**NEURO-OPHTHALMIC MANIFESTATIONS OF METASTATIC CANCER**
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**METASTASES**
With known history of cancer, always consider metastatic process.

In those patients, any new neuro-ophthalmic finding should be considered a metastatic process until proven otherwise.

Keep in mind that patients may have metastases without being previously aware of a primary cancer.

**SITEs OF METASTASES**
- Brain
- Bone
- Leptomeninges
- Lymph nodes
- Others (less applicable to us)

**BRAIN METASTASES**
- among the most common mass lesions in brain
- increased incidence traced to an increase in the median survival of patients with cancer
  - modern therapies, increased availability of advanced imaging techniques for early detection, and vigilant surveillance protocols for monitoring recurrence
  - most systemic treatments (eg, the use of chemotherapeutic agents, which may penetrate the brain poorly) can transiently weaken the blood-brain barrier (BBB) and allow systemic disease to be seeded in the CNS, leaving the brain a safe haven for tumor growth

**BRAIN METASTASES**
- Radiology appearance
  - usually at the junction of the gray/white matter
  - often with surrounding edema
  - dural based mets may mimic meningioma
  - often enhance with contrast
    - solid enhancing
    - ring-enhancing
- Sites of Origin
  - Lung
  - Breast
  - Melanoma
  - Lymphoma
  - Renal
  - Colorectal
  - Osteosarcoma
  - Head/Neck Cancers
Brain Metastases

- Location of Brain metastases
  - Based on blood supply, since the metastases occurs through the bloodstream
    - Cerebrum (80-85%)
    - Cerebellum (10-15%)
    - GI cancer
    - Melanoma
    - Brainstem (5-10%)
- Number of Brain metastases
  - If there appears to be an isolated brain metastasis on CT, there are often found to be multiple metastasis on MRI
    - Isolated
      - Thyroid cancer
      - GI cancer
      - Renal cancer
    - Multiple
      - Melanoma
      - Lung cancer
      - Breast cancer

Bone Metastases

- Primary bone cancers are rare
- Associated with lytic lesions and pain
- Sites of Origin
  - Prostate
  - Breast
  - Lung
- Sites of metastases (to cause neuro-ophthalmic disorder)
  - Chord
  - Skull base

Leptomeningeal Carcinomatosis

- Also called neoplastic or carcinomatous meningitis
- Invasion to and subsequent proliferation of neoplastic cells in the subarachnoid space
- Substantial rates of morbidity and mortality
- MRI with contrast can detect leptomeningeal enhancement
- Diagnosis confirmed with CSF cytometry
- Sites of origin
  - Lung
  - Breast
  - Melanoma
  - Medulloblastoma

Case 1, 2 & 3

Brain Metastases

Case 1
70 year-old man

- c/o a funny sensation on his right lower eyelid and under his right eye, and involving his right nose and upper lip.
- He suddenly noticed this about 1 month ago, and it seems constant since then, with nothing making it better or worse.
- He doesn’t feel the right side above his lip when he shaves, or the upper right teeth/gums when brushing his teeth
- He denies any other visual, ocular, or neurologic symptoms.

He mentioned this to his PCP and cardiologist

- They did not feel any additional work-up was necessary.

- Hypertension x 12 years
- Hypercholesterolemia
- Osteoarthritis
- Coronary artery disease
- Status post 2 stent placements in 2000
- Status post spinal surgery because of herniated discs.
- Medications
  - Lipitor, Metoprolol, and 81 mg aspirin.
- Ocular history is unremarkable.
- Social history is remarkable for a past history of tobacco use, which was discontinued 15 years ago.

VA: 20/20 OD, 20/20 OS
- Color: 5/6 OD, 5/6 OS
- PERRLA (-) RAPD
- CF: full OU
- EOMs: no restrictions
- No ptosis or proptosis

- Normal slit lamp exam
- Decreased corneal sensation OD as compared with OS
- IOP: 16 OD, 16 OS
- BP: 135/80
- DFE: 0.3 x 0.3 cupping OU
- (-) edema (-) pallor

NEUROLOGIC EXAMINATION:
- Reduced sensation in the distribution of V2 on the right side as compared with left side
• 3 enhancing intraparenchymal lesions
• 2 demonstrate peripheral enhancement
• 1 demonstrates solid enhancement
• Lesions demonstrate surrounding edema
• Largest lesion (2cm) is in the right frontal lobe, measuring 2 cm
• Highly concerning for metastatic disease
• None of the masses explain the symptoms (location).
• Enhancement of the foramen rotundum on R explains symptoms

• V1 = SOF
• V2 = foramen rotundum
• V3 = foramen ovale
• The patient has no known history of cancer.
• A work-up is needed to find the primary site
• He reports he had a normal colonoscopy a few months ago

• He now admits to some frontal headaches
  – X 1-2 months
  – May be getting more frequent
  – Relief with ibuprofen
• Sometimes he gets a funny sensation when he scratches his head
• No changes in weight or appetite
• No longer able to tolerate alcohol (pain)

**BRAIN METASTASES**

• Result from systemic cancers involving:
  • Lung ****
  • Breast ***
  • Melanoma ****
  • GI tract (colon, pancreatic)
  • Lymphoma
  • Genitourinary (kidney, testes, ovary, cervix)
  • Thyroid

• What is the number of brain mets?
  – Isolated brain met: breast, thyroid, renal, colon
  – Multiple brain mets: lung and melanoma

**WORK-UP:**

  Chest x-ray: nodular density in the right lower lobe (shadow vs. nodule)
  • CT of chest / abdomen / pelvis with contrast:
    - Confirmed lung cancer (carcinoma)

  Tx: radiation to brain, chemotherapy

**CASE 2**
68 year old man
• Recent onset horizontal diplopia x 8 days
• Worse at distance and in right gaze
• Recent problems with balance x 4 weeks
• Feels like he is drunk when he walks
• Using a cane to walk
• Yesterday notices left leg numbness

(-) DM x 8 yrs
• Tobacco use x 50 years
• Prostate cancer 5 years ago (s/p surgery)
• Small cell lung carcinoma 3 yrs ago
  — Radiation and chemo
• Recent PET scan showed suspicious lymph node
  — Has started chemo and about to begin radiation

VA OD 20/25 OS 20/25
• PERRL (-)APD
• CF: Full OU
• IOP normal
• BP normal
• DFE: (-) pallor OU, (-)edema OU

Abduction Deficit
• Problem with:
  — Muscle (restrictive)
    • Thyroid
    • Positive Forced Duction Test
  — Junction (Neuro-Muscular Junction)
    • Myasthenia Gravis
  — Nerve — CN VI
    • Subarachnoid space (papilledema)
    • Clivus
    • Cavernous sinus (check CN II, IV, V1, V2)
    • SOF / orbit (look for proptosis, features of optic neuropathy)
  — Brain – Pons
    • Look for CN VII, corticospinal involvement, etc
Neurologic Exam
- CN V, VIII-XII intact
- (+) left finger-to-nose ataxia
- Left lower extremity weakness

Work-Up
- MRI of the brain with and without gadolinium
- Special attention to pons, cerebellum

Metastatic Lesions Found
- Large lesion in right pons
- Lesion in cerebellum
- Small lesion in frontal lobe
- TX: getting daily radiation treatment to brain

CASE 3
52 year-old man

- Family indicates he lost 20 lbs in past yr
- Problems with walking and balance
- He keeps holding his chin up
- Changes in mental status and behavior
  - Pt thinks all problems are from glasses & clothing
- Hasn’t seen a doctor in > 10 years

- VA: OD 20/40 and OS 20/40
- Color: OD 7/7 and OS 7/7
- CF: full OU
- Palpebral apertures: OD 10 mm and OS 10 mm
- Exophthalmometry: OD 17 mm and OS 17 mm
- Normal SLE
- TA: OD 14 mm Hg and OS 17 mm Hg
- DFE: normal optic nerves and retina OU
- Neurologic exam:
  - Broad-based, ataxic gait
  - Positive Rhomberg sign
  - Slow, slurred speech
DORSAL MIDBRAIN SYNDROME

- TECTAL PUPILS
- UPGAZE PARESIS (DOWNGAZE PARESIS, OR BOTH)
- CONVERGENCE RETRACTION NYSTAGMUS
- EYELID RETRACTION

Diagnosis

- Multiple lesions noted, not only in midbrain, but throughout brain
- Characteristic of metastatic lesions
- No known history of a primary cancer
- Work-up to find primary site revealed multiple organs involved

CASE 4, 5 & 6
Bone Metastases

CASE 4
• 66 YO man
• Sudden onset blurry vision 4 days prior to consultation
• Notices a “glare” in left gaze, no diplopia
• Wife notes that OS sometimes turns in
• Examined at ER 2 days ago, told of BP 190/90 as cause of blur
• Hx of HTN (10 yrs), prostate CA-chemo tx q 3 m – no surg/rad
• HCTZ, Nifedipine, unspecified chemotherapeutic agent
• Denies eye / head pain, GCA symptoms, vision loss

VA: OD 20/30  
OS 20/25

- Pupils isocoric, (-)RAPD
- CF: OD full  OS full
- Color: OD 14/14 OS 14/14
- Exophthalmometry: OD 23mm OS 22mm
- SLE: mild cataracts
- DFE: unremarkable

- Slowed saccades to left OS
- Negative forced duction test OS

Prostate cancer mets to clivus
• S/P radiation treatments to involved areas
• Now 90% normal abducting capacity OS

CASE 5

Additional Work-up Revealed Previously Undiagnosed Breast Cancer

CASE 6

40 y/o Woman
• Hx of breast CA & S/P mastectomy
• Recent onset lid droop OS
• + anhydrosis & decreased tearing OS
Phrenic Nerve Syndrome

- Usually females
- Hoarse
- Hiccough
- Horner
- Can be from metastatic breast CA

CASE 7
Carcinomatosis Meningitis
Leptomeningeal Carcinomatosis

63 year old woman
- 3-week history of left eye and head pain
- The pain keeps her up at night
- Then, the left eyelid began to droop
- 2 weeks ago, she noticed double vision
- Decreased appetite
- Weakness and fatigue

CASE 7
SYSTEMIC HISTORY:
- Lung cancer 2 years ago
- Surgery, radiation, chemo
- Still undergoing treatment
- Otherwise unremarkable
• VA OD 20/40 OS 20/40
• Normal color vision
• Anisocoria greater in bright
• (-)APD
• CF: Full OU
• IOP normal
• BP normal
• ONH: (-) pallor OU, (-)edema OU

• Emergent hospitalization to rule out aneurysm
• MRI and MRA negative
• While in hospital CN III palsy progressively worsened
• Cerebral angiogram negative
• Lumbar puncture
• Diagnosed with meningeal carcinomatosis

CASE 8

Metastatic vs. Primary?

59 year old man

• difficulty reading words at distance and near x 3 months
  • letters look fragmented with a ghost image
  • cannot see entire word / has to scan more to read
• peripheral vision seems reduced on both sides
• “Ocular Migraines” x 2 years
  • large spot in the center of his vision x 20 minutes
  • 1-2 x week after physical exercise (riding his bike)
• Headaches – worsening over the past few months
  • daily - mild to moderate (4 out of 10) headaches
    • improvement with aspirin or Tylenol
  • 2 severe headaches in the last month
    • one woke him out of sleep
• **SYSTEMIC HISTORY:**
  - hypercholesterolemia (diet controlled), benign prostate hypertrophy
  - 25 years ago - herpes zoster outbreak on right face
    - affected the cornea - last flare up 3 months ago
    - question if related to recent vision issues

• **MEDICATIONS:**
  - multivitamin, aspirin 81 mg, fish oil, lutein,
  - sonata, Viagra

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**Clinical Examination**

- VA: OD 20/20 and OS 20/20
- Color Vision (Ishihara) OD 14/14, OS 14/14
- PERRL (-) | RAPD
- No ptosis or proptosis
- Ocular Motility: normal ductions, versions, and saccades
- SLE: right corneal opacity from past zoster involvement
- TA: normal OU
- BP: 130/90
- DFE: 0.3/0.3 cupping OD and OS
  - Normal optic nerve, macula, vasculature

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Radiologically the lesion was thought to be a glioblastoma multiforme (Grade IV Astrocytoma)

However, after surgical removal and biopsy, it was determined to be a rare primary CNS melanoma

WITH ANY NEW NEURO-OPHTHALMIC MANIFESTATION IN THE SETTING OF A HISTORY OF CANCER, ALWAYS CONSIDER METASTASIS.
THANK YOU.
ANY QUESTIONS?

SALUS UNIVERSITY