Imaging of Perineural Tumor Spread in Head and Neck Cancer

Lawrence E. Ginsberg, MD
Departments of Diagnostic Radiology and Head and Neck Surgery
University of Texas M.D. Anderson Cancer Center
Houston, Texas

Perineural Tumor Spread (PNS)
- Definition: dissemination of tumor from the primary site along tissue planes of the neural sheath
- Small vs. large nerve PNS
- Clinical settings:
  - salivary gland-parotid, minor salivary gland (palate)
  - mucosal (SCCa)-palate/RMT, nasopharynx (via MS, PPF)
  - skin (SCCa, desmoplastic melanoma)
  - previously treated/forgotten disease
- Symptoms: pain, paresthesias, motor denervation, but up to 40% may be asymptomatic
- Implications: serious finding associated with decreased survival. Detection will often affect treatment

Perineural Tumor Spread (PNS)
- Failure to recognize PNS (big problem)
  - common pitfall in head and neck imaging
  - good way to get sued
  - guarantees disease recurrence
- Because may be asymptomatic, up to radiologist to think of PNS and detect it
- Rarely, site to which tumor spreads perineurally may present prior to detection of primary cancer. Therefore, must consider PNS whenever lesion is seen in Meckel’s cave, pterygopalatine fossa, or cavernous sinus

Perineural Tumor Spread-Imaging
- Widening/destruction of or excessive enhancement within neural foramina (ovale, rotundum, palatine, stylomastoid foramen/descending facial canal, vidian canal)
  - CT better for bone destruction (late finding)
- Loss of normal fat density (CT)/T1 signal intensity (MR) or excessive enhancement/widening of the pterygopalatine fossa
- Enlargement/excessive enhancement within cavernous sinus or Meckel’s cave
- MR technique: 16-18 cm FOV, 3 mm slices, fat-suppressed, post contrast T1-weighted images
What should a normal Meckel’s Cave look like?

**Ophthalmic Nerve V₁**
- Provides sensory innervation to the eye, lacrimal gland, conjunctiva, and skin of the nose, supraorbital region, and frontal scalp
- Course-cavernous sinus to SOF, orbit, divides into branches-lacrimal, nasociliary, frontal
- Lacrimal branch also carries parasympathetic innervation originating in the facial nerve, via the GSPN and ultimately a small twig from the zygomaticotemporal branch of V₂
- Main nerve involved in PNS is frontal nerve, which divides into (or is formed by the joining of) the supratrochlear and supraorbital branches

58-y/o man, s/p resection SCCa left medial forehead, locally recurrent 5 months later, with PNS on supratrochlear branch V₁, extending to frontal nerve

72-y/o man presented with left forehead numbness, subsequently developing fullness. Imaging (Brain MR) allegedly normal. Biopsy of left eyebrow region SCCa. Post-bx developed diplopia attributable clinically to left abducens palsy. Note tumor going through superior orbital fissure.

**(PNS) Anatomic Considerations**
- Maxillary nerve, V₂-sensory to the mid-face, palate, sinonasal region, upper oral cavity. Common pathway to PPF, foramen rotundum, cavernous sinus, Meckel’s cave
- Mandibular nerve, V₃-sensory to lower face and oral cavity, motor innervation to muscles of mastication. Common pathway to foramen ovale, Meckel’s cave
- Antegrade PNS-Meckel’s cave to cavernous sinus or downward along V₃, Cavernous sinus anteriorly along V₂, PPF along palatine or infraorbital nerves
- Facial nerve, generally from primary parotid lesions or lesions that secondarily extend into the parotid
Fair-skinned 74-y/o male with left cheek melanoma, and V₂ hypesthesia

62-y/o man, now with left V₂ paresthesias following Mohs surgery for left cheek SCCa. Recurrence with infraorbital nerve PNS

64-y/o female presents with sudden onset of left cheek numbness. Unsuccessfully treated for sinusitis. PE confirmed V₂ sensory abnormality and was otherwise normal

Palatal/maxillary alveolar ridge ACCa, PNS to PPF, rotundum
(PNS) Anatomic Considerations

- Maxillary nerve, V2-sensory to the mid-face, palate, sinonasal region, upper oral cavity. Common pathway to PPF, foramen rotundum, cavernous sinus, Meckel's cave

- Mandibular nerve, V3-sensory to lower face and oral cavity, motor innervation to muscles of mastication. Common pathway to foramen ovale, Meckel’s cave

- Antegrade PNS-Meckel’s cave to cavernous sinus or downward along V3. Cavernous sinus anteriorly along V2, PPF along palatine or infraorbital nerves

- Facial nerve, generally from primary parotid lesions or lesions that secondarily extend into the parotid

---

Recurrent SCCa in the right masticator space, growing up V3

Prior left buccal SCCa, now recurrent to masticator space, and then PNS along V3 into Meckel’s cave

PNS in Nasopharyngeal Carcinoma

- Requires extension into:
  - pterygopalatine fossa (V2, PNS)
  - direct extension through pterygoid plates
  - anterior extension into nasal cavity and laterally through the sphenopalatine foramen
  - both
  - masticator space (V3, PNS)
  - lateral extension
47-y/o woman with several year hx/o HA, left otalgia, s/p XRT for never-biopsied “left cavernous sinus meningioma.” Dx: NPC with bilateral PNS to PPF and left foramen rotundum

NPC to V3/Ovale

**Inferior Alveolar Nerve**

- Branch of mandibular nerve (V3)
- Provides sensory innervation to lower gingiva and teeth, and cutaneous sensory innervation to the chin via the mental nerve
- Enters the mandible through the mandibular foramen
- At risk for PNS from lower lip primaries or any tumor that invades the mandible
- May be involved in downhill or antegrade PNS

56-y/o man presenting with left “numb chin” syndrome, outside radiologist interpreted MR as osteomyelitis. Dx: lymphoma
40-y/o man, s/p WLE left lower lip desmoplastic melanoma late 90’s, and resection of recurrence 2/05. Did well until 4/06 when he started experiencing numbness in the left lower teeth. Patient required hemimandibulectomy. Intramandibular inferior alveolar nerve perineural recurrence

| 2/05 | 4/06 |

**Auriculotemporal Nerve**

- Branch of mandibular nerve (V₃)
- Arises just below foramen ovale
- Provides cutaneous innervation to lateral face, preauricular, external ear, and TMJ
- Also acts as conduit for post-ganglionic parasympathetic fibers (originating as LSPN), that provide secretomotor innervation to the parotid gland
- ATN and therefore V₃ at risk for PNS in 1° or 2° malignancies of parotid gland and skin cancers in its cutaneous distribution
- Evaluation of all parotid malignancies should include foramen ovale and proximal course of V₃

**Auriculotemporal nerve**

**Pre-auricular carcinoma, invasive of parotid, with PNS along auriculotemporal nerve to foramen ovale**

**Recurrent left lower lip SCCa with proven PNS along the mental/inferior alveolar nerve to level of main trunk V₃**
66-y/o man developed right-sided trigeminal pain, progressing to numbness, unresponsive to steroids and acyclovir. Shortly thereafter developed facial neuropathy. History notable for removal of several skin cancers including left medial canthus and right nasal dorsum (SCCa) and several left facial BCCs.

Initial outside imaging showed tumor along right V3, but precise site or origin unclear.

Repeat imaging at MDACC scans read as likely right temporal subcutaneous primary (or recurrence), with V3 PNS. Surgeon did not read report and patient was on table for craniotomy, Meckel’s cave biopsy, which was aborted when soft tx biopsy proved SCCa. There is retrograde spread onto the main trigeminal trunk, and antegrade spread into foramen rotundum.

59-y/o man with multiple recurrences right facial SCCa, now with parotid region recurrence and facial palsy.

PNS-Anatomic Considerations-Facial Nerve

- Generally related to parotid pathology, either primary parotid malignancy, or lesions, generally skin cancers, that secondarily invade the parotid, at diagnosis or at recurrence
- Less commonly, skin cancers that have not yet invaded the parotid
- Beware the subdermal skin cancer, that is difficult to detect clinically
- When is “Bell’s Palsy” a Bell’s Palsy?

How Can Cancer Access the Facial Nerve Perineurally?

- Via peripheral branches and back into main trunk
- Directly into the stylomastoid foramen
- Back along GSPN (to follow)
79-y/o man with recurrent scalp SCCa left parotid

Outside brain, radiologist told "Bell's Palsy," no mention of prior skin cancer

No mention of parotid met

Facial nerve enhancement attributed to "Bell's Palsy."

Relationship Between CN 5 and 7

- Distal branches of V serve as conduits for small branches of VII and IX. These represent real or potential routes of PNS

- Potential sources of PNS:
  - chorda tympani-tongue, SM/SL glands
  - LSPN (runs with auriculotemporal nerve)-parotid gland

- Greater superficial petrosal nerve (GSPN)
  - Branch of CN7 originating in nervus intermedius
  - Preganglionic fibers, motor root of SP ganglion
  - Post ganglionic supply to palate, nasal, lacrimal
  - Potential for perineural tumor spread quite real

Course of the GSPN

Facial hiatus

Geniculate ganglion

Vidian canal

Foramen lacerum
43-y/o woman with right facial pain and numbness. Dx: ACCa of the hard palate with PNS to the PPF and vidian nerve

69-y/o man with ACCa left nasomaxillary. Spread to PPF facilitates PNS to vidian and rotundum

62-y/o woman with several year history of left ear discomfort and placement of tympanostomy tube for treatment of eustachian tube dysfunction. More recently developed left trigeminal sensory neuropathy, and oh yeah, just noticed she’s NOT TEARING FROM THE LEFT EYE. Outside brain MR read as cavernous sinus meningioma, patient referred for proton therapy.

Repeat imaging obtained primarily for XRT planning. How to make a very long story short...?
Unusual Pathways of PNS

- Nasociliary nerve
- Great auricular nerve
- Supraclavicular nerve
- Other cranial nerve

Nasociliary Nerve

- Branch of V1
- Provides cutaneous sensory fibers to skin of lateral nose, and sensory innervation from the frontal dura, sphenoid and ethmoid sinus mucosa, nasal mucosa, and medial canthus

Great Auricular Nerve (GAN)

- Superficial branch of the superficial cervical plexus.
- GAN provides sensory innervation to the skin over the parotid and lower pre-auricular region.
- GAN leaves plexus, courses over and around the SCM (Erb’s point) and then upward toward the ear.
- Has communicating branches with the facial nerve within the parotid gland, and with the auricular branch of the vagus nerve
- GAN at risk for PNS in its cutaneous distribution


68-y/o man with prior skin resections, now with recurrent SCCa left parotid, and PNS along auriculotemporal and greater auricular nerve

72-y/o man with multiply recurrent SCCa left face, now with recurrence over the left lower parotid region

Supraclavicular Nerves

- Branches of cervical plexus
- Formed by twigs from C3, C4 spinal nerve ventral rami
- Provide sensory innervation to skin over the clavicle, anteromedial shoulder, upper chest
- Anterior, posterior, intermediate branches

61-year-old man with recurrent SCCa, left supraclavicular region.

Rare Nerves—advanced, slow growing malignancies can spread to 3rd, 6th cranial nerves, maybe others, if cavernous sinus involved

Advanced recurrent lacrimal ACCa

Advanced recurrent facial melanoma, already had cavernous sinus disease. Progressive 3rd nerve involvement

Conclusion

- Perineural tumor spread is a very serious and potentially life-threatening complication of head and neck cancer
- Because it may be asymptomatic at presentation or masked at recurrence due to prior therapy, it is critical that the radiologist make the diagnosis
- Diagnosing PNS requires careful attention to imaging technique and a solid understanding of the relevant neuroanatomy