CEREBELLOPONTINE ANGLE TUMORS: DIAGNOSIS AND MANAGEMENT

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Grand Rounds Presentation
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Outline

- History of CPA tumors
- Discuss Relevant Anatomy
- Epidemiology and Tumor Biology
- Signs/Symptoms of CPA tumors
- Brief overview of other CPA tumors
- Treatment options
- Present a case presentation
Overview of CPA Tumors

- Represent 10% of all intracranial tumors
- Vestibular Schwannomas/Acoustic Neuroma represent 78% of these tumors (1)
- Differential
  - Meningiomas
  - Epidermoid
  - Other Cranial Nerve Schwannomas
  - Dermoid Tumors (Chordomas, Teratomas)
  - Arachnoid Cysts
  - Lipomas
  - Metastatic Tumors
  - Vascular Tumors (Hemangioma/Glomus Tumor)
History of CPA Tumors

- Sir Charles Balance (2,3)
  - 1894 First successful removal of Vestibular Schwannoma
  - 1907 Patient still alive but had CN VII paresis

- Harvey Cushing
  - 1917 Monograph described CPA syndrome
  - Pioneered subtotal resection through bilateral suboccipital craniectomy
History Continued

- **Walter Dandy (5)**
  - Advocated debulking with capsule removal and decreased operative mortality to 10%

- **William House (6-8)**
  - Advocated Translabyrinthine approach 1960’s
  - Introduced the microscope and dental drill to identify the facial nerve
  - Introduced middle cranial fossa approach
Ipsilateral Hearing Loss

Facial Hypesthesia

Hydrocephalus

Respiratory Failure and Death
Autopsy series have shown incidence of 1.7 to 2.7% (9,10)

MRI of 10,000 patients seen for non-otologic reasons showed 7 positive cases or 0.07% (11)

Denmark reports of 1.3 per 100,000 population (12)
1. They are not Neuromas

2. They rarely are found on the acoustic portion of the nerve

*Involvement of the acoustic portion of the nerve often leads to erosion of the cochlea.
Arise from Schwann cells within the IAC (1)
Equal frequency between inferior and superior divisions of the vestibular nerve.
Arise from Scarpa Ganglion instead of Obersteiner-Redlich zone.
- Scarpa’s ganglion has highest density of schwann cells
NF 2 Gene found at 22q12
- Tumor suppressor gene preventing schwann cell proliferation

Sporadic Variety (95%) (13)
- Hypothesized that there are two hits to the normal NF gene

Neurofibromatosis type II
- Autosomal Dominant
- Inherit one abnormal and one normal gene with one hit to the normal allele.
- Blood tests available to screen family members.
Biochemical Effects

1. Neuregulin
   - Expressed by schwann cells to control proliferation and survival of schwann cells

2. Chemokines
   - FGF, TGF-β, VEGF, PDGF (14-17)

3. Sex Hormones (18)
   - Previous studies showed increased growth in pregnancy
   - Recent studies have not shown growth modulation or receptors for sex hormones
Workup

- History and Physical Exam
- Audiologic testing
- Vestibular Testing
- Imaging
Symptoms

- **Intracanalicular tumors**
  1. Hearing Loss
  2. Tinnitus
  3. Vestibular dysfunction/Vertigo

- **CPA extension**
  1. Disequilibrium/Ataxia

- **Brainstem Extension**
  1. Midface Hypesthesia
  2. Hydrocephalus (vision loss and headache)
  3. Other Cranial Neuropathies

*SNHL > tinnitus > disequilibrium > facial hypesthesia (13)
Unilateral Hearing Loss

- Present in >85% of patients (19)
- 5% of patients with VS have no associated hearing loss (20)
- Speech discrimination out of proportion to HL
  - Many notice difficulty on the telephone
Association with SSNHL

- Occurs in up to 20% of patients (13)
- 1% of patients with SSNHL have a vestibular schwannoma (21)
- 48% of patients with SSNHL will have some recovery of hearing (21)
  - Don’t rule out VS if they recover
Tinnitus

- 2nd most common presenting sign
- Often precedes hearing loss
- Can be present without hearing loss
- Can be high pitch, hissing, or a roar
- Can localize to the opposite ear
- Unilateral tinnitus should be evaluated
36-50% of patients describe disequilibrium (1)

Vague, transient lightheadedness

Acute vertigo is presenting symptom in 27% of patients but is associated with smaller tumors.
Facial Hypesthesia

- Presenting symptom in 4% of patients
- Larger tumors >2cm
- Maxillary division 1st
- Corneal reflex is the first to go
- Facial weakness is rare
  - If present should assume a different type of tumor.
Ocular Complaints

- Rare
- Loss of corneal reflex
- Nystagmus (toward affected side)
- Diplopia
  - Involvement of CN VI
- Blurry vision
  - Papilledema and optic atrophy from compression
Signs

- **Hitselberger Sign**
  - Decreased sensation of EAC
  - Sensory VII more sensitive than Motor VII
- Absent corneal reflex, nystagmus
- Hypesthesia to pinprick and touch
- Weakness of Temporalis/Masseter muscles
- Other cranial neuropathy’s
- Gait disturbances or difficulty with finger to nose testing
Audiologic Testing

- Downsloping high frequency SNHL 65% (22)
- 5% of patients show no hearing loss (23)
- Rollover: Speech discrimination worse than expected and worse with increased sound intensities
  - Retrocochlear losses more common than cochlear
# Hearing Classification Scales (24)

<table>
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<tr>
<th>AAO-HNS classification</th>
<th>Class</th>
<th>Pure tone average (0.5, 1, 2, 3 kHz measured in dB HL)</th>
<th>Speech discrimination score (%)</th>
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<td>Speech discrimination score (%)</td>
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<td>A</td>
<td>0–30</td>
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<td>C</td>
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<td>Any</td>
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<th>Gardner-Robertson Classification</th>
<th>Class</th>
<th>Pure Tone/Speech Reception Threshold (dB HL)</th>
<th>Speech Discrimination Score (%)</th>
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<td>Class</td>
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<td>Pure Tone/Speech Reception Threshold (dB HL)</td>
<td>Speech Discrimination Score (%)</td>
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<td>&gt;90</td>
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<th>Word Recognition Scores</th>
<th>Class</th>
<th>Word Recognition Score (%)</th>
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<td>I</td>
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<tr>
<td>III</td>
<td>1–50</td>
<td>w C</td>
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<tr>
<td>IV</td>
<td>0%</td>
<td>w C</td>
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Acoustic Reflexes

**Positive test has 85% sensitivity for identifying retrocochlear problem

- **Acoustic Reflex Threshold**
  - Increased (compared with cochlear norms) or absent if retrocochlear process
Auditory Brainstem Evoked Response

- Sensitivity of 85 to 90% (25)
- False Positive rate 10%
- False Negative rate 18-30% for intracanalicular tumors
  - Number larger than in the past
- Five waveforms are produced with the most common being a latency in wave V compared to the normal ear of >0.2msec.
- Recommended as a screening test for those with low suspicion of vestibular schwannoma.
70-90% of patients will show some abnormality (26)

50% of small tumors produce no abnormalities (27)

Caloric testing is commonly the only abnormality

Inferior vestibular nerve tumors may be missed

- Superior nerve showed decrease in 98%
- Inferior nerve shows decrease in only 60% (28)
- Therefore not used as a screening test
90% of vestibular schwannomas will enhance with contrast

Frequently misses tumors that are not intracanalicular and do not extend >5mm to the CPA.

- 63% accuracy at diagnosis (29)
MRI

- Gold Standard for Vestibular Schwannomas
  - Can identify tumors as small as 3mm (30)
- Gadolinium is preferentially taken up by tumor
  - Better visualization of small tumors
- Gadolinium enhanced studies
  - Hyperintense on T1 and T2 studies
- Non-contrasted studies
  - Hypointense T1, Isointense on T2
- Some recommend T2 fast spin-echo MRI as screening test but most will likely require at thin slice MRI if abnormalities are found (31)
VESTIBULAR SCHWANNOMA

- Centered on IAC
- Globular appearance
- Ice cream cone appearance in IAC
- Bony erosion of IAC
- Cystic degeneration or hemorrhage may be present

MENINGIOMA

- Extend along petrous ridge
- Sessile appearance
- “Dural Tail” at periphery
- Iso/Hypointense on T1
- Hypo to Hyperintense on T2
Acoustic vs Meningioma
Differential Diagnosis
Meningiomas

- 3% of all CPA tumors (13)
- Do not metastasize but do recur due to bony invasion
- Are formed from cap cells around arachnoid villi near dural sinus’ and where CN’s enter their foramina
- Generally are not intracanalicular so must be larger to cause hearing concerns
Meningioma

- Signs and Symptoms (32)
  - Usually cause spontaneous nystagmus, facial hypesthesia, and gait ataxia
  - If inferior can cause hoarseness, dysphagia, tongue atrophy
  - If within the IAC can produce similar symptoms as Vestibular Schwannoma

- Hearing tests will show retrocochlear process if large enough, and 25% will have normal ABR’s (33)
Meningioma

- **Treatment**
  - **Surgical Excision**
    - Must remove rim of normal dura and possibly bone
  - **Poor hearing**
    - Translabyrinthine approach
  - **Good hearing**
    - Suboccipital or Middle Fossa Approach
    - Middle Fossa is better for more superiorly based tumors.
Epidermoids

- Identical to cholesteatoma
- Develop from epithelial rest cells
- Slow growing
  - Commonly don’t present until 20-30’s
- Arise adjacent to brainstem and infiltrate areas of least resistance
  - Can have irregular shape and infiltrate widely
Epidermoids

- **Signs/Symptoms**
  - Facial twitching is commonly described
  - Can become quite large before causing symptoms
  - Progressive facial paralysis more common than schwannomas

- **Audio/ABR/Speech discrimination consistent with other retrocochlear losses**

- **Treatment is surgical excision**
MRI Epidermoid (13)
MRI Arachnoid Cyst (13)
Facial Schwannoma

- Histologically identical to Vestibular Schwannomas

- Characteristics
  - Rarely restricted to IAC
  - Commonly have skip lesions
  - Generally involve part of geniculate ganglion
Facial Schwannoma

- **Signs/Symptoms**
  - Unilateral hearing loss
  - Tinnitus
  - Vertigo
  - Aural fullness (if distal to geniculate)
  - Facial weakness is rare unless very large

- Hearing tests show retrocochlear process but impedance testing can show ipsilateral absent acoustic reflex
Facial Schwannoma

- Treatment is observation
- If growth or facial nerve dysfunction
  - Resection of nerve with cable grafting
  - Translabyrinthine approach most commonly used
- Facial nerve decompression can be used if paresis is developing
Other CPA Tumors (1)

- **Glomus Tumors**
  - Jugular Foramen Syndrome (IX,X,XI), Surgical excision

- **Hemangiomas**
  - Centered on geniculate, slow progressive facial weakness, surgical excision with facial nerve grafting

- **Arachnoid Cysts**
  - Treatment is drainage

- **Cholesterol Granulomas**
  - Bright on T1 and T2, Drained via infralabyrinthine approach

- **Embryonic tumors (Dermoids, teratomas, chordomas)**
  - Excision with dysfunction

- **Primary Axial Tumors of CNS (glioma, hemangioblastoma, medulloblastoma)**
  - Surgical excision +/- radiation therapy
Management

- Observation
- Surgery
- Stereotactic Radiosurgery
- Radiation Therapy

**Generally tumors <3cm can be treated with stereotactic radiosurgery but microsurgery is the treatment of choice**
Growth rates vary from 0 to 2cm per year with an average of 2mm (34)
38.9-82% have some growth at ≥38 months (24)
14 to 24% of patients watched will go on to have some treatment (12)
Age should not be determining factor
1. Young patient with small tumor
2. Older patient with large tumor
3. Older patient with small tumor
Single MRI is not adequate
   ▪ Repeat at 6 months and then again yearly
Longstanding hearing loss may represent a slow growing tumor (35)
Radiation Therapy
First Introduced Leskell in 1969

Gamma Knife
- Uses 201 ionizing beams of gamma rays from cobalt 60 source
- One session

LINAC
- Uses multiple beams from a linear accelerator
- One session

Fractionated Radiotherapy
- Newer therapy to eradicate cells in different cell cycle stages
- Multiple sessions

Goal is to stop tumor growth, not shrink or remove tumor
Stereotactic Radiosurgery (24)

- Local control = not requiring salvage therapy
  - 87 to 100% local control rates all three combined
- 23% of cases have transient increase tumor volume due to central necrosis
  - 6mo to 5yr to disappear
  - Therefore some patients receive unnecessary salvage therapy
Hasegawa et al. 2005 (36)

- 317 patients
- Median follow up 7.8 years
- 10 yr local control >92%
- Partial or complete radiographic response 62%
- Progression free survival
  - 96% if <15cm³ vs 57% if >15cm³ \( p<0.001 \)
  - Better with no brainstem compression/4th ventricle obstruction \( p<0.001 \)
- Most tumor progression within 3 years
Freidman et al. 2006 (37)

- 390 patients
- Median follow up 40 months
- Median dose of 12.5 Gy
- 5- and 10-year local control 90%
- Only 1% of patients required surgery for treatment failure
Many different regimens studied
Dose 15-57.6 Gy/3-32fx
Median Follow ups of 48 months
5- year local control of >90%

**Relatively new idea so no long term outcomes available**
Radiosurgery vs FSRT (38)

- **Tumor Control**
  - 73.8 to 100% for Radiosurgery
  - 91.4 to 100% for FSRT

- **Tumor Shrinkage**
  - 38 to 76.2% for Radiosurgery with single dose
  - 34 to 76% for FSRT

- **Tumor Growth**
  - 0-26.2% for Radiosurgery
  - 0-12.5% for FSRT

- **Hearing Preservation**
  - 47-71% for Radiosurgery
  - 57-100% for FSRT
Hearing Preservation

- Defined as G-R class I/II
- Early studies 16Gy = 46%
- Later Studies 12-13Gy = 68-78% with no change in control (24)
- Prasad et al. (39)
  - 153 patients
  - Median follow up of 4.2 years
  - Useful hearing preservation rate of 58%
  - Size matters
    - <1cm³ = 75% hearing preservation
    - >1cm³ = 57% hearing preservation
GK vs FSRT

Andrews et al. 2001 (40)
- 109 patients
  - 63 GK at 12Gy
  - 46 FSRT at 50Gy/25fx
- Follow up was 3 years
- 33% vs 81% hearing preservation (GK/FSRT)
- 98% vs 97% local control (GK/FSRT)

Thought is that lower dose in multiple fractions leads to decreased late normal tissue damage
Facial Neuropathy

- GK dose decrease from 16Gy to 12-13Gy decreased rates from 15% to 0% (41)

- LINAC dose decrease of 16Gy to 12.5Gy showed drop in neuropathy from 4.4% to 0.7% (37)

- RS vs FSRT ranges of 0-52% vs 0-4% (38)
GK dose decrease from 16Gy to 12-13Gy decreased rates from 16% to 4.4% (41)

LINAC dose decrease of 16Gy to 12.5Gy showed drop in neuropathy from 3.7% to 0.7% (37)

RS vs FSRT ranges of 2.4-29% vs 0-16% (38)
Other complications

- Hydrocephalus
  - 0-11% (24), with highest rates in FSRT
- Tinnitus
  - 0.2 to 5%
- Ataxia
  - 1.4 to 3.6%
- Vertigo
  - 1.4 to 1.7%
- Peritumoral cyst formation
  - 3.6%
- Malignant transformation
  - 0 to 0.3%
  - 3 cases in all studies reviewed with time to presentation of 5, 7.5, and 18 yrs post therapy
- Disequilibrium
  - 33% likely due to weaker central compensation (42)
1. Translabyrinthine Approach
2. Middle Cranial Fossa Approach
3. Retrosigmoid-Suboccipital Approach

**All will require discussion/collaboration with Neurosurgery**
Translabyrinthine Approach (43)

ADVANTAGES

- Least cerebellar retraction
- Wide exposure of posterior fossa
- No size limit for resection
- Facial nerve easily identified throughout
- Ease of facial nerve repair if damaged/resected during removal
- Low recurrence
- Low headaches

DISADVANTAGES

- Residual hearing is sacrificed
- Requires abdominal fat graft
Middle Cranial Fossa Approach (43)

**ADVANTAGES**

- Best hearing preservation
  - <30db PTA
  - >70% speech discrimination
- Good exposure of lateral IAC, CPA, and clivus
- Drilling is extradural decreasing morbidity

**DISADVANTAGES**

- Limited to tumors <2cm in greatest dimension
- Temporal lobe retraction
- Must dissect around facial nerve due to its superior position
- Limited posterior fossa exposure
<table>
<thead>
<tr>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
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<tbody>
<tr>
<td>Can attack any size tumor</td>
<td>Must be medially located with &lt;2cm CPA extension</td>
</tr>
<tr>
<td>Hearing preservation possible</td>
<td>Lateral tumors risk injury to endolymphatic sac and vestibular labyrinth</td>
</tr>
<tr>
<td>Wide exposure of brainstem and lower cranial nerves</td>
<td>Cerebellar retraction occulomotor abnormalities and postop disequilibrium</td>
</tr>
<tr>
<td>Neurosurgeon familiarity</td>
<td>Increased air embolism risk (Sitting vs Park Bench position)</td>
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<tr>
<td>Consistent facial nerve identification</td>
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Microsurgery Control Rates

- **Translabyrinthine**
  - Total Resection 99.5 to 99.7% (44-45)
  - Near total resection (<25mm² or 2mm thick)
    - Visible on MRI in 50% of patients with 3% risk of recurrence (46-47)

- **Middle Cranial Fossa**
  - Total Resection 98% (48)

- **Retrosigmoid**
  - Total resection 95% (49)
Hearing Preservation

- Serviceable hearing defined as class A/B or 1/2 (24)
  - Middle cranial fossa 51%
  - Retrosigmoid 31%

- Meyer et al. 2006 (50)
  - 162 consecutive patients via MCF approach
  - Class A/B hearing preserved in 41%
  - 56/113 (50%) with WR >70% preoperatively maintained that level.
    - Tumor 0.2-1.0cm = 59%
    - Tumor 1.1-1.4cm = 39%
    - Tumor 1.5-2.5cm = 33%
Facial Nerve Paralysis

- Reporting function at 6-12 month point is gold standard
  - Preserved = Grade I/II (24)
    - Retrosigmoid 91%
    - Middle Cranial Fossa 88%
    - Translabyrinthine 77%
- Delayed paralysis (>72hrs after surgery)
  - Described by Grant et al. 2002
  - Incidence 5% (51)
  - 79% regain postoperative function by 1 yr
CSF Leak

- Pooled data from 19 studies 360/4297 (8%) rate (52)
  - MCF approach 6%
  - TL approach 8%
  - RS approach 11%
- Occurs at two different time points
  - POD 2-3 (Early)
  - POD 10-14 (Late)
Occurs roughly 10% of patients >3 months postop (52)

- RS approach 21%
- MCF approach 8%
- TL approach 3%

Mechanisms

1. Bone dust contacting CSF/Meninges → Aseptic Meningitis
2. Occipital nerve entrapment
3. Scarred neck muscles and dura
4. Migraine
Other Microsurgical Complications (53)

- **Mortality**
  - 1% due to neurovascular injury

- **Meningitis**
  - 1-8%
  - Aseptic more common than bacterial (bone dust/inflammation)
  - *S. aureus* most common pathogen

- **Tinnitus**
  - 50% with preop tinnitus will have resolution postop

- **Balance abnormalities**
  - Occurs in most patients but gone by 6-9 months

- **Seizure/Hydrocephalus/Stroke (24)**
  - Rare and <2% of cases
Myrseth et al 2005 (53)

- Retrospective review 189 patients tumors ≤3cm
  - 86 by microsurgery vs. 103 by GK
  - 5.9 year mean follow up
  - Local control rates of 89.2% Surgery vs 94.2% GK
  - HB 1-2 in 79.8% Surgery vs 94.8% GK \( p=0.0026 \)
  - Quality of life significantly lower in surgery group compared to gamma knife group

*MCF approach was not utilized*
Pollock et al. 2006 (54)

- Prospective cohort of 82 patients unilateral VS <3cm
  - 36 Surgery vs 46 GK
- Average follow up of 42 months
- Local control 96% Surgery vs 100% GK p= 0.50
- HB 1/2 in 75% Surgery vs 96% GK p<0.01
- Hearing Preserved 5% Surgery vs 63% GK p<0.001
- Quality of life all statistically better for GK
  - Physical functioning
  - Bodily pain scores
  - Dizziness Handicap Inventory
Vestibular schwannomas are the most common CPA tumor

Unilateral Tinnitus or SNHL must be evaluated

Tumors <3cm in size treated with radiosurgery
  - GK or LINAC have comparable results
  - FSRT may prove more beneficial but requires more than 1 day of treatment

For patients with no serviceable preoperative hearing, translabyrinthine approach is best choice

For Hearing Preservation options the middle cranial fossa approach appears to be slightly better than the retrosigmoid approach due to decreased rates of complications.
55 y/o female with 2 year history of falls and disequilibrium

Falls are now progressive and daily

Denies true vertigo just imbalanced

Also has tinnitus, neck spasms, and migraines

She denies any hearing loss but family feels otherwise
Case Report

- PMHx:
  - HTN, Hypothyroidism
- PSHx:
  - Partial hysterectomy and R thyroid lobectomy
- FHx:
  - Noncontributory
- SHx:
  - 45 pack year history of smoking, -EtOH
- Medications:
  - HCTZ, metoprolol, sydol prn, soma, and ambien prn
- Allergies:
  - Sulfa
- ROS:
  - Otherwise negative. No vision or constitutional problems
General: NAD oriented x3
Head: NCAT
Eyes: No nystagmus, PERRLA, EOMI
ENT: TM’s intact, Tuning forks normal
Neck: No masses or lymphadenopathy
Neuro: CN II-XII intact, unsteady Romberg, tandem gait falling to the left, and left finger to nose ataxia
Case Report

- **Audiogram**
  - Normal hearing with mild high frequency SNHL at 4000Hz bilaterally

- **ENG**
  - Decreased accuracy on horizontal smooth pursuit
  - 54% weakness on left air caloric testing

- **MRI**
  - 1.5 to 2cm lesion closely associated with CN VII/VIII. It is intracanalicular with extension into CPA. No evidence of brainstem compression or ventricular obstruction
1. Finger to nose and gait ataxia
2. Essentially normal hearing
3. ENG positive for left lateral canal weakness
4. 2cm tumor, no hydrocephalus
Case Report

- Patient had previous MRI 2005 showing no tumor
- Therefore it is decided that we perform suboccipital craniotomy for excision of tumor
Images of Surgery

- Tumor
- Retracted Cerebellum
- Tentorium Cerebelli
Images of Surgery

- Tentorium Cerebelli
- CN VII/VIII Complex
- Tumor
- Retracted Cerebellum
Images of Surgery

- CN V
- Tentorium Cerebelli
- CN VII/VIII Complex
- CN VI
- Tumor
- Retracted Cerebellum
- AICA
- CN V
Final Pathology: Meningioma
No complications at this point
Tuning forks 256hz and 512hz normal
HB I immediately and 72 hours postoperatively
References

13. Cummings
References