NEURO-OPHTHALMIC MANIFESTATIONS OF PRIMARY CANCER

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Nothing to Disclose

PRIMARY CANCERS

Basic Types of Primary Cancers

- **Carcinoma** — cancers that are epithelial in origin
  - Lung, Breast, Colon, Prostate, etc. (Often these present as metastatic cancers)
- **Sarcoma** - any cancer of connective tissue or supportive tissue
  - Bone, cartilage, fat, muscle
- **Glioma** — originates in brain or spine tissue
  - Astrocytoma, Oligodendroglioma, Ependymoma
- **Meningiomas** — arise from meninges
  - Atypical, Anaplastic
- **Schwannomas** — nerve sheath / Schwann cells (acoustic neuroma)
- **Medulloblastomas** — a form of primitive neuroectodermal tumor (PNET) in the cerebellum / posterior fossa
- **Hematologic Malignancies** — blood, bone marrow & lymph nodes
  - Leukemia, Lymphoma, Myeloma

Types of Primary Carcinoma

- There is not much epithelial tissue in the brain. Epithelial tissues in the brain make-up the lining of blood vessels.
- Carcinoma causing neuro-ophthalmic manifestations is more often a metastatic process rather than a primary cancer.
- Adenocarcinoma is a cancer of an epithelium that originates in glandular tissue
- Neuro-ophthalmic manifestations occur from carcinoma arising at locations other than brain
  - Nasopharyngeal carcinoma
  - Lacrimal gland adenocarcinoma
  - Parotid gland adenocarcinoma

Types of Sarcoma

- Depend on the cell type from which the tumor originates
  - Osteosarcoma (bone)
  - Chondrosarcoma (cartilage)
  - Liposarcoma (fat)
  - Leiomyosarcoma (smooth muscle)
  - Rhabdomyosarcoma (skeletal muscle)
  - Etc.

Types of Glioma

- Astrocytoma
- Oligodendroglioma
- Ependymoma
ASTROCYTOMA

» Grade I – Pilocytic Astrocytoma
  - Slow growing, with little tendency to infiltrate surrounding brain tissue. Most common in children and adolescents.

» Grade II – Diffuse Astrocytoma
  - Fairly slow growing, with some tendency to infiltrate surrounding brain tissue. Mostly seen in young adults.

» Grade III- Anaplastic /Malignant Astrocytoma
  - These tumors grow rather quickly and infiltrate surrounding brain tissue.

» Grade IV-Glioblastoma Multiforme
  - An extremely aggressive and lethal form of brain cancer. Unfortunately, it is the most common form of brain tumor in adults, accounting for 67% of all astrocytomas.

OLIGODENDROGLIOMA

» make up 4% of brain tumors, mostly affect people over 45 years of age

» May have a viral association

» Arise from white matter of cerebral hemispheres

GLIOMA - EPENDYMOMA

» rare and make up 2% of all brain tumors

» however they are the most common brain tumor in children.
  - Often involve the 4th ventricle

» In adults, they tend to affect the spinal cord

» Can be associated with neurofibromatosis II

» They generally don’t affect healthy brain tissue and don’t spread beyond the ependyma.

» Ependymal cells surround the ventricles

Types of Meningioma

One-quarter of all brain and spinal tumors are meningiomas, and up to 85% of them are benign. Account for about 27 percent of all primary brain tumors.

Benign

» About 6% of all meningiomas exhibit increased tissue and cell abnormalities. These tumors grow at a faster rate than benign meningiomas and on occasion can invade the brain. Atypical meningiomas have a higher likelihood of recurrence than benign meningiomas.

» Anaplastic or Malignant – About 3-5% of all meningiomas increased cellular abnormalities, and grow at a faster rate than either benign or atypical meningiomas.

Types of Hematologic Malignancy

- Leukemia
- Lymphoma
- Myeloma

Hematologic Malignancy

LEUKEMIA

- Cancers of blood and bone marrow.
- The four most common types of leukemia are:
  - acute myeloid leukemia (AML)
  - acute lymphoblastic leukemia (ALL)
  - chronic myeloid leukemia (CML)
  - chronic lymphocytic leukemia (CLL)
Hematologic Malignancy

**LYMPHOMA**
- A group of blood cancers that develop in the lymphatic system – associated with lymphocytes (WBCs).
- The two main types are:
  - Hodgkin lymphoma
    - Contains a giant cell (Reed-Sternberg cell)
    - Respond better to radiation
  - non-Hodgkin lymphoma (NHL)
    - Contains 16 different conditions
    - Grouped by aggressiveness

**MYELOMA**
- Cancer begins in bone marrow (plasma cells)
  - Tests:
    - ESR, SPEP/immunofixation/UEP/bone marrow biopsy
  - Forms of myeloma:
    - Multiple myeloma is most common:
      - > 90% of people with myeloma have this type.
      - Affects several different areas of the body.
    - Solitary myeloma
      - Affects just one area of body - rare
    - Localized myeloma
      - Affects several areas relatively close to each other.
    - Extramedullary myeloma
      - Affects tissue other than bone marrow - skin, muscle, lung

Multiple Myeloma
- Can progress from MGUS
  - Monoclonal gammopathy of undetermined significance
  - M-spike on SPEP (serum protein electrophoresis)
    - We see M-spike sometimes in pts with optic neuropathy
  - Pts followed by hematology/oncology
  - Labs, bone scans, bone marrow biopsy

**SPEP – serum protein electrophoresis**
- Measures proteins in the blood to help identify certain diseases
  - Multiple myeloma
  - Macroglobulinemia
  - Amyloidosis
- Uses an electrical field to separate the proteins in the blood serum into groups of similar size, shape, and charge
- 2 major proteins in blood serum
  - Albumin
  - Globulin

**SPEP**
- Albumin and globulin are broken down into 5 smaller fractions
  - We focus on the gamma region

Immunoglobulins (IgA, IgM, IgG, IgE and IgD) are the only proteins present in the normal gamma region
- Spikes in the gamma zone can be
  - Narrow (Monoclonal Gammopathy or “M-spike”)
    - Can be malignant
    - Myeloma (usually IgA or IgG spike), Waldenstrom’s Macroglobulinemia, Amyloidosis, some Leukemias, MGUS (monoclonal gammopathy of undetermined significance)
  - Broad (Polyclonal Gammopathy)
    - Suggests infection or rheumatologic condition
    - Usually not neoplasm
CASE 1
Primary Carcinoma

63 year old man

• CHIEF COMPLAINT
  – Right facial droop noticed about 1-2 months ago
  – Ocular irritation OD
  – Pain in right cheek

• Past Work-Up
  – Previous PCP in another state ordered MRI for facial droop
    • MRI of the brain without contrast
    • Remarkable only for white matter lesions - known Multiple Sclerosis
  – Patient saw a neurologist in another state 2-3 weeks ago
    • Multiple sclerosis was stable
    • Notes stated that PCP was handling CN VII palsy
    • CN VII palsy not addressed on that visit

• HISTORY:
  – Hypertension x 16 years
  – Multiple Sclerosis x 13 years - discontinued Avonex last year because of insurance issues
  – Current medications: naproxen, baclofen, metoprolol, colchicine, and lisinopril
  – Glaucoma suspect, question of past optic neuritis
  – Smokes ½ pack of cigarettes per day x years

• CLINICAL EXAMINATION:
  – VA: OD 20/40 and OS 20/30
  – Color Vision ( Ishihara) OD 8/14, OS 9/14
  – PERRLA (-) RAPD OD
  – CF: full OD
  – Ocular Motility: Normal ductions, versions, saccades
  – Cover Test : orthophoric posture - comitant
  – Neurologic exam: Right lower motor neuron CN VII palsy
  – SLE: exposure keratopathy OD
  – TA: 11 mm Hg OD; 10 mm Hg OS
  – DFE: Large cupping 0.75 x 0.75 OD and 0.85 x 0.85 OS
    – No optic disc edema or neuro retinal rim pallor
**DIFFERENTIAL DIAGNOSIS:**
- Suspect right parotid mass. Since recent MRI was read as normal, we questioned if the parotid gland was imaged in that study. We called the radiologist where the MRI was performed. He looked at the study again, and informed us that he could not adequately view the right parotid gland in that study.

**DIAGNOSIS / TREATMENT:**
- Biopsy and pathology report revealed a poorly differentiated carcinoma. The patient underwent surgical resection of the mass and radiation treatment to the area.

- right neck dissection
- parotidectomy,
- infratemporal fossa neoplasm resection,
- right lateral temporal bone resection
- skin cancer resection surgery
- skin graft from the forearm
- reconstructive surgery, which involved lifting the lower right eyelid.

**Parotid gland tumors**
- Initial finding is most commonly a raised mass

- Infiltration of CN VII during tumor growth can lead to facial weakness.

- Paralysis of the facial nerve in conjunction with a parotid mass is highly suggestive of malignancy (adenocarcinoma).
  - Assumed malignant until proven otherwise.

- Facial nerve paralysis is seen in approximately 12% to 35% of parotid gland carcinomas
CASE 2
Primary Sarcoma

19 year-old boy
- 2nd opinion - chief complaint:
  "I can’t see out of my left eye!"
- Columbian immigrant (16 months)
- Medical History (Hx): Unremarkable
- Last medical exam: 2 years ago
- Medications: none
- Social history: smokes 6 cigarettes/day
- Family history: cancer (breast), macular degeneration

Ocular Hx: Unremarkable

Patient feels like he got something in his eye while in the shower. VA is blurry OS and eyes feel heavy
Duration: 2 months but worsened 3 weeks ago.
Initially sought care elsewhere
  - Current treatment: OS Pred Forte (10x day) and Timolol 0.5% (qd), s/p sub-tenon's Kenalog injection
Also complains of occasional deep pain in eye
Additional symptoms:
  - headaches, only when sunny outside
  - sleeping excessively (12 hours a day)
  - funny taste in mouth

Summary of Outside records

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<tr>
<th></th>
<th>8 wks prior</th>
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<td>APD</td>
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<td>Rare cell</td>
<td>Trace cell &amp; flare</td>
<td>Quiet</td>
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<tr>
<td></td>
<td></td>
<td></td>
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<td>Dx: macular thickening</td>
</tr>
</tbody>
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Clinical Examination at Presentation
- VA: 20/20 OD, Count fingers (OS)
- PERRL (3 +) APD OS
- Color Vision: Ishihara 14/14 OD, 0/14 OS
- CF: Full OD, significant constriction OS
- Normal ocular motility exam
- Exophthalmometry: OD 17 mm OS 18 mm
- Normal slit lamp exam
- IOP: 18 mmHg OD, 18 mmHg OS
MRI Results

- Large anterior skull base soft tissue mass centered in the superior ethmoid
- Size: 3.3cm x 4.5cm x 4.7 cm
- Superiorly elevates frontal bones
- Laterally destroys the medial orbital walls
- Posteriorly extends just anterior to the optic chiasm
- Completely encases the optic nerve
- DDX: Rhabdomyosarcoma, Malignant melanoma, Lymphoma

Biopsy / Treatment

- Grade III Chondrosarcoma
- Patient was then treated with complete surgical resection of the tumor
- Vision subsequently improved to 20/50 OS

Chondrosarcoma

- Chondrosarcomas are thought to originate from the embryonal cartilage that escapes resorption during endochondral ossification.
- Most commonly seen in caucasians.
- Second most common primary malignant bone tumor after osteosarcoma.
- Most common sites are pelvic and shoulder bones, but can occur in any bone in the body
- The skull is formed by both bony and cartilaginous matrix and is therefore can be a site for this neoplasm to develop.

Chondrosarcoma

- Rare: Chondrosarcoma originating in the cranium accounts only for 0.16% of all intracranial neoplasms.
- Can occur at any age, but tend to occur in the third to fourth decades.
- Aggressiveness depends upon grade
- Treatment is determined based on location, grade and size; involves complete surgical excision with radiation therapy and/or chemotherapy.
- Recurrence rate and metastasis is high and depends on Grade.

Chondrosarcoma

- Grade III chondrosarcoma has been reported to be associated with up to a 70% metastasis rate.
- Grade III chondrosarcoma has an overall survival rate of 10 years in 50% - 70% of patients.
- Reduced life expectancy
  - Due to the high recurrence rate and metastasis
  - Most common site of metastasis is the lung.
CASES 3, 4, 5
Primary Gliomas

CASE 3

9 year-old boy
- Longstanding history of intermittent left exotropia
- Systemic history: asthma (Singulair)
- c/o occasional headaches, dizziness, and hearing “blowing air” in his left ear
- Because of the complaint about his ears for several months, his mother took him to the PCP, who dx: wax build-up

- VA: 20/25+ OD, 20/25+ OS
- Color: 7/7 OD, 7/7 OS
- PERRLA (-) RAPD
- CF: full OU
- EOMs: no restrictions (25pd ILXT)
- No ptosis or proptosis
- SLE unremarkable
- IOP: 21 mm Hg OD and 21 mm Hg OS

ONH photos

Papilledema
- Medical emergency in any age pt
- Pt sent immediately to Children’s Hospital
- Dx: Hydrocephalus secondary to Astrocytoma (grade I-II) of midbrain blocking the cerebral aqueduct
CASE 2 – HOW WOULD YOU MANAGE THIS PATIENT?

10 YEAR OLD BOY

CASE 5

77 year old man

- Reports 3 week history of blurred vision OD
  - Notices especially when reading
  - Right-sided weakness

- Visual acuities 20/20 OD 20/20 OS
- PERRL (trace +) RAPD OD
- Confrontation fields: right homonymous hemianopia denser superiorly
- Medical history
  - Hypertension

Visual Field Results
GLIOBLASTOMA MULTIFORME

• A Grade IV Astrocytoma
• Most common and most aggressive malignant primary brain tumor
• Poor prognosis
  – Median survival time 14 months, even with treatment

CASE 6
Primary Meningioma

51 year old woman

• CHIEF COMPLAINT:
  • Gradual decrease in vision OD x months / year
  • C/o Pressure sensation behind right eye
  • Denies any other visual, ocular, or neurologic symptoms
  • (-)Headache

• SYSTEMIC HISTORY:
  • Has not been medically evaluated in 5 years
    – Due to lack of insurance
  • Thyroid dysfunction as a teenager – not currently treated
  • Osteoarthritis
  • Hit back of head in motor vehicle accident 3 yrs ago
    – No subsequent problems with eyes or vision

• FAMILY HISTORY:
  • - Remarkable for diabetes, hypertension and stroke
CLINICAL EXAMINATION: Initial Presentation
- VA: OD 20/40 and OS 20/20
- Color Vision (Ishihara) OD 0/14, OS 14/14
- + red desaturation OD
- + decreased brightness sense OD
- > 1.8 log RAPD OD
- CF: inferior temporal defect OD
- Palpebral Apertures OD 11 mm, OS 11 mm
- Exophthalmometry: 21 mm OD, 20 mm OS
- Ocular Motility: Normal ductions, versions, saccades
  - Cover Test: orthophoric posture - comitant
- SLE: mild lens changes OU
- TA: OD 17 OS 17
- BP: 120/70

SLE: mild lens changes OU

TA: OD 17 OS 17

5 Months later

CLINICAL EXAMINATION: Follow-up Presentation
- VA: OD Light Perception and OS 20/20
- Color Vision (Ishihara) OD 0/14, OS 14/14
- + > 1.8 log RAPD OD
- Palpebral Apertures OD 14 mm, OS 11 mm
- Exophthalmometry: 5 mm of proptosis OD
- Ocular Motility: restrictions OD
  - 80% abduction, 90% adduction, 50% infra/abduction
- TA: OD 16 OS 16

MRI RESULTS:
- large, right, anterior-temporal apparent atypical sphenoid wing meningioma, with temporal and frontal intraparenchymal edema, and mass effect on the ventricles
Treatment

• Pterional craniotomy and resection of apparent atypical meningioma
• Resection of portion of sphenoid wing with placement of prosthetic orbital roof and lateral wall
• PATHOLOGY REPORT:
  • Atypical meningioma with chordoid features
  • WHO grade II / III
  • Potential for more aggressive course
  • Radiation treatment recommended

Meningiomas are benign and slow-growing in about 90% of cases. They arise from the meningeal brain coverings.

• Benign meningiomas fit with the WHO grade I classification, and recur only 7-20% of the time
• Less commonly, meningiomas can be atypical or anaplastic
• 6-8% of meningiomas are atypical, and have the tendency for local recurrence even after complete resection. These atypical meningioma correspond with the WHO grade II classification, and recur at a rate of 29-38%
• 2-3% of meningiomas are anaplastic and show signs of malignancy. They can recur (50-78%) and metastasize to other locations. They are classified as grade III in the WHO scale

• There is a difference in cytogenetic alterations between the benign meningiomas and the atypical and anaplastic meningiomas
• Meningiomas are further classified into 5 types: Meningiothelial, Fibroblastic, Transitional, Psammomatous, and Chordoid (more rare)
• The patient presented here had a relatively rare chordoid meningioma. Chordoid meningiomas get their name because they exhibit features that appear similar to chordomas (clusters of spindle and epithelial cells in a myxoid matrix)
• Chordoid meningiomas have been associated with hematologic abnormalities (not in this case)

• Not all meningiomas are benign. They can recur, and less likely become malignant
• Meningiomas mainly cause morbidity due to mass effect and compression.
• Prompt diagnosis and treatment is important to preserve optic nerve function
• Lack of insurance is a real problem that can result in increased morbidity and mortality
CASE 7
Hematologic Malignancies

- 69 year-old man
- c/o right eye redness x 10 days
- No pain
- Horizontal diplopia in right gaze x 3 days

VA: 20/20 OD, 20/20 OS
Color: 14/14 OD, 14/14 OS
PERRLA (-) RAPD
CF: full OU
Palpebral apertures: 5mm OD, 8mm OS
Levator function: 15mm OD, 20mm OS
Exophthalmometry: 25mm OD, 21mm OS
• Slit lamp exam
  • Grade 2 conjunctival injection OD
  • R upper lid edema
  • R lacrimal gland enlargement
• IOP: 20 OD, 18 OS
• BP: 135/80
• DFE: 0.2 x 0.2 cupping OU
• (-) edema (-) pallor

• History of Non-hodgkin’s lymphoma 8 years prior
  • affecting right leg/groin region, including bone (s/p surgery)

MRI suspicious for lymphoma, especially with past history

Pt will be followed by oncologist & is scheduled for biopsy of lacrimal gland

THANK YOU.