Case Report of Nasopharyngeal Carcinoma with Ocular Involvement

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**I. Case History/Pertinent Findings:**

**11/30/2012**

- 23 y.o. Native American male
- **CC:** Diplopia
  - OU, Started 1½ wks ago, Worsening, (+) Eye strain, (+) h/o Migraine headaches, (-) Ocular/Head Trauma
  - Current ear infection
- **VA** OD: 20/20 OS: 20/20 (w/retinoscopy)
- **Pupils, EOMs, IOP, Cover Test:** Normal
- **Anterior/Posterior Segment:** Normal OU
- **Dx:** Diplopia
  - **F/U:** 1 week

**12/07/2012**

- **F/U** for diplopia
  - Pt reports distance only diplopia, but feels its better
  - **Pupils, EOMs, Cover Test:** Normal
  - **SRx:** OD +0.25-0.75 x 180 OS +0.25-0.50 x 180
  - **Dx:** Diplopia – resolved w SRx

**12/17/2012**

- **CC:** Diplopia
  - Binocular, Worsening (D>N), Started 1 month ago, (+) h/o Migraine headaches, (-) Ocular/Head Trauma
  - Current ear infection
  - “Can hear heartbeat in Right ear”
- **VA** OD: 20/20 OS: 20/20
- **Pupils, Lids, IOP:** Normal
EOM: Full OU, but diplopia in 1⁰ gaze, superior, & inferior

CT(D): 10⁷ CRET  CT(N): 6⁰ CRET

*****Unable to elicit any vertical component

Trial frame of last Rx resulted in diplopia

Anterior/Posterior Segment: Normal OU

Dx: Diplopia 2⁰ Acute onset RET
  • Phone consultation w/ ENT

II. Differential Diagnosis:

• Gradenigo’s syndrome
  • Infection of petrous bone secondary to otitis media causing ipsilateral CN VI & VII paresis, resulting in facial weakness and pain, and hearing difficulties

• Tumor

12/18/2012

• Patient seen by ENT
  • Abnormal EOMs, diplopia in 1⁰ gaze and worse when looking right
  • Dx: right otitis media, right nasopharynx lesion, and new onset diplopia
    • “Extremely concerning for a skull base aggressive lesion”
    • Needs MRI

III. Diagnosis/Treatment/Management:

12/19/2012

• MRI of the brain, skull base, & orbits w & w/o contrast:
  • Abnormally enhancing soft tissue thickening & infiltration within the posterior nasopharynx which extends deep to the nasopharyngeal fascia. The tissue results in obstruction of the right eustachian tube. Also, there is superior extension of soft tissue infiltration into the right inferior petrous apex with associated mild wall thickening of the right petrous apex portion of the right internal carotid artery.

  • There is mild abnormally enhancing soft tissue thickening along the dura of the medial aspect of right temporal lobe which is concerning for intracranial extension. In addition, there is inferior extension of infiltrating soft tissue especially into the right parapharyngeal space.
• DDx: squamous cell carcinoma, lymphoma, infection
• EOMS demonstrate no evidence of thickening or infiltration.
• No evidence of intraconal or extraconal mass.
• Optic chiasm is unremarkable.
• Enlarged lymph node in the posterior neck which probably measures greater than 3cm.
• Impression: An infiltrating process involving the posterior nasopharynx, right petrous apex, mastoid sinus, right parapharyngeal space. Right temporal lobe dural thickening concerning for intracranial extension. Neck lymphadenopathy.

○ Axial T2 MRI Scans – 12/19/2012
○ Coronal T1 MRI Scans – 12/19/2012
○ Coronal T2 MRI Scans – 12/19/2012

12/20/2012

○ Patient seen by ENT
  • MRI reviewed
    ○ “3 cm deeply invasive nasopharynx mask...highly suspicious for a nasopharyngeal carcinoma”
    ○ “Recommended he have a nasopharynx biopsy with nasal endoscopy and a right myringotomy and tube tomorrow in Flagstaff Medical Center”

12/21/2012

○ Surgical notes:
  • A 23 y.o. male is found to have serous otitis media and a mass on his nasopharynx. Invasive 3 cm mass in the skull base seems to arise from the nasopharynx, wraps around the carotid artery and Eustachian tube.
  • Biopsy was performed through nasal endoscopy and sent to pathology where a frozen section was consistent with undifferentiated carcinoma. A myringotomy was made in the tympanic membrane, and a Reuter bobbin tube was inserted.

01/10/2013

○ Percutaneous Endoscopic Gastrostomy tube placement for chemotherapy

  • Chemotherapy to start 01/14/2013

IV. Discussion:
Epidemiology

- “Distinct cancer of head & neck”
- Worldwide: 80,000 incident cases & 50,000 deaths/yr
- US & Western Europe: RARE – 0.5 to 2/100,000
  - Incidence increases w/ increasing age
  - Major peak 50 yrs of age, minor peak ages 10-25
- Southern China (endemic): 25/100,000
  - Incidence peaks around 50-59 y.o.
  - Incidence has declined over past 30 yrs (unclear reason)
  - 2-3 x higher in Males

Etiology

- Endemic populations: appears due to interaction of
  - Epstein-Barr virus (EBV)
  - Genetic predisposition – 1st degree relative ↑ risk
  - Environmental factors (high intake of preserved foods, smoking)
  - United States & Europe: more commonly associated w/ alcohol & tobacco
- Human Papilloma Virus – small group of pts, all have extension into oropharynx
- Epstein-barr virus
  - Much evidence supports role as primary etiologic agent
  - 95% of adults in all ethnic groups in the world are healthy carriers of EBV→ NPC is not simply a consequence of EBV infection
  - Likely results from a viral reactivation coupled w/ genetic predisposition, environmental carcinogens, immune defects
    - The detection of EBV-related serological alterations can be detected a long time prior to a clinically or radiologically detectable tumor
  - Present in almost all cells of primary and metastatic NPC tumors; regardless of histology, stage of disease, or patient geographic location

Clinical Presentation
Neck mass, Nasal obstruction w epistaxis, Serous otitis media, Hearing problems, Tinnitus, Dysphagia, Dysphonia, Anosmia, Headache, Diplopia, Facial pain, Numbness

Asymptomatic for prolonged period

Originates from the lateral pharyngeal recess (the fossa of Rosenmuller) and the eustachian tube ostium

CN involvement: upper (II-VI), lower (IX-XII), or both
  - Most commonly V or VI

Skull-base invasion in up to 65% of patients
  - Most common site is sphenoid bone

Tendency for early metastatic spread
  - Lymph node metastasis in 75-90%
  - Bilateral nodes in >50%
  - Distance metastasis in 5-11%
  - Bone, lung, liver, distant nodes

Histology

- Arises from epithelial lining

World Health Organization (WHO) classification:
  - 1. Keratinizing squamous cell carcinoma
    - Less radiosensitive than non-keratinizing carcinoma
    - Less association with EBV
  - 2. Differentiated non-keratinizing carcinoma
  - 3. Undifferentiated non-keratinizing carcinoma
    - Endemic form, strongly associated w EBV, more favorable prognosis
    - North America: 25% type 1, 12% type 2, 63% type 3
    - Southern China: 2% type 1, 3% type 2, 95% type 3

Diagnosis/Imaging

- Only definitive on endoscopically-guided biopsy
- MRI preferred over CT
  - Better at showing skull-base involvement & intracranial extension
  - Superior soft tissue contrast & multi-planar imaging capability
- PET scanning to determine other systemic involvement
  - High risk (N3) disease should also have chest radiography, bone scan, liver ultrasonography
- EBV testing

**Therapeutic Intervention**

- **Radiation therapy** is mainstay
  - External or brachytherapy
- **Chemotherapy**
  - Neoadjuvant – before radiation therapy; used to reduce the sub-clinical metastases and to improve local control by shrinking tumor volume
  - Adjuvant – used to reduce the risk of distant metastases
  - Concomitant radio-chemotherapy – increase local control and decrease probability of distant metastasis
- **Intensity-modulated radiation therapy** – improves tumor target coverage & spares sensitive normal tissue
- **VEGF** – angiogenic growth factor that contributes to angiogenesis & important to tumor growth, invasion, & metastasis
  - Expression is found at a higher rate in nasopharyngeal carcinoma compared to normal nasopharynx
  - Expression is statistically significantly increased in advanced disease compared to early stage

**TNM Classification**

**Prognosis**

- Clinical stage
  - 5 year survival ranges from 90% for Stage I to 50% for Stage IV
- Distant metastasis (main cause of death)
- MRI over CT when used to stage
  - Had better tumor control rate & survival
Better if only lower or upper CN involvement
Better survival if recovered from CN palsy
  • Roughly 50% have complete remission of CN palsy
  • Median time to complete remission is 14 days from initiation of radiation therapy

Necessary Follow-up

Endoscopic examination: To detect superficial tumors
  • q4-6 months during initial 3-5 years

MRI: To evaluate for tumor recurrence or post-radiation complications
  • q4-6 months during initial 3-5 years

Eye clinic: To manage residual CN palsy
  • Appearance of CN palsy several years after radiotherapy may not indicate recurrence

Dental clinic: To manage Mucositis, infection, xerostomia, taste changes

References


I. Case History

- 50 Year old white male, right handed, oriented P, P & T normal affect
- Presents seated in a wheelchair, wearing glasses, squinting one eye shut
- Gives history in a hoarse scratchy voice

**Chief complaint:** Diplopia

Other symptoms: Blurry vision, wiggling vision (oscillopsia), spatial distortion of doorways into trapezoidal shape, feels pulled to the right so he leans left, balance disturbance, dizziness, hiccups, dysarthria, swallowing difficulty

**History of Present Illness:**

- Recent hospitalization for right lateral medullary stroke
- IV-tPA administered
- Aspiration on swallowing, PEG tube placed
- Uncomplicated hospital course, followed by inpatient rehabilitation

**Past Medical history:**

- Gout
- Testicular cancer (treated with orchiectomy)
- Radiation therapy
- New onset hypertension

**Medications:**

- Duonebs
- Norvasc
- Vitamin C
- Ecotrin
- Thorazine
- Heparin
Family History
- Mother lung cancer, hypertension and hyperlipidemia at young age
- Father MS and seizure disorder

Ocular history
- Last eye exam routine and one year ago
- Wears PAL
- No other ocular issues self or family

II. Pertinent findings

- Clinical
  - Current Rx -0.25 sphere OD and OS +1.25 Add PAL
  - Distance VAcc 20/60-2 OD and 20/50-2 OS, NI PH
  - Near VAcc 20/100 OD and 20/100
  - Cover Test: 10 prism diopters left hyper in primary gaze at distance and 8 at near. Worse in right gaze.
  - Hypometric saccades to the left and Hypermetric saccades to the right
  - Horizontal torsional nystagmus on gaze holding and smooth pursuits
  - Right ptosis and miosis (Right Horner’s syndrome)
  - 15 degrees counterclockwise torsion OD and 10 degrees CC OS
  - Normal confrontation fields and convergence

- Physical
  - Feels as if being pulled to the right so he leans left (lateropulsion)
  - Dizzy and off balance, sits in wheelchair, walks with supervision
• Laboratory studies
  ○ Pre-admission lab studies on file in patient medical chart
  ○ Consistent with hyperlipidemia diagnosis
• Radiology studies report
  ○ MRI of brain indicates right lateral posterior medulla infarction

III. Differential diagnosis

• Lateral medullary stroke with Wallenberg’s syndrome
• Central acquired Horner’s Syndrome with multiple process
• Other forms of diplopia and balance disturbances

IV. Diagnosis and discussion

• Ocular Diagnoses:
  ○ Diplopia oblique
  ○ Skew deviation with ocular skew torsion, ocular tilt reaction
  ○ Torsional nystagmus
  ○ Oscillopsia
  ○ Decreased visual acuity
  ○ Horner’s Syndrome
  ○ Hypermetric /Hypometric saccades
  ○ Lateral pulsion
  ○ Graviceptive pathway dysfunction
  ○ Vestibular /ocular dysfunction

• Unique features
  ○ Diplopia and nystagmus are reduced when patient is fully reclined
  ○ Graviceptive pathways are not evoked in reclined position

• Discussion of the neuro-anatomy in the lateral medulla
  ○ Vestibular nucleii
V. Treatment, management

- Treatment and response to treatment
  - Increased Add to +1.75D OU, 20/40 near VA OD and OS
  - Fresnel Press on Prism, 10 prism diopters base down OS eliminated diplopia in most positions of gaze while patient is upright
  - Reclined visual rehabilitation, occupational and physical therapies will reduce symptoms related to graviceptive pathways, skew diplopia, nystagmus and oscillopsia
  - Range of motion and fusion, smooth tracking saccades and VOR are the visual rehab activities for the reclined position
  - Gradual inclination on tilted bench introduced over time allows gradual adaptation of the vestibular system

VI. Conclusion

- Clinical pearls: Knowledge of neuro-anatomy predicts signs and symptoms associated with a lesion
- Diplopia comes in many varieties, can be associated with other neurologic findings, and is treatable with prism and rehab therapies
• Understanding of the relationship between the visual and vestibular system allows a more complete view of patient symptoms in this case

• A non-traditional diagnostic and therapeutic technique of reclining the patient and repeating testing revealed the effects of the graviceptive pathways in skew deviation

VII. Bibliography


"THE INCREDIBLE SHRINKING BRAIN"

A 46yo man presents with abnormal vertical saccades with convergence spasm / divergence insufficiency. MRI shows cerebellar hemispheric and vermian atrophy. Differential diagnoses including spinocerebellar ataxias, OPCA, ethanol toxicity, lysosomal storage diseases, among others, are considered.

CASE REPORT:

Case History

- **Patient Demographics:** 46 year-old man
- **Chief Complaint:** walking / balance / gait issues, difficulty going down steps, feels like in a fog, no diplopia

  **Ocular / Medical History:** hypercholesterolemia (diet controlled)

  **Medications:** none

  **Other Salient Information:** few concussions from HS football, reports drinking 1-2 beers/day

Pertinent Findings:

- **INITIAL VISIT**
  - **Clinical:** (photos included in presentation where appropriate)
    - OVA 20/20 OD and 20/25+ OS.
Ishihara color plates: 14/14 OD and 14/14 OS,
Pupils were isocoric with no relative afferent pupillary defect
Confrontation fields: full bilaterally
Palpebral aperture: OD 10 mm  OS 10 mm, Exophthalmometry: OD 19 mm  OS 20 mm
Ocular motility: ductons full OU; versions/saccades: mild conjugate / dysconjugate dysmetria (overshoots, post-saccadic drifts, glissades); vertical saccades – intermittent convergence in up and down gaze; mild gaze evoked nystagmus.
Slit lamp examination unremarkable OU / IOP: normal OU / Blood pressure: normal
Dilated fundus examination: No disc edema, Moderate cupping, NRR pink, Normal retina OU.

Physical: Neurologic examination: cranial nerves V, IX - XII intact
Motor, sensory, and coordination testing: mild finger-to-nose ataxia, mild difficulty with rapid alternating hand movements

Diagnostic laboratory Testing: (INITIAL WORK_UP)
CBC, ESR, C-reactive protein, platelet count, TSH, vitamin B12, myelin associated glycoprotein IgM, vitamin B1, CMP, ANA, RF, SPEP, folate, creatine kinase, etc.
All unremarkable

Imaging Studies: (INITIAL WORK_UP)
MRI of brain and orbits with and without contrast
Remarkable for dilation of sulci and ventricles, greater than expected by age, few focal defects in periventricular white matter, cerebellar hemispheric and vermian atrophy with secondarily large 4th ventricle

FOLLOW-UP VISITS (including with neurology)

Chief Complaint: continued episodes of balance / gait issues
Additional Work-Up:
- EMG: no evidence of peripheral neuropathy or Charcot-Marie Tooth syndrome

iii. ER Visit: unsteady gait, confusion, occipital headache, and extreme sleepiness.

Blood alcohol level very high at 297. Pt first claimed drank 7 beers 72 hours prior, then said last drink was 10 hours ago (5 beers).
Additional Work-Up: recheck alcohol level, thiamine, B6 levels
**Differential Diagnoses:**

1. **Chronic Traumatic Encephalopathy:** associated with atrophy of the frontal and temporal cortices and medial temporal lobe.

2. **Cerebellar Ataxias:**
   - Hereditary Ataxias - May be autosomal dominant, autosomal recessive or x-linked
     - Autosomal Dominant Cerebellar Ataxias:
       - Spinocerebellar ataxia: progressive, degenerative genetic disease with up to 60 types
         - May occur at any age / many are polyglutamine diseases
         - Slowly progressive incoordination of gait and is often associated with poor coordination of hands, speech, and eye movements.
       - Marie's ataxia, olivopontocerebellar atrophy, cerebello-olivary atrophy
     - Autosomal Recessive
       - Friedreich's ataxia, Spinocerebellar ataxia, Ataxia telangiectasia, Vasomotor ataxia, Vestibulocerebellar, Ataxiadynia, Ataxiophobia, Olivopontocerebellar atrophy, and Charcot-Marie-Tooth disease.
   - OPCA – can be inherited or sporadic with no known family history
     - The cause of the sporadic form is not known; it progressively worsens
     - The average age of onset is 54 (earlier with inherited form); more likely in men
     - Balance problems, walking issues, slurred speech, abnormal eye movements
   - Lysosome storage diseases - group of approximately 50 rare inherited metabolic disorders
     - Lysosomal dysfunction usually as a consequence of deficiency of a single enzyme required for the metabolism of lipids, glycoproteins or mucopolysaccharides
     - Most are autosomal recessively inherited such as Niemann-Pick disease, type C, few are X-linked recessive such as Fabry disease and Hunter syndrome.
     - Affect mostly children - often die at a young age, within few months or years of birth
     - Development delay, movement disorders, seizures, dementia, deafness, blindness.

3. **Diagnosis and Discussion:** Ethanol Toxicity / Alcoholic cerebellar degeneration
• one of the most common neurological complications in alcoholics
  
• both cerebellar vermis and hemispheres can be involved
  
• caused by irreversible toxic degeneration of Purkinje cells, and is clinically characterized by impaired gait, tremor and predominantly truncal ataxia.
  
• combination of nutritional deficiency and alcohol neurotoxicity, likely involving glutamate.
  
• Typically, the disease develops after more than 10 years of heavy drinking, though there is no direct relation between the "dose" of alcohol and severity of symptoms
  
• Cognition remains intact (unlike Wernicke-Korsakoff syndrome)
  
• The anterior and superior vermis are preferentially affected, giving rise to a remarkably stereotypic syndrome of ataxic stance and gait. Alcohol is directly toxic to the cerebellum, causing degeneration of the anterior superior vermis and hemispheres

○ Treatment / Management:

  ○ Treatment / Response:

    ○ Patient advised to completely discontinue all alcohol use / vitamin supplementation

  ○ Bibliography / Literature Review:

    
    

Conclusion:

• Cerebellar degeneration can be associated with balance issues as well as abnormal eye movements
  
• There are several neurologic causes of cerebellar atrophy/degeneration and ataxia, but ethanol toxicity must always be considered.
  
• Patients with alcohol overuse will not be forthright about their levels of alcohol consumption
  
• Alcohol overuse can affect the eyes in many ways, either directly (toxic nutritional optic neuropathy) or indirectly (cerebellar degeneration).
  
• Patients with alcoholic cerebellar degeneration may not have any other obvious features of ethanol toxicity, such as optic neuropathy.