An Introduction to Benign Brain Tumors

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Objectives

- Discuss the features of benign primary brain tumors
- Review the three most common types of benign brain tumors, their symptoms, diagnostic tests, and management
- Review peri-operative risks specific to these patients
What makes a brain tumor benign?

- Pathology: mostly normal cells, slow growing, low ki 67, few or no mitotic figures per hpf
- Graded WHO I, WHO II
- Well defined borders, usually amenable to surgical resection, potential cure
### Malignant/high grade

- **GROSS DESCRIPTION:**
  - A. Received fresh, the specimen is labeled "right frontal brain tumor" and consists of 2.5 x 1.5 x 0.6 cm aggregate of pink-tan focally necrotic soft tissue. Representative sections for frozen section. Following the specimen is 100% submitted. Summary of sections: AFSC1-AFSC2; A1-A2-remaining tissue.
  - B. Received fresh, the specimen is labeled "right frontal brain tumor" and consists of a 3.4 x 2.4 x 1.5 cm aggregate of pink-tan, focally necrotic soft tissue covered by clotted blood. 100% submitted. Summary of sections: B1-B4. (LR/KCP)

- **DIAGNOSIS:**
  - A. Brain, right frontal lobe (resection): Glioblastoma multiforme (WHO Grade IV), see note.
  - B. Brain, right frontal lobe (resection): Glioblastoma multiforme (WHO Grade IV), see note.

  **Note:** The tumor is composed of a hypercellular proliferation of pleomorphic, malignant glial cells. There are foci of tumor cells that have oligodendrogial features. Necrosis, endothelial proliferation, and frequent mitoses are present. Immunohistochemistry demonstrates that the tumor cells are diffusely positive for GFAP and EGFR, and up to 20% are positive for p53. The proliferation rate by ki67 staining is 30-40%. There is preservation of PTEN in 20% of the tumor.

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### Benign/Low grade

- **GROSS DESCRIPTION:**
  - A. Received fresh, the specimen is labeled "skull base tumor-frozen" and consists of a 0.5 x 0.4 x 0.4 cm aggregate of firm, light tan soft tissue. The specimen is frozen in its entirety for frozen section diagnosis. Summary of sections: A1FSC-frozen section control.
  - B. Received in formalin, the specimen is labeled "skull base tumor" and consists of a 3.5 x 2.0 x 0.8 cm aggregate of rubbery tan-white tissue. Representative sections are submitted. Summary of sections: B1-B2. (LRC/PAD)

- **DIAGNOSIS:**
  - B. Skull base tumor (excision): Meningioma (WHO grade I).

  **Note:** The tumor consists of bland meningothelial cells with ovoid to spindled nuclei. The cells are arranged in a streaming pattern with whorl formation. No mitotic figures are identified.
Most Common Benign Tumors

- Meningioma: 35%
- Glioblastoma, WHO IV: 16%
- Pituitary lesions: 13.5%
- Nerve sheath tumors: 8.5%
  - 63% Vestibular Schwannoma

Extraaxial Lesions

Meningioma

- Represent up to 35% of all primary brain tumors
- Arise from protective layer of the brain, the meninges, not brain tissue itself
Meningioma

- Incidence: most common brain tumor, 6.84/100,000 person-years
- Females > males
- All ages
- 90% benign (WHO I), 5% atypical (WHO II), 1-3% malignant (WHO III)
- 5 year survival rate: 70-95%

Meningioma: Symptoms

- Asymptomatic
- Seizures, in 20-50% of patients, most common presenting symptom, not correlated to tumor aggressiveness
  - Pre-operative seizures lead to increased post-operative risk of seizure
  - Up to 1/3 of patients have post-operative epilepsy

Meningioma: Symptoms

- Headaches
  - Usually not sole presenting symptom
  - Severe, new-onset requires immediate investigation w/imaging
  - Can be caused by ICP, involvement of the meninges and vessels, inflammation, edema
- Focal neurologic deficit
- Mental status changes
- Other symptoms depending on location and size...
**Meningiomas: Risk Factors**

- **Exposure to ionizing radiation**
  - Therapeutic radiation
  - Dental x-rays? (2012)
- **Genetic disorders: NF2**
- **Sex: females > males**
  - Males are greater risk of malignancy
- **Hormones?**

AND...

### Meningioma Risk factor: Increasing Age

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Most common Histology</th>
<th>Second most common Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-34</td>
<td>Pituitary</td>
<td>Meningioma</td>
</tr>
<tr>
<td>35-44</td>
<td>Meningioma</td>
<td>Pituitary</td>
</tr>
<tr>
<td>45-54</td>
<td>Meningioma</td>
<td>Glioblastoma</td>
</tr>
<tr>
<td>55-64</td>
<td>Meningioma</td>
<td>Glioblastoma</td>
</tr>
<tr>
<td>65-74</td>
<td>Meningioma</td>
<td>Glioblastoma</td>
</tr>
<tr>
<td>75-84</td>
<td>Meningioma</td>
<td>Glioblastoma</td>
</tr>
<tr>
<td>85 +</td>
<td>Meningioma</td>
<td>Neoplasm, unsp.</td>
</tr>
</tbody>
</table>

Meningioma: Diagnosis & Management

- Complete Physical Exam
- MRI Brain, with and without contrast
- Refer to neurology if seizure is present
- Refer to neurosurgery for review
Depending on size, symptoms, pt’s age and comorbidities, treatments may include:

- Observation, serial imaging; 3-6 months, then annually
  - Many lesions do not grow
- Medical Management: anti epileptics, dexamethasone for edema and/or symptom control
Meningioma Management, cont.

• Resection: Craniotomy
• Indicated for symptomatic lesions, or those demonstrating growth over 4-6 month period
• Curative in 68-80%
  • WHO I: 5% recurrence @ 5 yrs
  • WHO II 40% recurrence rate
  • WHO III 50-80% recurrence rate
    • MEDIAN SURVIVAL< 2 YRS

Meningioma Post-op Follow up

- Follow-up based on pathology, grade
  - Radiation
  - Serial imaging
  - Follow-up with neurology for seizure medication

Meningioma: Peri-operative risks

- Cerebral edema
  - Steroids: dexamethasone
- DVT/PE
  - Craniotomy patients high risk
  - Meningioma may be higher
- Infection

Patients who do better: < 70 yrs old, <3 cardiac medications, Few comorbidities, and gross total resection

AANS
Case study #1

- 49 yr old healthy right-handed male reported one week of new-onset numbness in his right upper and lower extremities, with tingling.
- Difficulty with writing, walking was becoming more difficult as his leg felt “heavy.”
- Presented to his local ER: CT scan negative for CVA, showed “broad-based mass in left superior frontal lobe;” MRI recommended and showed “well circumscribed, lobular, avidly enhancing extra axial mass lesion at the left parietal vertex that abuts superior sagittal sinus”
- Given dexamethasone 4 mg q 6hr, Keppra 500 mg bid
Case Study #1: MRI
Case Study #1

- PE revealed WNWD male in NAD, with notable right upper and lower extremity weakness and sensory deficits
- Underwent left frontal craniotomy
- Pathology: Meningioma, WHO I, with fewer than 4 mitoses per hpf
- Strength is improving
- PLAN: MRI in 3 months, then q 6-12
Pituitary Tumors

- Pineal gland
- Hypothalamus
- Pituitary gland
- Spinal cord
- Anterior pituitary
- Infundibulum
- Posterior pituitary

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Pituitary Tumors

- 14% of all primary brain tumors
- Incidence: 2.71 per 100,000 person years
- Any age, both sexes, more common in 30’s-40’s, women of childbearing age especially
- Most are adenomas; small percent are carcinoma
- Most grow on anterior part of gland
- Functional and non-functional tumors

National Brain Tumor Society: BrainTumor.org
Pituitary Lesions: Symptoms

- Depends on type of adenoma
- Non functional: Symptoms may be caused by compression of nearby structures
  - Asymptomatic if small (micro adenoma)
  - Macroadenomas (>1 cm) may cause:
    - Headache
    - Nausea, vomiting
    - Vision loss (optic chiasm): bitemporal hemianopsia, unilateral optic atrophy, and contralateral hemianopsia
Pituitary Gland: Secreting Adenomas
# Symptoms of Secreting Pituitary Lesions

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Endocrine abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypersecretion</strong></td>
<td>Amenorrhea, galactorrhea (in women)</td>
</tr>
<tr>
<td>Prolactin</td>
<td>Impotence (in men)</td>
</tr>
<tr>
<td>Growth hormone</td>
<td>Acromegaly</td>
</tr>
<tr>
<td>TSH</td>
<td>Hyperthyroidism</td>
</tr>
<tr>
<td>ACTH</td>
<td>Cushing syndrome, Nelson syndrome</td>
</tr>
<tr>
<td>FSH, LH</td>
<td>Hypogonadism, asymptomatic</td>
</tr>
<tr>
<td><strong>Hyposcretion</strong></td>
<td>Impotence, loss of libido, osteoporosis</td>
</tr>
<tr>
<td>FSH, LH</td>
<td>Central obesity, reduced muscle mass</td>
</tr>
<tr>
<td>Growth hormone</td>
<td>Premature atherosclerosis</td>
</tr>
<tr>
<td>TSH</td>
<td>Psychiatric manifestations</td>
</tr>
<tr>
<td>ACTH</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Vasopressin</td>
<td>Addison disease</td>
</tr>
<tr>
<td></td>
<td>Polydipsia, polyuria, nocturia</td>
</tr>
</tbody>
</table>

TSH: Thyroid stimulating hormone  
ACTH: Adrenocorticotropic hormone  
FSH: Follicle-stimulating hormone  
LH: Luteinizing hormone

Blue Books of Neurology: 54-70.
Pituitary Lesions: Diagnosis & Management

- Complete PE
- Labs: Endocrine panel
- MRI Brain and Pituitary, with and w/o contrast

Management:
- Referral to endocrinology
  - Prolactinomas can usually be treated medically (Bromocriptine, Cabergoline)
- Referral to ophthalmology for visual field testing
- Referral to neurosurgery
Surgery: Indicated for lesions secreting GH, ACTH, or TSH, or symptomatic non-secreting lesions

Endoscopic, endonasal transphenoidal resection

Done with ENT surgeon

Pituitary Lesions: Surgical Management

- Leads to improvement in visual symptoms in ~90%
- Long term remission of Cushing disease (50-98%), acromegaly (50-85%) and TSH adenomas (80-91%)
- Prolactinomas refractory to oral medication also helped (91%)

Pituitary Lesions: Surgical Management

Post-op complications:
- DI: 30%, usually resolves
- Delayed hyponatremia: 1-9%
- Adrenal insufficiency: steroid replacement
- CSF leak: 0.5-3.9%
- Recurrence: 10-20% recur within 10 years
- Secreting adenomas can recur after 10 years

Pituitary Lesions: Long Term Management

- Radiation treatment may follow surgery
- Endocrine lab abnormality followed post-op
- Ophthalmology follow up
- Surveillance MRI 3 months post op, then q 6-12 months depending on pathology
Case Study #2

- 50 yr old male, chief complaint of loss of pigmentation on his face and body in April 2012.
- Seen by dermatology and was referred for endocrine evaluation for possible thyroid dysfunction as part of vitiligo workup.
- Endocrinology lab work: All normal except IGF-1: 838 (61-285)
- MRI brain & pituitary showed left lateral pituitary mass, 1 x 1 x 0.7 cm
During office visit, reported increase of shoe size over the past years from size 12 to 14. His ring and glove size had increased as well. Decreased libido.

PE: notable for prominent supraorbital ridge ("frontal bossing")
- large jaw
- elongated hands, large feet
Individual with acromegaly photographed over a 37-year span. Ages in years are in lower left corner of each photograph.

http://open.umich.edu/education
Case Study #2, Acromegaly Features

Hands of individual with acromegaly (left) compared to hand of non-acromegalic adult (far right).

http://open.umich.edu/education
Case study #2, continued

- Resection of Pituitary lesion
- Pathology: pituitary adenoma, WHO I
- Post-op MRI: no evidence of residual
- IGF levels taken post-op slowly lowered
  - 3 months post-op normalized

PLAN

- MRI, IGF1 levels in 3 months
- Follow with PMD, cardiology, endocrinology
Vestibular Schwannoma

- Also called acoustic neuromas
- Evolve from the Schwann cell sheath of the superior division of the vestibular nerve
- Caused by a mutation of chromosome 22, either sporadic or inherited as in NF2 patients
Vestibular Schwannoma

- 5% of all primary brain tumors
- 1.06 per 100,000 person-years
- Typically occur on 8th cranial nerve but can occur on other brain or spinal nerves
- Males = females
- Any age, but peaks in 65-74 yr olds

Greenberg, M. Handbook of Neurosurgery. 7th edition. Thieme. 2010
Vestibular Schwannoma
Vestibular Schwannoma: Symptoms

- Hearing loss (insidious and progressive)
- High pitched tinnitus
- Disequilibrium (rarely true vertigo)
- Headache
- Facial numbness and/or weakness
- Diploplia

Vestibular Schwannoma: Signs

Signs on PE:
- 66% have no other signs than hearing loss due to VIII involvement
  - Weber test lateralizes to uninvolved side, Rinne will usually be normal (AC>BC)
- Nystagmus
- Facial palsy
- Papilledema

National Brain Tumor Society: BrainTumor.org
Vestibular Schwannoma: Diagnosis

- MRI with and w/o contrast, Brain and IAC
- Audiology evaluation
- If <40, evaluate for NF2
  - (referral for genetic eval)

Vestibular Schwannoma: Management

Depending on size of lesion, symptoms, pt’s age:

- Observation, serial imaging
- Surgery
- Radiation treatments (SRS, XRT)
- Chemotherapy (Avastin)
- Symptom control: dexamethasone, supportive care

Vestibular Schwannoma: Surgical Risks

- Tumor resection techniques are improving
- Major challenge is preservation of facial nerve
- Facial nerve preservation inversely correlated to tumor size
  - < 2cm: 95-97% preservation of House-Brackman grade I or II function
  - 2-3.9 cm: 61-73%
  - >4 cm: 28-57%

Vestibular Schwannoma: Surgical Risks

- House-Brackmann grading

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal</td>
<td>Normal facial function in all areas</td>
</tr>
<tr>
<td>II</td>
<td>Mild dysfunction</td>
<td>Slight weakness noticeable on close inspection; may have very slight synkinesis</td>
</tr>
<tr>
<td>III</td>
<td>Moderate dysfunction</td>
<td>Obvious, but not disfiguring, difference between 2 sides; noticeable, but not severe, synkinesis, contracture, or hemifacial spasm; complete eye closure with effort</td>
</tr>
<tr>
<td>IV</td>
<td>Moderately severe dysfunction</td>
<td>Obvious weakness or disfiguring asymmetry; normal symmetry and tone at rest; incomplete eye closure</td>
</tr>
<tr>
<td>V</td>
<td>Severe dysfunction</td>
<td>Only barely perceptible motion; asymmetry at rest</td>
</tr>
<tr>
<td>VI</td>
<td>Total paralysis</td>
<td>No movement</td>
</tr>
</tbody>
</table>
Vestibular Schwannoma: Surgical Risks

- Inability to wrinkle brow
- Drooping eyelid; inability to close eye
- Inability to puff cheeks; no muscle tone
- Drooping mouth; inability to smile or pucker
Another challenge is preserving ipsilateral hearing
Also related to tumor size
20-60% cases preserved where tumor < 3 cm
Larger tumors fare worse

Vestibular Schwannoma: Post-op Follow up

- Radiation may be recommended after surgery
- Serial Imaging with MRI
- Audiology follow-up
- Symptom control
Conclusion: Parting thoughts

- Histologically benign brain tumors may pose significant clinical morbidity and reduce QOL.
- Most patients will follow with the “Neuro team” as well as their primary care providers:
  - Neurosurgeon, neuro-oncologist, radiation oncologist, seizure doctor, endocrinologist
- Psychological support
- Primary care providers have a pivotal role of helping with early diagnosis, surveillance, detecting new symptoms of recurrence or side effects from treatment, and continuing preventive care.
Thank You!
References

- American Brain Tumor Association: ABTA.org
References