Paraganglioma of the Skull Base

Ross Zeitlin, MD
Medical College of Wisconsin
Milwaukee, WI
Case Presentation

• 63-year-old female presents with right-sided progressive conductive hearing loss for several years
• Mild pulsatile tinnitus
• No other neurologic complaints
• Physical exam: Red-purple mass located behind right tympanic membrane, no cranial nerve (CN) deficits
Case Presentation

• CT temporal bone and MRI internal auditory canal: 4 mm soft tissue mass along the right cochlear promontory consistent with a glomus tympanicum

• Underwent right tympanoplasty with tumor resection, with pathology demonstrating paraganglioma

• Lost to follow-up until 4 years later, with progressive disequilibrium, right sensorineural hearing loss, and right pulsatile tinnitus
Case Presentation

- Repeat CT temporal bone (right; orange arrow denotes tumor) in comparison to initial pre-operative CT (left):
  - Evidence of recurrence in right middle ear cavity in the hypotympanum (red arrow) with new moth-eaten osseous destruction of the temporal bone (yellow arrow)
Case Presentation

• MRI brain with contrast:
  – Enhancing tumor (red arrow) along the medial margin of the right internal jugular vein, centered at the right jugular foramen with slight extension below the foramen.
Background

- Affects approximately 1 case per 1.3 million patients per year
- Most common tumor of the middle ear
- Female predominance
- Most occur in patients aged 40-70
- Mostly benign, but <5% can metastasize
Terminology

• Jugulotympanic paraganglioma are also termed:
  – Glomus jugulare tumors
    • Arise from Jacobson nerve (branch of CN IX) or Arnold nerve (branch of CN X) within the jugular foramen
  – Glomus tympanicum tumors
    • Arise from the Jacobson nerve in the middle ear/cochlear promontory
Pathophysiology

• Neuroendocrine tumors arising from autonomic paraganglia (small organs of neuroendocrine cells derived from the embryonic neural crest)
• Most parasympathetic paragangliomas are non-secreting, distributed along vascular or neural structures of the skull base and neck
• Histologically, they are comprised of clusters of chief cells in a highly vascular stroma
• Can be locally invasive within the temporal bone/skull base and adjacent structures
Classification

• Fisch Classifications:
  – Type A: Limited to middle ear cleft/arise along tympanic plexus
  – Type B: Invasion into hypotympanum/limited to tympanomastoid area with no infralabyrinthine compartment involvement
  – Type C: Involves the infralabyrinthine compartment of the temporal bone, extending to the petrous apex
  – Type D: Intracranial extension
Classification

- Glasscock-Jackson:
  - Type 1: Involves jugular bulb, middle ear, mastoid process
  - Type 2: Extends under internal auditory canal
  - Type 3: Extends into petrous apex
  - Type 4: Extends beyond petrous apex into clivus or infratemporal fossa
    - Note: Types 2-4 may have intracranial extension
Clinical Presentation

• Gradual onset of symptoms
• Middle ear involvement: Conductive hearing loss, ear fullness, pulsatile tinnitus, otorrhea; otalgia is uncommon
• Involvement of inner ear: Vertigo, sensorineural hearing loss
• CN IX-XI involvement: Dysphonia, dysphagia, loss of gag reflex
• Intracranial involvement: Headache, nausea
Work-Up

• Thorough neurologic and otoscopic exam
• Audiogram
• CT temporal bone with contrast and with thin slicing
  – Delineates extent of osseous involvement
• MR brain with contrast
  – “Salt and pepper” appearance of intermixed high-intensity signals and signal voids: represents fast flowing blood
• MR angiogram may be helpful for further tumor delineation
Treatment options

• Observation
  – Asymptomatic, tumor size <2-3 cm

• Surgery
  – Early stage tumors: Tympanoplastastic resection
  – More advanced tumors or those with jugular involvement: Resection using infratemporal approach

• Radiotherapy
  – Often used when resection would require extensive sacrifice of critical vascular or neural structures as well as for recurrent tumor after prior surgery
  – May utilize either fractionated external beam radiation therapy (EBRT) or stereotactic radiosurgery (SRS) approaches
Surgical Treatment

• Tympanoplastastic surgery
  – Low risk of damage to cranial nerves

• Resection using infratemporal
  – More extensive
  – One systematic review of retrospective series reports high risk of post-operative cranial neuropathies
Radiotherapy: Principles

• Goal: Achieve durable radiographic and clinical stability

• However, tumors often do not regress in size
  – Locally symptomatic lesions should be considered for surgery when anatomically feasible
Systematic Review: RT vs Surgery

- Suarez et al: Systematic study examining efficacy and safety of surgery (n=715 in 41 studies), fractionated RT (n=461 in 20 studies), and SRS (n=254 in 14 studies) for jugular paragangliomas (JPGs)
- Mean duration of follow up: 65.6 months
- Surgery vs RT in JPGs:
  - Tumor control: 78.2% vs 91.5% (SS)
  - Major complications: 28.2% vs 11.4% (SS)
  - CN palsies after treatment (per patient): 0.9 vs 0.08 (SS)
- Conventional EBRT vs SRS in JPGs:
  - Tumor control: 89.1% vs 93.7% (NS)
  - Major complications: 10.4% vs 6.5% (NS)
  - CN palsies after treatment (per patient): 0.15 vs 0.002 (NS)
- Conclusions: EBRT and SRS offer similar chance of tumor control with lower risks of morbidity compared to surgery in patients with JPGs.
Retrospective Series: Fractionated RT

- Dupin et al: Retrospective series examining survival and toxicity outcomes for head and neck paraganglioma patients (n=66) receiving fractionated RT (mean dose 45 Gy in 25 fractions)
- Median follow up: 4.1 years
- Outcomes:
  - Local control: 100% at 5 years, 98.7% at 10 years
  - Cause-specific death: 2 patients within 6 months following RT
  - Acute toxicity: 9 patients hospitalized for weight loss, nausea, mucositis, or ophthalmic zoster
  - Late toxicity: 2 patients with vascular complications (middle cerebral artery and carotid stenosis) and 2 patients with RT-related meningiomas 15 and 18 years post-treatment
- Conclusion: Conventional fractionated EBRT is effective and safe, and achieves excellent local control.
Systematic Review: SRS

- Guss et al: Systematic review and meta-analysis of data on management of jugular paraganglioma tumors using SRS (n=335 patients in 19 studies) with either Gamma Knife-, CyberKnife-, or linear accelerator-based technologies.
  - Clinical control of 95% and tumor control of 96% at mean or median follow up time of > 36 months
Retrospective Series: SRS

- Sheehan et al reports a multicenter retrospective analysis examining outcomes after SRS in 132 patients undergoing 134 procedures.
- Median dose 15 Gy; median follow up 50.5 months
- Outcomes:
  - Overall tumor control: 93% at 5 years
  - Pulsatile tinnitus improved in 49% of patients
  - New or progressive CN deficits noted in 15% of patients
  - Improvement in preexisting CN deficits noted in 11% of patients
- Conclusions:
  - Gamma knife SRS was well tolerated, provides high rate of local control, and improves symptomatic tinnitus in approximately ½ of patients.
  - Overall neurologic status and CN function were preserved or improved in the majority of patients after SRS.
Radiotherapy: Treatment Planning

• Fractionated EBRT:
  – Dose: 45-50.4 Gy at 1.8-2 Gy/fraction to the PTV

• SRS:
  – Dose: 12-15 Gy in single fraction to ~50% isodose line

• Choice of approach depends on tumor size, normal tissue constraints, and tumor delineation.
Radiotherapy: Treatment Planning

• Target Definition:
  – GTV: Grossly visible disease as defined by contrast-enhanced CT and/or MRI
  – CTV: Typically none is used unless the disease is poorly defined
  – PTV: 1-5 mm depending on image-guidance and immobilization
Case Presentation: Fractionated RT

• Given the concern for tumor delineation on MR for SRS planning, the patient underwent fractionated RT to a dose of 50.4 Gy in 28 fractions at 1.8 Gy per fraction.
Case Presentation: Treatment Planning
Case Presentation: Treatment Planning

• DVH Summary:

<table>
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<tr>
<th>Structure</th>
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<tr>
<td><strong>PTV</strong></td>
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<tr>
<td>GTV</td>
<td>V(5400 cGy) &gt; 95%, 28 Fx@193 cGy/Fx.</td>
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<tr>
<td>PTV</td>
<td>V(5040 cGy) &gt; 95%, 28 Fx@180 cGy/Fx.</td>
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<tr>
<td>Eye_R</td>
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<tr>
<td>Lens_L</td>
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<tr>
<td>Lens_R</td>
<td>Dmax &lt; 300 cGy</td>
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<tr>
<td>OpticNerve_R</td>
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<tr>
<td>Brainstem</td>
<td>Dmax &lt; 5600 cGy</td>
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<tr>
<td>Inner Ear_L</td>
<td>Dmax &lt; 4500 cGy</td>
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<tr>
<td>Spinal Cord</td>
<td>Dmax &lt; 4500 cGy</td>
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Note: Delta is the difference between the achieved and wished values.
Toxicities

• Acute: Fatigue, skin reactions, transient mucositis, ear congestion, middle ear effusion, xerostomia

• Long-term: Decreased hearing, hypopituitarism, xerostomia; more rarely, osteomyelitis, bone necrosis, brain necrosis, vascular compromise due to stenosis
Follow-Up

• Extrapolated from NCCN, clinical and radiographic follow up every 6-12 months for the first 3 years, then annually thereafter for 10 years, as recurrence can take several years to present
References


