used to consider tumor metabolism

Adam and Dixon, eds. (2008), sagittal view
Grangier and Allison’s Diagnostic Radiology

Barkovich (2005) Pediatric Neuroimaging
Menu of tests for posterior fossa masses

- Magnetic Resonance Imaging (MRI): the clinical gold standard
  - Multiplanar imaging capabilities
  - Compatible with computerized navigation techniques
  - CT imaging can have tissue artifacts, especially in the posterior fossa
  - Sensitivity: Can identify spread to subarachnoid spaces

Barkovich (2005) Pediatric Neuroimaging
Menu of tests for posterior fossa masses

- Magnetic Resonance Imaging (MRI): the clinical gold standard
  - Multimodal approach using MR suite of tests
    - (Patient history and exam)
    - Conventional, structural MR imaging
    - MR perfusion - hemodynamic characterization
    - MR diffusion - restricted movement of nuclei
    - MR spectroscopy - biochemical environment of nuclei
Menu of tests for posterior fossa masses

- Magnetic Resonance Imaging (MRI): the clinical gold standard
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Patient Presentation

- 3 3/4 year old girl

- PMH: Asthma, RSV infection (1 yo)

- 3 weeks of headaches of increasing intensity
  - two weeks ago: one episode daily, lasting 1-2 minutes
    - debilitating (pt stops what she is doing, but she is responsive)
  - last week: several/day
  - this morning: 3 episodes
  - pain localized to the top of her head
  - frequently occurs in the morning, can awaken her from sleep
  - AM emesis

- Family Hx: noncontributory

- Physical Exam
  - active, alert, oriented; in no apparent distress
  - no seizures
  - no focal weakness
  - unsteady, with a wide-based gate; normal tone
  - no observed papilledema
Indications for neuroimaging in pediatric headache

- Headaches of <6 months duration (no response to medical tx)
- Headache associated with abnormal neurologic findings
- Persistent headaches without family history of migraine
- Persistent headaches associated with substantial episodes of confusion, disorientation or emesis
- Headaches that awaken a child repeatedly from sleep or occur immediately on awakening
- Family/medical history predisposes to CNS lesions and clinical/lab findings suggestive of CNS involvement
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Index Patient: Initial Imaging

axial CT w/o contrast

large, dense, singular mass (infratentorial)

area adjacent to mass, poorly attenuating = surrounding edema

areas of high attenuation within = internal calcifications

dilated temporal horns = hydrocephalus
1) Patient Age and History of the Present Illness

2) Infratentorial area of focal, low attenuation with internal calcifications, surrounding edema and concomittant hydrocephalus

Nonneoplastic or Neoplastic

Could MR imaging techniques distinguish between these?
- nucleus with nonzero spin → magnetic moment
- exogenous magnetic field, $B_0$

Storey (2006), Chp.1, *Methods in Molecular Medicine*
MRI: Basic Physics

Storey (2006), Chp.1, *Methods in Molecular Medicine*
MRI: Basic Physics

Longitudinal relaxation (E loss): T1
Transverse relaxation (Loss of phase coherence): T2 and T2*
MR Diffusion: phase-disrupting pulse sequence
MR Spectroscopy: chemical shift

Storey (2006), Chp.1, *Methods in Molecular Medicine*
MR Spectroscopy

myo-inositol (mI):
- astrocytic marker
- osmolyte
- phosphatidyl inositol metabolism

4 yo child
T2-weighted, axial MRI ROIs (boxed)

Panigrahy et al. (2010) Seminars in Perinatology
MR Spectroscopy

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T2-weighted, axial MRI ROIs (boxed)

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Choline (tCho, complex):
- breakdown of phosphatidyl choline
- increased membrane turnover
- increased cell density

Panigrahy et al. (2010) Seminars in Perinatology
**MR Spectroscopy**

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**Creatinine/phosphocreatinine (Cr):**
- tissue energy metabolism
- used to replenish ATP levels

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Glutamate+Glutamine (Glu+Gln):
- neurotransmitter
- energy consumption

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**N-acetyl aspartate (NAA):**
- normally functioning neurons
  - component of soma and neuronal processes

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Lactate:
- anaerobic metabolism
- concentration low in healthy tissue

Panigrahy et al. (2010) Seminars in Perinatology
Ordered Approach to reading MR Spectroscopy

1) Quality Control
- Patient Information
- Clinical History and Study

Rationale
- Procedural statements
- Basic utility of MR Spectroscopy
- ID scanner and echo times used
- Spectral Quality (“exposure”)
- Limitations (“exposure”), eg. sampling, motion artifact

2) Findings - repeat for each voxel
- Voxel Placement (“ROI”/location)
- Voxel Size (“ROI”/location)
- Echo time for region
- Detail metabolite levels
- Qualitative assessment

3) Impression (“Interpretation”)
Children’s Hospital,
Boston

Panigrahy et al. (2010) Seminars in Perinatology
1) Patient Age and History of the Present Illness

2) Infratentorial area of focal, low attenuation with internal calcifications, surrounding edema and concomittant hydrocephalus

Nonneoplastic or Neoplastic

Could MR imaging techniques distinguish between these?
Proton MR Spectroscopy distinguishes between nonneoplastic and neoplastic lesions

Index Patient

T1-weighted image, sagittal

Markedly depressed NAA

Elevated choline

Companion Patient #1 (same dx)
Proton MR Spectroscopy distinguishes between nonneoplastic and neoplastic lesions.

**Index Patient**

- Markedly depressed NAA
- Elevated choline

= suspicious for tumor

Cho/Cr ratio, 78.1% grouped cases correctly classified

Proton MR Spectroscopy distinguishes between nonneoplastic and neoplastic lesions.

**Index Patient**
- T1-weighted image, sagittal

**Companion Patient #1**
- Markedly depressed NAA

**Companion Patient #2**
- Axial T2-weighted image hyperintense

**Canavan Disease:** diffuse confluent demyelination
Index Patient: Differential Diagnosis

1) Patient Age and History of the Present Illness

2) Infratentorial area of focal, low attenuation with internal calcifications, surrounding edema in posterior fossa and concomittant hydrocephalus

- Infratentorial Tumors (%)
  - Medulloblastoma (32.4)
  - Pilocytic Astrocytoma (28.3)
  - Ependymoma (12)

Could MR imaging techniques distinguish between these?

Menkes, Harvey and Maria (2006) *Child Neurology*
Do common neoplastic lesions of the posterior fossa have distinct MR spectra?

Index Patient

T1-weighted image, sagittal

Markedly depressed NAA
Elevated choline

Companion Patient #1
Medulloblastoma

Highly malignant tumor composed of very primitive, undifferentiated small, round cells; often situated within inferior vermis

CT(-): hyperdense

Variable appearance on MR

T1: hypo/isointense to grey matter

T2: hypo/isointense to grey (solid component), decreased diffusion

MRS: markedly elevated choline, markedly depressed NAA, lactate usually present

Barkovich (2005) Pediatric Neuroimaging
Pilocytic Astrocytoma

Mixed cystic/solid mass with variable surrounding edema; endothelial cells within tumor have open tight junctions and fenestrations

CT(-): iso/hypodense to grey

Variable appearance on MR
T1 (solid portion) iso/hypointense to grey
T2 (solid portion) iso/hyperintense to grey

MRS: high choline, modestly low NAA

Medulloblastoma

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Barkovich (2005) Pediatric Neuroimaging
Ependymoma
Slow growing tumor of differentiated ependymal cells of the floor and roof of the 4th ventricle; often solid with calcifications (50%)
CT(-): iso/hyperdense to grey with punctate calcifications and small cysts
Homo- or heterogeneous on MR
T1: heterogeneous, usually slightly hypo- to isointense
T2: heterogeneous, usually isointense with hypo- and/or hyperintense components

Medulloblastoma

Pilocytic Astrocytoma

Ependymoma

Barkovich (2005) Pediatric Neuroimaging
Companion Pt #1

Companion Pt #3

Companion Pt #4

Medulloblastoma

Pilocytic Astrocytoma

Ependymoma

long-echo-time $^1$H-MRS: 135-270 msec
Companion Pt #1

Creatinine

Sagittal T2-weighted image

Companion Pt #3

Sagittal T1-weighted image

Companion Pt #4

Sagittal T2-weighted image

Medulloblastoma

Pilocytic Astrocytoma

Ependymoma

Long-echo-time $^{1}$H-MRS: 135-270 msec
Companion Pt #1

Companion Pt #3

Companion Pt #4

Medulloblastoma

Pilocytic Astrocytoma

Ependymoma

sagittal T2-weighted image

sagittal T1-weighted image

sagittal T2-weighted image

long-echo-time $^1$H-MRS: 135-270 msec

Creatinine

NAA

$\text{NAA} / \text{Cr} = ?$
Medulloblastoma

Pilocytic Astrocytoma

Ependymoma

Cr/Cho = ?

long-echo-time $^1$H-MRS: 135-270 msec
Do common neoplastic lesions of the posterior fossa have distinct MR spectra?

Medulloblastoma/PNET

Pilocytic Astrocytoma

Ependymoma

Do common neoplastic lesions of the posterior fossa have distinct MR spectra?

- Medulloblastoma/PNET
- Pilocytic Astrocytoma
- Ependymoma

Our patient’s Naa:Cho and Cr:Cho ratios suggest a diagnosis of PNET.

Do common neoplastic lesions of the posterior fossa have distinct MR spectra?

**Medulloblastoma**

**Pilocytic Astrocytoma**

**Ependymoma**

**Short-echo-time $^1$H-MRS algorithm**

Does the spectrum meet the quality control criteria?
- Is the choline peak at least 5 times that of the noise?
- Are the creatine and choline peaks well separated?

**Is the ratio NAA/Cr > 4.00?**

- Yes
- No

**Pilocytic Astrocytoma**
- For completeness check that CrCho < 0.35, and Ins/NAA < 0.50

**Is the ratio CrCho < 0.75?**

- Yes
- No

**Ependymoma**

**MEDULLOBLASTOMA**

**NB:** Additional metabolic information may be obtained by short-echo-time $^1$H-MRS, which offers increased diagnostic value.

Harris et al (2007) *Pediatric Radiology*
Do common neoplastic lesions of the posterior fossa have distinct MR spectra?

**Medulloblastoma**

**Pilocytic Astrocytoma**

**Ependymoma**

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**Short-echo-time $^1$H-MRS algorithm**

**NB:** Additional metabolic information may be obtained by short-echo-time $^1$H-MRS, which offers increased diagnostic value.

Harris et al (2007) *Pediatric Radiology*
- In Diffusion-Weighted Imaging (DWI), the rate of microscopic water diffusion within tissues can be evaluated.

- Restriction of motion can been seen in normal white matter tracts (anisotropy).

- Restriction of motion can also be seen in hypercellular/solid tumors.

- DWI can be used to distinguish between:
  - epidermoid and arachnoid cysts
  - ring-enhancing brain abscesses and ring-enhancing cystic/necrotic high-grade gliomas

- Different tumor grades: greater restricted diffusion correlates to hypercellularity, and subsequently, higher tumor grade.

- Different tumor types: restricted diffusion is less for low-grade gliomas as compared to embryonal tumors (PNET, medulloblastoma and malignant teratoid-rhabdoid tumor).

Poussaint and Rodriguez (2006)
Patient follow-up: s/p Suboccipital Craniotomy

- No evidence of residual medulloblastoma
- No evidence of leptomeningeal spread or drop metastases
- Radiation course
- Chemotherapy course
- 4 yrs s/p GTR, no evidence of recurrent medulloblastoma
- Bone age by plain radiography (AP view): 6 y, 10 mo
  (chronological age: 7 y, 11 mo)
Future Directions

• MR Spectroscopy could be used as part of a suite of diagnostic tests for the noninvasive, comprehensive diagnosis of posterior fossa masses. This might include MR Diffusion (and MR Perfusion).

• MR Spectroscopy could be used to consider:
  • Tumor Grading (including tumor heterogeneity)
  • Planning of Treatment/Monitoring of Treatment Response
    • Tumor therapy: chemotherapy/radiotherapy, surgical planning/need for complete resection
  • MR Spectroscopy provides a novel, noninvasive way to ask more basic questions about tumor biology.
    • Privileged patient population
    • Intervention, even biopsy, carries risks.
    • Masses are often inaccessible.
  • As imaging resolution improves, we can ask about heterogenous environments within the tumor that may be important in oncogenesis. In addition, one could possibly monitor metabolic responses to therapy in situ.
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Barkovich, A.J. *Pediatric neuroimaging* (Lippincott Williams & Wilkins, Philadelphia, 2005).


Panigrahy, A., Borzage, M. & Bluml, S. Basic principles and concepts underlying recent advances in magnetic resonance imaging of the developing brain. *Seminars in perinatology* 34, 3-19.


