The Patient with Glossopharyngeal Neuralgia

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Learning Objectives

• Define the syndrome of glossopharyngeal neuralgia
• Briefly review anatomy of CN IX, the glossopharyngeal nerve
• Discuss pathologies that are associated with the clinical entity of GPN

Glossopharyngeal Neuralgia

• An uncommon CN hyperactivity-pain syndrome
  – Occurs in adults, esp females >50 yrs, L>R
• Severe, transient, sharp pain in ear, base of tongue, tonsillar fossa, or beneath angle of jaw
  – Distribution of auricular and pharyngeal branches of glossopharyngeal (IX) and vagus (X) nerves
  – Commonly provoked by swallowing, talking or coughing
    • Specific trigger zone can be difficult to identify
  – 0.2-1.3% of facial pain syndromes; ~2% bilateral
• Can be associated w cardiac arrhythmia or syncope (2-3% of cases)
  – Called “vagoglossopharyngeal neuralgia”
  – Pain followed by bradycardia/asystole
  – Related to circuit interconnections between CN’s IX, X

GPN: Abbreviated History

• 1910: severe pain in distribution of glossopharyngeal nerve described (patient had a CPA tumor)
• 1920: syndrome rx’d w extracranial nerve avulsion
• 1921: current nomenclature of “GPN” introduced
• 1926, 1927: rx w intracranial sectioning of nerve; continued into 1970’s
• 1977: Laha, Jannetta: observed nerve compression by vertebral artery and proposed rx w microvascular decompression (MVD)
• 2015: medical rx (AED’s), MVD are mainstay
  – Rx of underlying lesion if identified

CN IX: Glossopharyngeal Nerve

<table>
<thead>
<tr>
<th>Modality</th>
<th>Function</th>
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<tbody>
<tr>
<td>General</td>
<td>Somatic sensory information from parts of ear, posterior 1/3 of tongue, soft palate, upper pharynx, mastoid region</td>
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<tr>
<td>Sensory Afferent</td>
<td>Viscerals sensory information from carotid body, carotid sinus</td>
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<tr>
<td>Visceral Afferent</td>
<td>Taste from posterior 1/3 tongue</td>
</tr>
<tr>
<td>Special Afferent</td>
<td>Branchial motor to stylopharyngeus muscle</td>
</tr>
<tr>
<td>General Visceral Efferent</td>
<td>Visceral motor (parasympathetic) to parotid gland</td>
</tr>
<tr>
<td>Special Visceral Efferent</td>
<td>Branchial motor to stylopharyngeus muscle</td>
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Relevant branches: tympanic, tonsillar, lingual, carotid, pharyngeal
Proximity of CN 9, CN 10

- CN IX, X are in close anatomical proximity as they exit the medulla and traverse the cerebellomedullary cistern en route to the jugular foramen (JF)
  - Anastomoses exist between rootlets of the nerves
  - Also shared nuclei in lower pons and medulla

Diagnostic Criteria for Classic GPN

- A. Paroxysmal attacks of pain lasting from a fraction of a second to 2 minutes
- B. Pain has the following characteristics:
  - 1. Unilateral location
  - 2. Distribution within posterior part of tongue, tonsillar fossa, pharynx, or beneath angle of lower jaw and/or ear
  - 3. Sharp, stabbing and severe
  - 4. Precipitated by swallowing, chewing, talking, coughing, and/or yawning
- C. Attacks are stereotyped in the individual patient
- D. No clinically evident neurological deficit
- E. Not attributed to another disorder


Criteria for “Symptomatic” GPN

- Includes pain as defined for classic GPN with the proviso that aching pain may persist between paroxysms and sensory impairment may be found in the distribution of the glossopharyngeal nerve
  - Additionally, a causative lesion has been demonstrated
- Examples of causative lesions: CPA or JF tumor, carotid space lesion, UADT malignancy, leptomeningeal disease, brainstem lesion (MS), Eagle syndrome

Imaging Evaluation

- Etiology typically NV compression
  - So looking for an impinging vessel, typically PICA, vs AICA or vertebral a
- MR is study of choice
  - High-resolution heavily T2-weighted images to assess basal cisterns
- MRA may help evaluate vessels
  - CTA can contribute as well
  - High-resolution: relationship of vessels to bony anatomy
  - CT portion useful to assess for Eagle syndrome
- Gadolinium to assess for inflammation, infection, neoplasm

Normal Imaging Anatomy: CT

- CN IX, X exit medulla
- Traverse CM cistern to pars nervosa (IX) or pars vascularis (X) of jugular foramen
- Below SB: carotid space
- CN IX exits anteriorly at NP level to pharynx
- CN X continues into thorax, abdomen

Normal Imaging Anatomy: MR

- Glossopharyngeal n
- Vagus n
- From superior to inferior
Glossopharyngeal Neuralgia: Cases

Neurovascular compression is by far the most common cause, but multiple pathologies have been associated w GPN

- Brainstem lesions:
  - Infarction, demyelination, tumor, hemorrhage
  - More typically give multi CN palsies, not GPN
- Cisternal lesions
  - Tortuous vessel vs aneurysm or AVM
  - Leptomeningeal tumor, nerve sheath tumor
- Jugular foramen lesion
  - Nerve sheath tumor, meningioma, metastasis
- Carotid space lesion/extracranial lesion
  - Consider Eagle syndrome

33 F w paroxymal pain in R pharynx, ear

Dx: neurovascular compression by PICA, eventually rx'd w MVD

70 F w increasingly frequent episodes of R ear and pharyngeal pain

Dx: R PICA aneurysm. Patient currently considering treatment options.

80 M w intermittent R pharyngeal pain

Dx: presumed CN IX schwannoma

65 M w occasional ear pain

Dx: arachnoid cyst

55 F w R ear fullness and pharyngeal pain as well as increasing dysphagia and hoarseness. A middle ear mass was present on otoscopic examination.

Dx: meningioma. Bpsed, then rx'd w Cyberknife radiosurgery

63 F w/o breast cancer and new headaches as well as lower cranial nerve palsies. Though the patient complained of minor throat pain, she did not have classic symptoms of glossopharyngeal neuralgia.

Dx: leptomeningeal carcinomatosis.
69 M, progressive lower CN dysfunction, Horner syndrome, unrelenting pain in R ear, neck and throat.

Dx: metastatic poorly differentiated carcinoma. Patient subsequently expired due to tumor progression and aspiration pneumonia.

**Eagle Syndrome**
- Uncommon sequel of abnl elongation (>3 cm) and/or ossification of stylohyoid ligament
  - Symptoms include recurrent throat pain + anterolateral neck pain, w referred pain to ear
  - Presumed due to compression of neurovascular structures in neck
- Often included in ddx of GPN
- Typically rx’d surgically

**Treatment of Classic GPN**
- Medical: carbamazepine, gabapentin, phenytoin
- Surgical: microvascular decompression
  - Rhizotomy as a back-up procedure
- Other: glossopharyngeal nerve block, antidepressants, opioids, steroids, RF nerve ablation, stereotactic radiosurgery (target: distal portion of CN IX, X at jugular foramen)

**Summary**
- GPN is an uncommon pain syndrome in the head and neck
- Typical etiology is neurovascular compression
- Imaging is performed not only to assess for neurovascular compression but also to exclude alternative etiologies and to assist with treatment planning
Evaluating hoarseness: vocal cord paralysis

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Hoarseness

- 30% life-time prevalence
- Evaluation: patient history & laryngoscopy
- Imaging indicated only when:
  - Mass lesions
  - Vocal cord paralysis

Roy K et al. Laryngoscope 2005;115: 1988–95
Potestio PM. BMJ 2008;337:1165–8

Vocal cord paralysis (VCP)

- Immobile of the vocal cords due to neurologic impairment
- A sign of a disease process & not a diagnosis in itself
- Variable morbidity and mortality
- 30% - 50% of unilateral VCP are asymptomatic

Anatomy CN X
Brainstem & cisternal segment

From CW Baker: Head and neck anatomy. Thieme Medical Publishers, 2002, with permission
Etiology

- Neurologic (3% - 5%): stroke, tumor, Parkinson, ALS, myasthenia gravis...
- Mass compression (13%): lung, esophagus, thyroid, skull base, neck
- Inflammatory & infectious (6%-8%)
- Medications: vinka alkaloids, ...

Brainstem
Right CN X - XI paralysis in a 72 year old male

Middle & lower nucleus ambiguous stroke

Skull base
Right CN X - XII paralysis in a 55 year old male

Chordoma

Jugular foramen
Right CN X paralysis and otalgia in a 29 year old male

DD: Paraganglioma, schwannoma
Jugular foramen:
Right CN X paralysis and otalgia in a 29 year old male

DOPA PET CT: Malignant paraganglioma

Carotid space & parapharyngeal
Right RLN and CN XI paralysis in a 39 year old male

Nasopharyngeal SCC

Carotid space
Left CN X & right RLN paralysis in a 44 year old female

Bilateral vagal schwannoma

Thyroid
Left RLN nerve paralysis in a 54 year old male

Castle carcinoma

Thyroid
62 year old female with goiter

Benign goiter with left RLN paralysis

Mediastinum
Left RLN paralysis in a 57 year old female

Lung tumor with mediastinal LN metastases
Ortner's syndrome

- Compression of the left RLN due to cardiovascular origin

Pulmonary artery hypertension

Treatment VCP

- Goal: improve voice & prevent aspiration
- Speech & swallow therapy
- Surgical:
  - VC injection
  - Medialisation thyroplasty
  - Arytenoid adduction
  - Laryngeal reinnervation

Thyroplasty

Right RLN paralysis with autologous fat injection

Take home points VCP

- Imaging after clinical assessment & laryngoscopy
- Imaging VCP: brainstem to carina
- Dedicated high res images, 2D & 3D MPR
- Do not miss VCP in patients imaged for other causes
- Be aware of imaging pitfalls of VCP
Horner’s Syndrome

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Learning Objectives

- Review the anatomy of the Oculosympathetic pathway (OSP)
- Learn to localize lesion based on clinical findings
- Learn pathology encountered at various levels in the OSP

Introduction

Horner’s Syndrome (HS) occurs when there is interruption of the oculosympathetic pathway (OSP). The clinical symptoms may cause little if any functional impairment in most patients. However, since both benign and malignant disease processes are associated with HS a thorough clinical evaluation is required.

Anatomy of the OSP

- Consists of three neurons:
  - **FON** - Posterolateral hypothalamus
  - **SON** - Ciliospinal center (C8-T2)
  - **TON** - Superior cervical ganglion (C2-C3)

First Order Neuron (FON)

- **Location**: posterolateral hypothalamus
- **Course**: PGF descend in the reticular formation (brainstem, cervical and thoracic cord) to synapse in the intermediolateral (IML) gray substance of the spinal cord at level C8-T2 (Ciliospinal center of Budge-Waller)

Second Order Neuron (SON)

- **Location**: Ciliospinal Center of Budge-Waller
- **Course**: PGF exit in the ventral spinal root, pass through the inferior cervical ganglion or stellate ganglion (fusion of inferior cervical and first thoracic ganglion) and middle cervical ganglion in route to the TON in the superior cervical ganglion.
Third Order Neuron (TON)

- **Location**: SCG
- PGF travel with the ICA for a short distance to the cavernous sinus where they attach to CN VI then to V1 and enter the SOF (via the ophthalmic nerve ON). The long posterior ciliary nerve, a branch of the ON innervates Muller’s muscles and the dilator muscles of the iris.
- PGF travel with the ECA to the blood vessels to the face and are responsible for sweating.

**Clinical Findings**

**Classic Triad**
- Ptosis
- Miosis
- Anhydrosis

**Ptosis**

- **Muller’s muscle**: in the upper eyelid is a thin smooth muscle arising from the undersurface of the levator palpebrae superioris muscle.
- This muscle elevates the upper eyelid and controls the resting position of the upper eyelid (when the eye is open).
- Innervated by the sympathetic nervous system. Interruption of the sympathetic nerve supply results in a moderate droop of the upper lid (ptosis).

**Miosis**

Decrease in pupil size due to paralysis of the dilator muscles. The *sphincter* and *dilator muscles of the iris* are innervated by the autonomic nervous system.

**Innervation**

- **Sympathetic** - Sphincter
- **Parasympathetic** - Dilator

**OS Innervation**

**IPSILATERAL**

- Sweat glands body and face
- Dilator muscles of the iris
- Retractor muscles of the eyelids

**Sympathetic and Parasympathetic Innervation of the Iris**

When the sympathetic innervation is interrupted the parasympathetic innervation of the sphincter muscle is unopposed, therefore the pupil constricts.
Anhydrosis

- Lack of sweat production due to interruption of the sympathetic innervations of the sweat glands
- Unilateral absence of sweat to the forehead, face, or body is a good indication of Horner’s syndrome

Other Clinical Findings

- Conjunctival hyperemia
- Upside down ptosis
- Iris Heterochromia
- Harlequin Sign

Transient Early Signs of Acute Horner’s Syndrome

Conjunctival hyperemia
Sympathetic denervation causes vasodilatation of the capillaries in the conjunctiva (“blood shoot eyes”)

Upside Down Ptosis

- Best demonstrated when the upper lid is in the resting position
- Sympathetic fibers innervate retractor muscle fibers (Muller’s muscle) in the lower lid.
- The lower lid will rise slightly in Horner’s Syndrome (“upside down” ptosis)
- This, in conjunction with the upper lid changes causes narrowing of the palpebral fissure and may give the false appearance of enophthalmus

Iris Heterochromia

- The iris is blue or gray at birth. An intact OSP is required for pigmentation of the iris to develop in the first year of life.
- Lesions interrupting the OSP in the first year of life lead to iris heterochromia (light colored iris)

Harlequin Sign

- Unilateral facial flushing seen in children with congenital HS
- Areas that do not flush correspond with areas of anhidrosis
- Decrease skin temperature on the affected side
- Due to impaired vasodilatation
**HS Classification**

- **Preganglionic HS**
  - lesion proximal to the superior cervical ganglion
- **Postganglionic HS**
  - lesion anywhere from the superior cervical ganglion to the eye

**Preganglionic HS**

Proximal to the SCG
- Central (FON HS): from the hypothalamus to the lower cervical to upper thoracic cord before the PGF synapse with the SON
- Peripheral (SON HS): lesion located anywhere from the SON to before the PGF synapse with the TON in the superior cervical ganglion

**Postganglionic HS**

- **TON HS**
  - Caused by lesions that occur anywhere from the SCG to the eye

**Clinical Evaluation**

- Anisocoria (unequal pupil size) may be due to a number of causes i.e. aging, sympathetic or parasympathetic dysfunction
- Examination in the dark will help determine the etiology

**Anisocoria**

- Anisocoria (unequal pupil size) may be due to a number of causes i.e. aging, sympathetic or parasympathetic dysfunction
- Examination in the dark will help determine the etiology

**Dilation Lag**

- The sympathetic denervated pupil dilates slower than the normal pupil in the dark
- This is best identified when photographs are taken after 5 and 15 seconds in the dark
Pharmacological Testing

- Ideally sequential pharmacological testing using cocaine (5-10% solution) and hydroxyamphetamine (1% solution) should be performed
- Poor response to cocaine confirms the diagnosis of HS
- Response to hydroxyamphetamine helps determine if the Horner’s is pre or postganglionic

5 - 10% Cocaine

- If the sympathetic pathway is intact, norepinephrine is released from the nerve innervating the dilator muscles
- Normal pupil – dilates
- Horner’s - poor response

Apraclonidine can be used instead of cocaine to confirm the diagnosis of HS.

Hydroxyamphetamine

- Releases norepinephrine from the postganglionic nerve endings to the dilator muscles
- Preganglionic Horner’s (FON and SON) pupil dilates
- Postganglionic Horner’s (TON), pupil will not dilate because norepinephrine is depleted from the nerve endings
- Cocaine inhibits the uptake of HO therefore wait at least 24 to 72 hours to insure maximum sensitivity to HO

First Order Neuron HS

- Lesion location: from the hypothalamus to the Ciliospinal Center of Budge Waller (C8-T2) before the PGF synapse with the SON
- Least common location of Preganglionic HS

Clinical Findings

- Miosis may be the only evidence of a central Horner’s Syndrome
- Usually present with cerebellar or brain stem findings
- Anhidrosis Distribution ipsilateral entire half of the body
**Etiologies**

- Brain stem infarcts - Lateral medullary syndrome (Wallenberg Syndrome)
- Tumor (hypothalamus, brain stem, or spinal cord)
- Trauma
- Inflammation (poliomyelitis, transverse myelitis)
- Syringomyelia
- Demyelinating disease i.e. Multiple sclerosis

**Imaging Modalities**

- FON HS with brain or brain stem symptoms: 
  Brain MR +/- MRA, diffusion weighted imaging
- FON HS with myelopathic features: 
  Cervical and Upper Thoracic Spine MR

**LMP (Wallenberg)**

- Most common cause of FON HS
- Occlusion of the PICA or the vertebral artery can produce infarct in the region
- CN palsy and FON HS

**Hypothalamic Pilocytic Astrocytoma**

13 yr old boy with headaches and left anisocoria. Pharmacological testing suggested a left preganglionic HS.

**Syringohydromyelia**

Intramedullary cyst that contain CSF can causes compression of the gray and white matter. HS may alternate from eye to eye.

**Multiple Sclerosis**

The presence of HS in a patient with a history of demyelinating disease such as MS suggest the possibility of spinal cord involvement. MS plaques tend to occur in the dorsolateral aspect of the cord. This is where the sympathetic fibers travel in the cord.
First Order Neuron HS

Multiple Sclerosis

Second Order Neuron HS

Horner’s Syndrome

Peripheral Preganglionic HS

• Lesion location: from the SON to before the PGF synapse with the TON
• The majority of cases of Preganglionic HS are secondary to lesions in this region.

Second Order Neuron HS

Clinical Findings
• Often have the full syndrome of ptosis, miosis, and anhidrosis
• May have a brachial plexus palsy
• Anhidrosis distribution: ipsilateral face and neck

Second Order Neuron HS

Etiologies
• Surgery or trauma of the thorax and neck
• Pancoast tumor
• Primary spinal nerve root tumors or lesions compressing or destroying the nerve root (osteophytes and nerve root avulsions)
• Sympathetic chain lesions (neoplasm and surgery)
• Neck masses (nodal disease or primary neck masses such as an enlarged thyroid)

Second Order Neuron HS

Imaging
• Lesions can be located in the SON, nerve roots of C8- T2 or neck up to the level of C2- C3
• If a mass is present on PE or a lesion is seen the lung apex on a CXR – usually do a CT covering the area of interest
• If clinical findings suggest spine or nerve root involvement - MR
• Otherwise you need to cover the area from C2- C3 to T2
Non small cell bronchogenic carcinomas (squamous or adenocarcinoma)
• Located in the lung apex (superior sulcus)
• Cause SON HS secondary to inferior cervical ganglion involvement and brachial plexopathy when the inferior trunk of the brachial plexus is involved

Second Order Neuron HS
Pancoast Tumor

58-year-old male with weight loss, right brachial plexopathy and preganglionic HS

Second Order Neuron HS
Sympathetic Ganglion Schwannoma

19 yr old male with a right preganglionic HS.

Second Order Neuron HS
Cervical Sympathetic Chain (CSC)
The CSC runs longitudinally over the longus colli and capitis muscles, posteromedial to the CS, deep to the prevertebral fascia. Lesions involving the CSC typically cause anterior or anterolateral displacement of the CS.

Second Order Neuron HS
Sympathetic Schwannoma (SCS)
Nerve sheath tumors can arise from the sympathetic chain. HS may be part of the initial presentation but is more often encountered after surgery for the removal of the lesion.
Arises from the neural crest blast cells in the adrenal gland or cervical sympathetic chain. Less than 5% of these lesion occurs in the neck. These lesion should be look for in children who present with HS, iris heterochromia and no history of cervical trauma.

Neuroblastoma

2 yr old male with a right preganglionic HS, iris heterochromia and no history of birth trauma.

Metastatic Breast Carcinoma

Any lesion that compresses the sympathetic chain can produce a HS.

50 yr old female with breast cancer had a left preganglionic HS.

Goiter

35 yr old female with a thyroid mass and a left preganglionic HS

Third Order Neuron Horner’s Syndrome

Postganglionic HS

• Lesions can be located anywhere from the from the SCG to the eye
Clinical Findings

- Full syndrome usually present: ptosis, miosis and anhydrosis
- Orbital lesions: proptosis, chemosis and conjunctival hyperemia are often present
- Cavernous sinus: ipsilateral extraocular pareses esp CN VI without brain stem signs
- Carotid dissection: hx of trauma, neck pain, ipsilateral vision loss and acute onset of postganglionic HS

Anhidrosis

- Ipsilateral face and neck if the lesions occurs in the SCG
- Ipsilateral nose and forehead if the lesions is distal to the SCG

Anhidrosis

- Ipsilateral face and neck if the lesions occurs in the SCG
- Ipsilateral nose and forehead if the lesions is distal to the SCG, because sympathetic fibers travel with the IAC to this region.

Etiologies

- Carotid dissection above the SCG
- FMD
- Cluster or Migraine headache
- Trauma
- Neoplasm/ infection in the orbit, pericarotid and cavernous sinus regions

Imaging

- NO ASSOCIATED CLINICAL FINDINGS
  NO IMAGING
- If clinical findings are focal, the scan should cover the suspected area
- If history suggest a carotid dissection, CT/CTA or MR/MRA

Fibromuscular dysplasia
Carotid Dissection

Carotid dissection should be r/o if a pt has a hx of trauma, neck pain, ipsilateral vision loss and acute onset of postganglionic HS

High signal around the left ICA with an eccentric flow void.

Nasopharyngeal Carcinoma

46-year-old Chinese female with left TON HS.

Invasive Aspergillosis

45-year-old immune compromised male, presented with left proptosis, chemosis, conjunctival hyperemia and left postganglionic HS.

Summary

Before this lecture what lesions would you have list as potential causes of HS?

- Chest Radiologist
  - Pancoast tumor

- Pediatric Radiologist
  - Birth trauma
  - Neuroblastoma

- Neuroradiologist
  - LMP infarct
  - Carotid dissection

Now you know there is more to HS “THAN MEETS THE EYE”
Last but not least: Cranial XI and XII

Anatomy where are the nerves
Denervation patterns
XI
XII
Pathology
Primary
Secondary invasion
Perineural spread
Carotid dissection
Other

XI Accessory
XII Hypoglossal
Landmarks
- Pars Nervosa (medial jugular foramen)
- Jugular spine
- Jugular tubercle (occipital)
- Hypoglossal canal

XI
Spinal accessory n. crosses anterior to the jugular vein most commonly but occasionally posterior. Gives of branches to the sternocleidomastoid before extending to the Trapezius

XII
Hypoglossal n. initially follows the carotid artery then curves anteriorly passing lateral to the internal and external carotid. The nerve is medial to the digastric muscle and passes through the glosso-mylohyoid gap between the hyoglossus m. and mylohyoid into the sublingual space and tongue.
Denervation patterns

Xi  SCM and Trapezius

XII Tongue muscles
  spares mylohyoid and digastric
Etiology of denervation
Persistent hypoglossal artery

Venous Varix

Meningocele

Artwork by Robert Galla
