Understanding Your Tumor: Tumors of the Brain Lining and Nerves

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• I have no stocks, patent rights or employment with any company

• I have consulting/advisory board agreements with: Springworks (paid), AstraZenica and Exelixis (unpaid)

• I have pre-clinical laboratory and/or clinical trial support from the following companies: GlaxoSmithKline, Bristol-Myers Squibb, Lily

• Who I am:
  • Neurologist Neuro-Oncologist
    • I take care of patients with primary brain tumors that happen sporadically or as part of genetic conditions
    • I conduct research to develop new therapies for primary brain tumors by testing new drugs as well as working to define the ways we measure success
1. Brain lining surrounds (but is not in) the CNS.
2. Nerves are in the PNS.
# Meningiomas and Schwannomas

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Percentage of All Nervous System Tumors</th>
<th>Percentage of All Benign Nervous System Tumors</th>
<th>Common Location(s)</th>
<th>Primary Neurologic Morbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningiomas</td>
<td>36.6%</td>
<td>53.2%</td>
<td>Meninges</td>
<td>Headache, focal neurologic deficit, seizures, altered mental status</td>
</tr>
<tr>
<td>Schwannomas</td>
<td>8.2%</td>
<td>12.0%</td>
<td>Cerebellopontine angle or peripheral nerve</td>
<td>Hearing loss, vestibulopathy, facial nerve dysfunction, radiculopathy</td>
</tr>
</tbody>
</table>
What is a meningioma?

A. A tumor that grows inside brain tissue

B. A tumor that grows on the coverings around the central nervous system (CNS) called the meninges

C. A tumor that grows inside the spinal cord
A meningioma is a tumor that forms from arachnoidal cells. These cells are inside of a “wrapping” around the brain and spinal cord called the meninges. Meningiomas are therefore close to but not inside the brain or spinal cord tissue (with very rare exceptions).
Meningioma
Meningioma

- The most common form is World Health Organization (WHO) grade I
  - 7.6 per 100,000 in the United States (higher prevalence in women and African Americans)
  - Incidental meningiomas seen on autopsy in 1.4% of all people
  - Increase in prevalence with advancing age

- Benign (non-malignant)
  - Account for > 1/3 of all intracranial tumors across the world
  - Often found incidentally and without symptoms
  - Most are single and occur sporadically
    - Major risk factors are:
      - Prior radiation treatment in the area
      - Genetic conditions: NF2, schwannomatosis
        - This should be suspected in people with multiple meningiomas or meningioma at a young age.
  - Depending on age and features, can monitor with imaging or examination or both
• However, depending on location, even benign meningiomas can cause:
  • Headache
  • Seizures
    • The presentation for roughly 40% of people who have symptoms associated with their meningioma
  • Focal weakness or sensory changes
  • Blockage of CSF flow
  • Change in vision / loss of vision
  • Disruption of hormonal function
  • Nerve injury

• If there are symptoms, there is a need to treat

Sanai et al, J Neurosurg, 2010
Meningioma Locations

• Location:
  • 50% are in the brain convexities
    • Tumors in convexities can be associated with headache, focal weakness, seizures, change in thinking
  • 20% are at the skull base
    • Dysfunction of the nerves that travel through or near the dura
      • Vision loss; swallow dysfunction
  • Additional locations are: cavernous sinus (major draining veins), intraventricular (in the spinal fluid cavities)
  • Least common location is spinal cord
Meningioma Imaging Features

- Imaging features
  - Computed Tomography
    - Hyperdense lesions
    - May have calcifications
    - Can have bone remodeling or there can be hyperstosis
  
- Magnetic Resonance Imaging
  - Isointense on T1-weighted images
  - Variable on T2-weighted images
  - Densely enhancing with contrast enhancement
If no symptoms and no change over time, observe

- Surveillance, Epidemiology, and End Results Program database indicated that more than 60% of WHO grade I meningiomas had no treatment, and the 5-year survival estimate was 85.6% (95% confidence interval, 85% to 86.2%).

- After initial diagnosis, for low risk tumors can monitor with CT or MRI
  - Advantage of MRI is has FLAIR sequence
    - FLAIR change can indicate a biologic change in brain tissue around the meningioma and does not have radiation
  - Advantage of CT is no need for contrast enhancement, low cost, rapid

- Interval for imaging is dependent of lesion features. For low risk lesions the following is reasonable:
  - Imaging and clinical surveillance at 3, 6, and 12 months post diagnosis.
  - If stable at 1 year, the surveillance interval is increased to every 6 or 12 months for 5 years and once every 2 to 3 years thereafter.

NCCN guidelines, 2019
What are symptoms that could lead to the recommendation to treat?

**Table 2. Symptoms of Brain Tumors.**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Low-Grade Gloma</th>
<th>Malignant Gloma</th>
<th>Meningioma</th>
<th>Primary Central Nervous System Lymphoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>40</td>
<td>50</td>
<td>36</td>
<td>35</td>
</tr>
<tr>
<td>Seizure</td>
<td>65–95</td>
<td>15–25</td>
<td>40</td>
<td>17</td>
</tr>
<tr>
<td>Hemiparesis</td>
<td>5–15</td>
<td>30–50</td>
<td>22</td>
<td>24</td>
</tr>
<tr>
<td>Mental-status</td>
<td>10</td>
<td>40–60</td>
<td>21</td>
<td>61</td>
</tr>
<tr>
<td>abnormalities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DeAngelis, NEJM, 2001
DeAngelis&Posner, 2009
Prevalence of seizures differs by histology

### Table 4. Tumor pathology and occurrence of seizures (n = 711)

<table>
<thead>
<tr>
<th>Tumor Pathology</th>
<th>Patients</th>
<th>With seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Low-grade astrocytoma</td>
<td>53</td>
<td>22</td>
</tr>
<tr>
<td>Anaplastic astrocytoma</td>
<td>30</td>
<td>13</td>
</tr>
<tr>
<td>Glioblastoma</td>
<td>106</td>
<td>27</td>
</tr>
<tr>
<td>Oligodendroglioma</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td>Ependymoma</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Mixed glioma</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Medulloblastoma</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>Schwannoma</td>
<td>27</td>
<td>0</td>
</tr>
<tr>
<td>Meningioma</td>
<td>124</td>
<td>47</td>
</tr>
<tr>
<td>Anaplastic meningioma</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Hemangioblastoma</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Metastatic tumor</td>
<td>105</td>
<td>16</td>
</tr>
<tr>
<td>Without histology</td>
<td>138</td>
<td>17</td>
</tr>
</tbody>
</table>

The pathology of 59 tumor patients with very low incidence (<5) is not given.

* p < 0.05, ** p < 0.005, *** p < 0.001.
Seizures in the Setting of Meningiomas

• Presenting sign of tumor: 30-40%
• In the course of living with the tumor: 40%
  • Can be from meningioma or from interventions:
    • 15-20% who did not present with seizure, develop seizures post-operatively
    • 50-90% of patients presenting with seizures gain seizure control post-operatively
What are the indications for use of anti-seizure medications in patients primary brain tumors?

A. Presence of lesion on MRI
B. Presence of swelling on MRI
C. Has had at least one seizure
D. Ongoing use of stimulant medications
E. Presence of anxiety
F. Patient and physician preference
What are the indications for use of AEDs in patients primary brain tumors?

A. Presence of lesion on MRI
B. Presence of swelling on MRI
C. Has had at least one seizure
D. Ongoing use of stimulant medications
E. Presence of anxiety
F. Patient and physician preference
Seizure prophylaxis: AAN Guideline

- Review of 4 randomized clinical trials (level I evidence) and 8 cohort studies (level II evidence)
- Total of 1017 patients
  - 678 metastasis (67%), 276 glioma (27%), 46 meningioma (5%), 17 other (2%)
- 26% incidence (range, 14%-51%) of seizures before/at diagnosis
- Anti-seizure drugs: dilantin, valproate, phenobarbital
- Results:
  - 42% receiving prophylaxis has sub-therapeutic levels
  - No studies favored the prophylaxis group
  - 24% experienced side effects leading to change or discontinuation of anti-seizure drugs

Anti-seizure treatment is appropriate for patients with seizures

- Older agents (dilantin, phenobarbital, carbamazepine) induce P450 enzymes
  - Alter levels of corticosteroids and chemotherapy agents
- Newer agents have fewer interactions and are generally preferred
  - Levetiracetam, topiramate, lamotrigine, lacosamide
  - No trials comparing efficacy of newer agents for brain tumor patients
  - Valproate may be beneficial for patients receiving radiation and temozolomide
- Most patients have good seizure control with one agent

- Exceptions to the guidelines:
  - Meningiomas with edema: there are studies showing edema is associated with a higher risk of seizure (odds ratio 3.5) and I often recommend an agent like leviteracitam in that setting

Weller et al, Neurology, 2011
Simis et al, Surgical Neurology, 2008
• Treatment for grade I meningioma
  • If there is concerning progression, or development of symptoms:
    • First line therapy is surgical resection
      • If complete surgical resection is feasible, there is a <10% chance of recurrence over 10 years
        • Can proceed with monitoring alone post-operatively
      • If there is incomplete resection, there are recurrence rates between 20-40% over 10 years
        • Hence, depending on the degree of resection, radiation may be indicated
    • If surgery is not feasible, radiation therapy is first line therapy

Psammoma bodies
Whorls

Lefkowitz MA, Neurosurgery Focus, 1997
• Grade II lesions = Atypical meningiomas
  • Roughly 15% of meningiomas
  • On pathology:
    • > 4 mitoses per 10 high-power fields; high cellularity, small cells with high nuclear to cytoplasmic ratio, prominent nucleoli, sheet like growth, and areas of necrosis
    • Or grade I features with evidence of brain invasion
  • These features increase the risk for recurrence after treatment (surgery, radiation or drug)

• Grade III lesions = Malignant meningiomas
  • Roughly 2% of all meningiomas
  • On pathology:
    • As above, except more mitoses (20 mitotic figures per 10 high-power fields)
    • Can be identical to sarcomas
Treatment of Atypical and Malignant Meningioma

- Atypical meningiomas
  - Surgical resection
    - If this is complete, radiation can be considered, not obligate
      - If there is incomplete surgical resection, radiation therapy is indicated

- Malignant meningiomas
  - Resection followed by radiation therapy and consider chemotherapy
    - The chemotherapy with the best activity to date is sunitinib
      - People with progressive grade II or grade III meningiomas after surgery and radiation therapy were treated with sunitinib 50 mg/d with a 6 month progression free survival of 42% and median overall survival of 25 months
      - Multiple clinical trials are ongoing including:
        - Immunotherapies
        - Receptor tyrosine kinase inhibitors targeted to specific pathways or mutations
• Most commonly seen in genetic conditions
  • Neurofibromatosis type 2 (NF2):
    • Neurogenetic condition caused by mutation in the NF2 gene on chromosome 22
    • Prevalence 1/56000
      • Pathognomonic finding = vestibular schwannomas on each eighth nerve
      • 60% of people with NF2 have >1 meningioma and meningioma burden is a major risk for mortality
        • However, many do not need any intervention
        • Need to monitor for signs of elevated intracranial pressure
Symptoms in NF2:

- Hearing loss
- Tinnitus
- Cranial neuropathies
- Ataxia or Balance problems
- Facial weakness
- Swallow dysfunction
- Muscle wasting
- Weakness
- Paralysis
- Sensory loss
- Gastropareisis
- Vision impairment
- Pain
The nerves that control the movement of the face, the movement of the eyes and functions like swallow are called the cranial nerves.

Are those nerves part of the central nervous system or the peripheral nervous system?

A. Central nervous system
B. Peripheral nervous system
C. Both
B. The cranial nerves have their function in the peripheral nervous system. However, *the cranial nerves start in the brainstem (the nuclei)*.
Schwannomas: Peripheral Nerve Sheath Tumor

What Schwann cells do for peripheral nerves:

Image from: www.quora.com
Schwannomas

- Benign tumors of the nerve sheath
- Relatively “bland” tumors - composed of Schwann cells

- What do they do?:
  - Often: nothing, can grow silently
  - But more often than we want, their growth causes:
    - Neurologic dysfunction
      - Sensory change
      - Weakness
    - Cranial nerve dysfunction
      - Hearing loss, facial weakness
    - Compression of neighboring organs/structures
    - Pain

Lin and Crane, Am J Neuroradiology, 2017
Cranial Nerve Schwannomas

- Schwannomas on the 8th cranial nerve, the vestibular nerve = vestibular schwannomas (VS; aka acoustic neuromas)
  - The most common schwannoma
  - Can cause hearing loss, imbalance, facial weakness and if large enough, can compress the brainstem

- People with the genetic condition, neurofibromatosis type 2 (NF2), commonly develop VS on both sides and so are at risk for deafness, facial weakness on both sides and severe imbalance.
Vestibular Schwannoma

- Arise from the vestibular portion of the VIIIth cranial nerve
- Present with auditory symptoms.
- Typically slow growing and cause slow deterioration in hearing.
- Balance and other cranial nerve functions may become impaired
- Brainstem compression and obstructive hydrocephalus can occur with large tumors.
- Bilateral VS are the primary sign of NF2.
The Critical Triangle

- Hearing
- Balance
- Facial weakness
- Facial sensation
- Swallow
- Taste
- Speech
Critical cranial nerve considerations with schwannoma

- Facial nerve (VII)

Courtesy of Kofi Boahene
Facial re-animation procedures

- By plastic surgery and ENT
- Small, targeted procedures (brow lifts, Botox)
- Large reconstructive surgeries
  - temporalis tendon transfer, digastric muscle tendon transfer
  - facial nerve-hypoglossal nerve, masseter to facial nerve transfer, cross facial nerve grafting
Voice and Swallowing Function

- N=42, median age 26 (3-64)
- CPA surgery:
  - 9 (21%) bilateral
  - 14 (33%) unilateral
  - 19 (45%) no surgery
- RT: 11 (26%)

<table>
<thead>
<tr>
<th>Cranial Nerve</th>
<th>Normal Function</th>
<th>Abnormal Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial nerve (CN VII)</td>
<td>17 (40%)</td>
<td>25 (60%)</td>
</tr>
<tr>
<td>Hearing (CN VIII)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>5 (12%)</td>
<td>3 (7%)</td>
</tr>
<tr>
<td>Mild/moderate loss</td>
<td>3 (7%)</td>
<td>34 (81%)</td>
</tr>
<tr>
<td>Severe/profound loss</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Balance (CN VIII)</td>
<td>15 (36%)</td>
<td>27 (64%)</td>
</tr>
<tr>
<td>Palate (CN X)</td>
<td>34 (81%)</td>
<td>8 (19%)</td>
</tr>
<tr>
<td>Tongue (CN XII)</td>
<td>32 (74%)</td>
<td>10 (24%)</td>
</tr>
</tbody>
</table>

Voice Handicap Index Scores distributions for normal (n = 26) and abnormal (n = 14) levels of self-perceived voice dysfunction in NF2 patients.

- 14/40 (35%) had self-assessed voice handicap
- 20/40 (50%) patients had a self-assessed swallow handicap
- 22/31 (71%) had vocal fold motion impairment
- 45% had velopharyngeal insufficiency
Nerves of greatest concern for swallowing

• Facial nerve (CN VII)
• Vagus nerve (CN X)
• Glossopharyngeal nerve (CN IX)
• Hypoglossal nerve (CN XII)

Oral Phase Swallowing Difficulties:
• Incomplete lip closure
  • Drooling
  • Difficulty drinking from a cup
  • Difficulty biting off items
  • Loss of food through the front of the mouth
• Lack of cheek tone
  • Loss of food/liquid to the space between the cheek and the teeth
• Trouble with chewing
• Extra time needed to prepare food for swallowing

Throat Swallowing Difficulties:
• Voice box (larynx)
  • Difficulty with choking while eating/drinking
• Palate
  • Food/liquid going up the nose
• Throat muscles
  • Food/liquids/pills getting stuck in the throat
• Sensory disturbance
  • Swallow may be slow to trigger
  • May not feel material in the throat to clear it
Safety concerns

- Choking
  - Family members should be trained in Heimlich maneuver

- Aspiration
  - Risk for developing pneumonia
  - Oral hygiene important for reducing pneumonia risk

- Weight loss
  - ? Need for supplements, diet changes, feeding tubes
  - Nutrition consultation
Spinal Schwannomas
Spinal Schwannomas: Clinical Presentation

- Often silent (asymptomatic)
- Sometimes pain or paraesthesias
- Rarely, progressive myelopathy
  - Tight, stiff muscles
  - Difficulty waking
  - Difficulty with bowel and bladder function
    - Requires surgery
Schwannomatosis

- Genetic condition
- The rarest form of NF
- Incidence: 1/60,000

- Genetic condition but mechanisms not well understood
  - Most frequently sporadic (no other affected relative)
  - Approximately 20% familial

- Genes associated
  - INI1 (SMARCB1) and LZTR1
    - Tumor suppressor genes

- Rare neurocutaneous syndrome (~1 in 40,000)
  - Diagnostic criteria established in 2005 (MacCollin) – Definite vs Probable
- Germline mutations in LZTR1 and SMARCB1 genes
- Multiple peripheral nerve or spinal schwannomas
- Pain is most common symptom, not correlated to tumor burden
- Surgery only current effective option (imperfect)
Clinical Findings in Schwannomatosis

- Multiple schwannomas are the hallmark feature of schwannomatosis
  - Spinal nerve roots
  - Distal nerves
- Meningioma is seen in about 5% of patients
- Segmental disease is seen in about 30% of patients
- Subcutaneous schwannomas are seen in 20-30% of patients
- Average age of symptom onset is 25-30 years
- Average age of diagnosis is 40 years
- Pain is the most common presenting symptom
- The overall tumor burden in patients with schwannomatosis has not been well characterized and is difficult to assess clinically
Symptoms in Schwannomatosis

- Chronic pain is common
  - Complex
  - Presents with mixed features
  - Can be difficult to manage medically and can become disabling
  - Most often not associated with a discrete mass

- Focal neurologic deficits:
  - Numbness
  - Weakness
  - Atrophy

- Tumor
  - Palpable vs. Radiographic
Symptom Management: Pain

Medications:

- **Anti-epileptics**
  - Gabapentin (Neurontin)
  - Pregabalin (Lyrica)
  - Carbamazepine (Tegretol)
  - Lamotrigine (Lamictal)

- **NSAIDS:**
  - Celebrex
  - Naproxen
  - Meloxicam
  - Ibuprofen

- **Anti-depressants**
  - Amitriptyline (Elavil)
  - Nortriptyline (Pamelor)
  - Cymbalta
  - Effexor

- **Benzodiazepines**
  - Diazepam
  - Clonazepam

- **Topical Agents**
  - Lidocaine Gel/Patches
  - Capsaicin

- **Opioid Analgesics**
  - Tramadol

- **Narcotic Agents**

- **Vitamin supplements**
  - Vit D, B12

Interventions:

- Nerve Block
- Injections
- Physical and Occupational Therapies
- Yoga
- Meditation
- Cognitive-Behavioral Therapy
- Surgery
Sporadic Peripheral Nerve Sheath Tumors: Natural History Study at Johns Hopkins

265 PNSTs
- Sex: 149 female (56%)
  - Age: 50.5 +/- 15.5 years
- Peripheral nerve: 91 (34%)
  - Brachial plexus: 36 (14%)
  - Spinal canal: 138 (52%)
    - Cord compression: 41 (30%)

148 initial observation
- Sex: 90 female (61%)
  - Age: 52.7 +/- 14.8 years
- Peripheral nerve: 37 (25%)
  - Brachial plexus: 19 (13%)
  - Spinal canal: 92 (62%)
    - Cord compression: 13 (14%)

117 upfront surgery
- Sex: 59 female (50%)
  - Age: 47.6 +/- 15.3 years
- Peripheral nerve: 54 (46%)
  - Brachial plexus: 17 (15%)
  - Spinal canal: 46 (39%)
    - Cord compression: 28 (61%)

124 long-term observation
- Sex: 73 female (59%)
  - Age: 53.1 +/- 14.6 years
- Peripheral nerve: 27 (22%)
  - Brachial plexus: 12 (10%)
  - Spinal canal: 84 (68%)
    - Cord compression: 8 (9%)

24 delayed surgery
- Sex: 16 female (67%)
  - Age: 50.9 +/- 15.5 years
- Peripheral nerve: 9 (38%)
  - Brachial plexus: 7 (29%)
  - Spinal canal: 8 (33%)
    - Cord compression: 5 (62%)
Histopathology of PNST by location

- Peripheral nerve (74 specimens)
  - Schwannoma 68 (92%)
  - Ganglioneuroma 2
  - Neurofibroma 2
  - NF/Schwannoma 2
  - MPNST 1

- Brachial plexus (27 specimens)
  - Schwannoma 23 (85%)
  - Neurofibroma 1
  - NF/Schwannoma 1
  - Myxoma 1
  - Myoepithelioma 1

- Spinal (66 specimens)
  - Schwannoma 55 (83%)
  - Myxopapillary ependymoma 5
  - Meningioma 3
  - Neurofibroma 2
  - Hemangioma 1
Long-term observation only for PNST

- **Rationale**
  - Asymptomatic finding most common: 115/124 (93%)

- **Location**
  - Spinal canal most common 84/115 (68%)
    - 8/84 (9%) had cord compression

- **Median 21 months follow up**
  - 41/124 (33%) grew → 2.2mm/yr
  - 12/124 (10%) had symptom progression
Delayed surgery for PNST

- **Rationale**
  - Symptoms, no imaging change 11/24 (46%)
  - Symptoms + imaging change 8/24 (33%)
  - Imaging change 4/24 (16%)
  - Patient preference 1/24 (4%)

- **Location:**
  - Peripheral nerve (38%), spinal canal (33%), brachial plexus (29%)
    - 62% of spinal tumors had cord compression

- **Median 9 months after initial consult**
  - 14/24 (58%) grew → 2.5mm/year
Upfront surgery for PNST

- **Rationale**
  - Symptoms: Pain 76 (65%), myelopathy 18 (15%), weakness 12 (10%), diagnosis 11 (9%)

- **Location:**
  - Peripheral nerve 54 (46%), spinal canal 46 (39%), brachial plexus 17 (15%)
    - 28/46 spinal tumors (61%) had cord compression

- **Outcome (median 6 months):**
  - 104 (89%) improved (40/46 spine, 15/17 BP, 49/54 PN)
  - 9 (8%) stable (5 spinal, 4 PN)
  - 4 (3%) deteriorated (2 BP, 1 PN, 1 spinal)
Conclusions about sporadic peripheral nerve sheath tumors

• Up to 2/3rd do not grow
• Schwannoma is most common lesion
• Incidental finding and pain most common presentations
• Observation a reasonable option in non-syndromic, extra-cranial nerve sheath tumors
  • Spinal lesions that are small, asymptomatic, and not causing cord compression likely most amenable

• No cases in this series had malignant conversion, although there are rare reports of this in the literature and there is some suggestion that the risk for malignant conversion is higher after radiation
Proposed Management Strategy for PNST

- Extra-cranial NST referral
  - History, physical, full neuro-axial MRI
  - Malignant features

- Non-syndromic NST
  - Incidental finding/asymptomatic
  - Location
    - Peripheral nerve/brachial plexus
    - Spinal canal
      - Max diameter < 10mm
      - No cord compression

- Symptomatic
  - Pain
  - Trial of observation
    - Yes
    - No

- Motor dysfunction/myelopathy
  - Malignant features on imaging or Growth > 2mm/year

- Surgical intervention**
Meningiomas are tumors of the lining surrounding the brain. Peripheral nerve sheath tumors are common and of various “flavors”; the most common are schwannomas – tumors of the cells that insulate the peripheral nerves. In both cases, a majority of the tumors are benign and only need intervention if they are causing symptoms or growing rapidly. The type of symptom is specific to the tumor location. Various care providers can be involved in management of the symptoms (neuro-oncology is a good place to start in general). Rarely, there can be more aggressive forms of these tumors that require cancer management.

Summary
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THANK YOU!

- Our patients and their families
- The Johns Hopkins Comprehensive Neurofibromatosis Center
  - Allan Belzberg
  - Verena Steadtke
  - Shannon Langmead
  - Emily Little
  - Leslie Morgan
  - Mary Brown
  - Simon Best
  - Kofi Boahene
  - Shivani Ahlawat
  - Laura Fayad
  - Alireza Mansouri