BRAIN & SPINAL LESIONS: NOT JUST A SCIENCE

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OVERVIEW

• Background
• Clinical Presentation
• Clinical Management
  – Surgery
  – Stereotactic radiosurgery
  – Systemic Therapies
BACKGROUND

• VHL gene 3p25-26
• >200 distinct disease-causing mutations
• 1 in 360,000 live births
• Men=Women
• ~40% sporadic hemangioblastomas have VHL gene mutation
• Progressive central nervous system (CNS) hemangioblastomas associated with significant symptoms
CNS MANIFESTATIONS

• Hemangioblastomas
  – Brain
  – Spinal Cord
  – Spinal Nerve Roots

• Endolymphatic Sac Tumors (ELST)
  – Dr. M. Gluth to discuss
HEMANGIOBLASTOMAS

- WHO grade I tumors
- pVHL inhibits breakdown of HIF1α
- Tumors composed of endothelial cells, pericytes, stromal cells
## VHL TYPES

<table>
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<th>Genetic Abnormalities</th>
<th>High Risk</th>
<th>Low Risk</th>
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<td>Type 1</td>
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<td>CNS hemangioblastomas, retinal hemangioblastomas, ccRCC</td>
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VHL, Von Hippel-Lindau; CNS, central nervous system; ccRCC, clear cell renal cell cancer.
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NEUROANATOMIC LOCATION

• Posterior Fossa (Infratentorial)
  – Cerebellum
    • Posterior >Anterior
  – Brainstem
    • Posterior medulla>Elsewhere in brainstem

• Supratentorial
NEUROANATOMIC LOCATION

• SPINAL REGION
  – Spinal Cord
    • Dorsal>Ventral
  – Spinal Nerve Roots
CLINICAL PRESENTATION

• Localizable Symptoms
  – Cerebellum
  – Brainstem
  – Spinal cord
  – Spinal nerve roots

• Non-Localizable Symptoms
  – Increased intracranial pressure (ICP)
CLINICAL PRESENTATION

- Median age of CNS hemangioblastoma diagnosis = 20s-30s
- Age of onset Male = Female
- Most are asymptomatic
- Symptoms due to tumor/cyst size/location
- Saltatory (72%), exponential (22%), linear (6%) growth rates
- Synchronous & Non-Synchronous growth phases
- Spontaneous regression not common
- Non-cystic tumors may develop cysts
CLINICAL PRESENTATION

• 60-90% VHL patients develop multiple CNS hemangioblastomas
• Location of existing lesions does not increase likelihood of lesions in the same region
• ~1/2 patients have hemangioblastomas in at least 2 regions
• Cysts >tumor in size (for example, cerebellar 34:1)
PREGNANCY

• Conflicting reports
• ??Change in rate of growth??
• ??Incidence of serious complications??
• VHLA→MRI at 4 months, routine neurological evaluation, increase if new symptoms
CLINICAL MANAGEMENT

• Symptoms or anticipated progression guide management
• Imaging influences management
• ***No similar size cut-offs as in RCC***
• Management Options
  – Surgery
  – Radiation
  – Systemic Therapies
NEUROSURGICAL RESECTION

• Often curative for specific hemangioblastoma
• Can prolong life and improve quality of life (QOL)
STEREOTACTIC RADIOSURGERY (SRS)

• Optimal targets
  – ***except cyst size***
• Limited prospective data
• Limited long-term follow up
• Better evaluated in non-VHL hemangioblastomas
• Local control at 2,5,10, and 15 yrs=91%, 83%, 61%, and 51%
• Recommended in patients with unfavorable risks associated with resection or in circumstances where multiple hemangioblastomas prevent definitive surgical resection
SYSTEMIC THERAPIES

- “Holy Grail”
- **NOT** recommended in front-line setting
- Clear signals for efficacy have *not* yet been established
- VEGFR TKI
  - sunitinib
  - semaxinib
- VEGF Ab
  - Bevacizumab
  - Ongoing trial NCT01015300 (www.clinicaltrials.gov)
- Thalidomide
- Interferon Alpha
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