Cancer of The Eye and Visual System

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Cancer: A Problem of Epidemic proportions

- Nearly 1 million Americans are afflicted each year with cancer of some type
- 2nd leading cause of death in the US

What Is Cancer?

- Neoplasia- “new growth”
  - An abnormal mass of tissue the growth of which exceeds that of normal tissue
    - progresses in the same manner even when the inciting stimulus is removed
  - Fundamental to the origin of neoplasms:
    - is a loss of responsiveness to normal growth controls
    - Neoplastic cells continue to divide/replicate oblivious to regulatory influences that control normal cell growth

Neoplasms

- Compete with normal cells and tissues for metabolic needs
  - Dependant on host for nutrition and blood supply
- Steadily increase in size regardless of local environment

Non-Neoplastic proliferations

- Hypertrophy: increase in normal cell size and volume
- Atrophy: decrease in normal cell size and volume
  - Both are adaptive responses

Non-Neoplastic proliferations

Hyperplasia
Metaplasia
Dysplasia
All are controlled and abate when inciting stimulus is removed
Non-Neoplastic proliferations

- **Hyperplasia**: an increase in the number of cells in a tissue or organ
  - Only occurs in tissues or organs capable of mitotic division, post embryonic life
  - Ex. Thyroid hyperplasia
  - Striated muscle cells and neurons incapable of hyperplasia

Non-Neoplastic proliferations

- **Metaplasia**: controlled abnormal cell growth
  - Adaptive substitution of one adult cell type to another
  - Ex. In the lungs: seen in tissue when stimulated by chronic inflammation in the pulmonary epithelium
  - Stratified squamous for columnar pseudo-stratified epithelium

Non-Neoplastic proliferations

- **Hyperplasia**
  - **Physiological**
    - Glandular proliferation in the female breast tissue at puberty
  - **Pathological**
    - Thyroid hyperplasia- stimulated by TS immunoglobulins
    - May produce clinical disease
    - Incur a risk of neoplasia

Dysplasia

- Encountered primarily in epithelial cells
- In the spectrum of non-neoplastic proliferations, it is the most disorderly state
  - Loss of uniformity of individual cells
  - Loss of cells architectural orientation
    - Cells lacking normal arrangement
      - A variation in size and shape
      - Unusually large nuclei
  - A precursor to cancer

Characteristics of Benign neoplasms

- Stays localized at its site of origin
- Does not have the capacity to infiltrate or to metastasize to distant sites as do cancers.
- Typically but not always encapsulated

Comparisons between benign and malignant tumors

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Differentiation/Anaplasia</td>
<td>Well differentiated, structure maybe typical of tissue of origin</td>
<td>Some lack differentiation with anaplasia, cell structure atypical</td>
</tr>
<tr>
<td>Rate of growth</td>
<td>Usually progressive and slow, may come to standstill or regress; mitotic figures rare/normal</td>
<td>Erratic; slow to rapid; Mitotic figures are numerous and abnormal</td>
</tr>
<tr>
<td>Encapsulation: Invasion</td>
<td>Usually encapsulated Cohesive/ expansive</td>
<td>Invasive without encapsulation, usually infiltrative</td>
</tr>
<tr>
<td>Metastasis</td>
<td>Absent</td>
<td>Frequently present; more likely the larger and more undifferentiated</td>
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Classification by origin/ Location

- **Primary ocular cancers**
  - starts within the eye
- **Secondary/Metastatic cancers**
  - Spread to eye from another organ

Malignant Tumors

The properties of invasiveness and metastasis identify a neoplasm as malignant

Malignant neoplasms

- Cancers grow by progressive infiltration, invasion, destruction, and penetration of surrounding tissue.
- Typically do not develop capsules

Malignant neoplasms

- Malignant neoplasms disseminate by one of three pathways:
  - Seeding within body cavities
  - Lymphatic spread
  - Hematogenous spread—through the blood

Most Common Ocular malignancies

- **Adults**
  - Choroidal/Uveal melanoma
  - Intra-ocular Lymphoma (non-Hodgkins type)
    - B-cell Lymphoma
- **Children**
  - Retinoblastoma
  - Medulloepithelioma
  - Rhabdomyosarcoma

Uveal melanoma

- Develop from pigment-making cells called melanocytes
- 8/10 intraocular melanomas develop in the choroid; nearly all the remaining intraocular melanomas start in the iris/CB
- Most common primary intraocular malignancy in adults
**Intraocular/ Uveal melanomas**

- **80%** ........ *Choroidal malignant melanomas*
- 10-15%..... Ciliary Body melanomas
- 5-8% ............ Iris melanomas

- ↑ Risk:
  - Light irides
  - Sustained light exposure
  - Dysplastic nevus syndrome

**Iris melanomas**

- Abnormally pigmented areas of iris tissue
- Tan to brown in color
- Lesions larger than 1 mm
- Increase in size documented
- Changes in local/surrounding tissues
- Intra-mass intrinsic vascularity

**Iris melanomas**

- Monitor with:
  - Anterior segment digital color photos
  - UBM
  - Spectral domain OCT

**Intraocular/ Uveal melanomas**

- Most frequently diagnosed in patients over the age of 50
- **Incidence:**
  - 1/1 million ........ before the age of 30
  - 7/1 million ........ before age of 70
  - 50/1 million ....... after age 70

**Intracocular/ Uveal melanomas**

**Circumscribed vs. Diffuse**

**Circumscribed**
- Highly elevated, “mushroom like”
- Smooth surfaced
- Mottled pigmentation
- Whitish to gray-green in color
- Usually > 10 DD in size
- Associated with serous RD
- Orange pigment

**Diffuse**
- More rare: 4-5%
- Flat diffuse growth pattern
- Poorly defined margins, less conspicuous lesion
- High rate of misdiagnosis
  - Choroidal nevi
  - Serous RD
- More malignant, poorer prognosis

**Choroidal melanoma**
**Intraocular melanomas**

- Generally made up of 2 kinds of cells
  - Spindle cells, long thin cells
  - Epitheloid cells, almost round/cuboidal

- Prognosis is better if the tumors are mostly spindle cells as opposed to mostly Epitheloid cells. Epitheloid tumors are more likely to metastasize.

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**Intraocular melanomas Management**

- Dependant on various factors
  - Tumor size
  - Tumor location
  - Invasiveness into adjacent tissues
  - Visual status of both affected and fellow eye

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**Intraocular melanomas Management**

- Photodocumentation
- Visual Fields- baseline
- Referral to retinal oncologist
  - Confirm with fine needle aspiration Bx.

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**Intraocular melanomas Management**

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- Standard Systemic Evaluation to R/O metastasis
  - Complete Physical exam
  - CT of the abdomen, brain
  - Chest X-ray
  - CBC with differential
  - Liver enzymes*
  - 95% of cases result in Metastasis to liver
  - 98% of patients with ocular melanoma have no systemic/metastatic disease at time of diagnosis

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**Malignant Melanoma Management**

- Management can include
  - Radiation
    - Brachytherapy
    - External charged particle beam therapy
  - Photocoagulation
    - Xenon, Argon, Krypton laser
  - Local resection- with iris melanoma
  - Cryotherapy
  - Enucleation- in large high risk tumors

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**Malignant Melanoma Management**

- Radiation therapy is most common
  - Brachytherapy- radio plaques sewn into the eye for 3-7 days (80-100 Gy)
  - External Charged particle beam therapy
    - Used to treat small to midsized lesions
    - Near ON or in posterior pole
  - Radiation carries risk; radiation retinopathy, optic neuropathy
Cases of choroidal melanoma

Hemorrhagic Choroidal Melanoma

Post treatment with brachytherapy
2 months
Choroidal melanoma

Not to be confused with.....

melanocytoma of the optic disc

Intra-ocular and orbital lymphoma

Intra-ocular and orbital lymphoma

• Typically caused by Non-Hodgkins B-Cell Lymphoma
• Incidence of Non Hodgkins Lymphoma
  – 7/100,000 (T or B-cell) origin
  – Leading cause of cancer deaths under age 55
  – When intra-ocular lymphoma is found in isolation
    • Know as primary ocular form
    • Often a sign of undetected systemic or CNS lymphoma

Intra-ocular lymphoma

• Lymphoma is a cancer that starts in immune system cells called lymphocytes
  – Usually starts in the lymph nodes
  – Can also present initially in the stomach, lungs, and eye
  – Presents typically in the elderly
    • Rarely in young patients (immune system problems)
    • Often associated with CNS lymphoma
Intra-ocular/orbital lymphomas

– Primary malignant intraocular/orbital lymphoma is caused by immature malignant lymphoid cells (large B-cells)
  • Non-Hodgkins B-cell lymphoma
– Typically presents later in life
– 3 Forms
  • Vitreo-retinal (most common)
    – Strongly associated with CNS lymphoma
  • Uveal
  • Orbital

Intra-ocular lymphoma: presentation

• White diffuse retinal infiltrates
• Associated vitritis
  – white clumps of cells in the vitreous

• Anterior uveitis with KP
• Optic neuropathy

Intra-ocular lymphoma: presentation

Orbital lymphoma

– Orbital lymphoma presents as a painless, slowly progressive unilateral or bilateral anterior orbital mass
  • Muscle restriction
  • Proptosis
  • Reduced vision
– Inspect conjunctiva for fleshy (salmon patch)
  • strongly suggests orbital lymphoma

Conjunctival Lymphoma

Orbital B-Cell lymphoma
7 mm proptosis OD with EOM restrictions

- Well circumscribed homogeneous mass superiority situated in the right orbit, which appears to lie in an extra-conal location. Measuring 3.8 cm (AP) × 3.0 cm (T) × 2.3 cm

Initial presentation of orbital NH Lymphoma

BAM!

After some urging and tumor resection

Intra-ocular lymphoma

Management and treatment
Intra-ocular/orbital lymphomas

- Once diagnosis is suspected immediate referral to retinal specialist/oncologist for vitreal biopsy
- Arrange for Referral to oncologist for treatment with retina if Dx. Confirmed
  - Complete systemic work up

Intra-ocular/orbital lymphomas treatment

- Treatment usually consists of
  - Chemotherapy
  - Radiation therapy (2400-4000 rads over 3 weeks)
- Prognosis is poor:
  - average life expectancy 2 years after Dx.
  - 25% chance of developing systemic lymphoma in 5 yrs.

Retinoblastoma

- Most common malignant congenital intraocular neoplasm in children
- Derived from neurosensory elements (retinoblasts) of the evolving fetal retina
- Both sporadic and inherited forms exist

Retinoblastoma: Clinical signs

- Leukocoria and strabismus
- Variable presentations
  - Flat diffuse form
  - Pinkish dome shaped lesion
  - Non rhegmatogenous retinal detachment
    - In larger tumors
  - Retinal hemorrhage
  - Involvement of ONH is ominous sign
Retinoblastoma

• Tumor typically is highly calcified
• Highly reflective on B-Scan and CT

Retinoblastoma: management

• Early identification is key
• Can metastasize to brain, bones, blood, liver, and lymphatics
• Can be a lethal cancer!
• Thorough SLE
• Ophthalmoscopic exam under anesthesia may be necessary

Retinoblastoma: management

• Treatment depends on tumor size, location, and laterality and associated findings
• Options include:
  – Plaque radiotherapy
  – Laser photocoagulation
  – Transscleral cryotherapy
  – Chemo-reduction
  – External beam radiotherapy
  – Enucleation (a last resort)

Rabdomyosarcoma

• Common tumor of soft tissue
• Most common malignant orbital tumor in childhood
• Thought to arise from undifferentiated embryonal mesenchyme
• More predominant in males
• 50% of all cases present in the retrobulbar muscle cone, 25% in the superior orbit
• No racial predilection or genetic relationship
Clinical signs of Rabdomyosarcoma:

• Rapidly progressive proptosis
• Motility problems
• Eyelid edema
• Ptosis
• Headache, sinusitis, nosebleeds
  (sinus involvement)

Rabdomyosarcoma management

• If suspected emergent incisional biopsy
• Complete systemic work up
  – Chest and abdominal CT
  – Lumber puncture
  – Bone scan
• Treatment: Combined radiation and chemotherapy is indicated over several weeks

Primary Brain Tumors Affecting The Visual Pathway

Primary Brain Tumors: other less common types

• Acoustic Neuromas/ Schwannomas (benign)
  – Tumors arising from nerve sheath or Schwann cell
• Medulloblastomas
  – Form of primitive neuroectodermal tumor
  – Arise from the posterior fossa (brainstem) before age 2
• Hematologic malignancies
  – Leukemia
  – Lymphoma
  – Myeloma

Primary Brain Tumors:

• Carcinomas - cancers that are epithelial in origin
  – Adenocarcinoma
• Sarcoma - cancer of connective or supportive tissue, type depends on cell type of origin
  – Osteosarcoma (bone)
  – Chondrosarcoma (cartilage)
  – Liposarcoma (fat)
  – Leiomyosarcoma (smooth muscle)
  – Rhabdomyosarcoma (skeletal muscle)
**Primary Brain Tumors:**

- **Gliomas**
  - **Astrocytomas**
    - Grade 1, Pilocytic Astrocytoma, slow growing, little tendency to infiltrate tissue
    - Grade 2, diffuse astrocytoma, slow growing will infiltrate
    - Grade 3, rapidly growing and infiltrative
    - Grade 4, Glioblastoma Multiforme—very aggressive and lethal
      - Unfortunately most common form of brain tumor in adults (67%)

- **Ependymomas**
  - Rare, make up 2% of brain tumors in adults, most common in children
  - Ependymomas are glial tumors that arise from ependymal cells within the CNS

- **Meningiomas**
  - Benign
  - Atypical, grow faster and can be invasive
  - Anaplastic or malignant (3-5%)
    - Grow the fastest
    - Invasive, metastasize

**Case TS**

- 26/aa/f referred for second opinion on papilledema
- HPI: patient reports
  - "feels like her eyes keep crossing" causing trouble with driving; she has developed constant double vision over the last two weeks and closes one eye when driving.
  - Headache “10” on the pain scale
  - Diplopia (side by side)
  - (+) Dizziness

**Medical / Ocular history**

- Medical Hx.: Leukemia 93’-96’ (in remission), GERD, migraine HA’s since 1992
  - Meds: Zantac, Amitriptyline for migraines
- Ocular Hx.: (-) surgery, trauma eye/ head
- Allergy: ASA

**HPI cont’d**

- Neuro symptom inventory:
  - (-) Paresthesias
  - (-) muscle weakness, tremor
  - (-) coordination issues, Loss of balance
  - (-) Tinnitus
  - (-) Slurred speech, dysphagia
  - (+) HA’s worse over the last six months

**Clinical Exam**

- DVA cc OD 20/20 OS 20/20
- Pupils: PERRL(-) APD
- Cover test: (D) sc 5 pd right ET constant
- EOM's: Slight right abduction deficit; neurogenic
- SLE: conjunctiva clear, cornea clear, Anterior chamber deep/quiet, Iris normal OU, lens, nuclear opacities OD, OS clear, vitreous clear
- Ta: 12 OD 11 OS @11:40 Pach 544 OD 538 OS
DFE:
- Vitreous cl, macula cl OU,
- Optic nerves:
  - marked edema OU without CWS or hemes
- Vessels: Normal OU
- Retinal periphery: Nml, (-) Tears, holes, RD’s

Retinal Photos

Testing: VF

OCT/NFL
**MRI review**

Orbital MRI: Normal

Brain MRI: Large mass lesion in the posterior horn of the lateral ventricle with a solid component (38 X 54 mm) on coronal view and (32 X 39 mm) on axial views; appears to remain within the ventricle.

**The Worlds Worst Anaplastic Malignant Meningioma**

**The Unluckiest Guy in the World**

Initial presentation
Case: HP

- 58/W/F cc. noticed no peripheral vision OD x 1 wk. Px. Was in town this weekend for a wedding; denies flashes, floaters, eye pain. No Hx. of trauma recent or old.
- No prior hx. of glaucoma or other ocular disease.
- CC: Has noticed she bumps into things and has a new HA x 2 days, no vomiting; (−) neurological symptom inventory
  - Medical Hx.: postmenopausal osteoporosis, taking Fosamax; denies HTN, DM, ASHD, and elevated cholesterol
  - Ocular Hx.: no prior hx. Of ocular diseases, trauma, or surgery
Case HP: Clinical Findings

- BVA cc: OD: 20/20  OS: 20/20-3
- Pupils: PERRL (-) APD
- External: NML  CF: RHH
- SLE:
  - cornea: CL OU
  - A/C: D/Q OU
  - iris: nml OU
  - lens: trace-1+ milky NS OU
  - Vitreous: syneresis with heavy floaters OU
- Ta: OD 16  OS 16  @ 10:45

Case HP: Visual Fields

Case HP: Grade III-IV malignant Astrocytoma

Metastatic Carcinomas to the Eye

- Most common adult intraocular malignancy
- The choroid is the most common site of ocular metastasis (80%)
  – Iris (5-8%)
  – Ciliary Body (10-15%)
  – Optic nerve (3-5%)
- Most metastatic tumors to the eye are carcinomas
  – Cutaneous melanoma
  – Rarely sarcomas
Primary Sites of metastatic Carcinomas

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
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<tbody>
<tr>
<td>Lung (35-54%)</td>
<td>Breast (78-85%)</td>
</tr>
<tr>
<td>Unknown (25%)</td>
<td>Lung (8-25%)</td>
</tr>
<tr>
<td>Skin melanoma (18%)</td>
<td>Unknown (4-8%)</td>
</tr>
<tr>
<td>GI/pancreas (12%)</td>
<td>GI/Pancreas (4%)</td>
</tr>
<tr>
<td>Kidney (6%)</td>
<td>Skin (2%)</td>
</tr>
<tr>
<td>Prostate (1%)*</td>
<td></td>
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</tbody>
</table>

*Very low incidence of metastasis to eye

Metastatic Carcinomas to the Eye

- Primary tumor may be anywhere
  - Highest incidence
    - Lung, males
    - Breast, females
- Clinical signs
  - Choroidal mass with decreased acuity
  - Absolute VF defects
  - Retinal detachment
  - photopsias
  - Classic lesion: creamy yellow post equatorial mass

Differential diagnosis

- CNVM
- CHRPE
- RPE Hyperplasia
- Choroidal hemangioma
- Melanocytoma
- Adenocarcinoma
- Choroidal osteoma
- Amelanotic melanoma
- Astrocytoma
- Lymphoma/leukemia
- Choroidal granuloma
- Posterior scleritis
- Disciform lesions

Metastatic Carcinomas to the Eye

Management

- Primary work up:
  - Ultrasound:
    - A-Scan, moderate to high reflectivity
    - B-Scan, Placoid or dome shaped, acoustically solid
  - MRI and CT
  - Fluorescein Angiography

Metastatic Carcinoma

- Secondary work up
  - Immediate referral to retinal oncology
  - Oncologist for complete systemic evaluation
    - Chest X-ray
    - Mammogram
    - CT of the brain, abdomen
    - Urinalysis
    - CBC, liver function tests
    - Complete physical exam

Metastatic Disease Seeding to Brain
Brain Metastases by location

<table>
<thead>
<tr>
<th>Location</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Cerebrum</td>
<td>80-85%</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>10-15%</td>
</tr>
<tr>
<td>Brainstem</td>
<td>3-5%</td>
</tr>
</tbody>
</table>

What we should be looking for....

- Horner’s syndrome
- CN palsies
- VF loss, especially neuro fields
  - Respect for vertical midline
  - Homonymous hemianopsias
- Ptosis and proptosis
- Cavernous Sinus syndromes
- + APD ?

*Unfortunately once ocular metastasis has occurred prognosis for survival is poor.

Case BS

- 61 yo/ AA/F referred by oncology for 2nd opinion on new eye swelling OS with inflammation; patient states eye became swollen previously, with itching and she was prescribed Bacitracin ung. Patient believes problem has returned, noticed this AM.
  - Poor historian: (swelling developed overnight!)
  - Patient being treated for diffuse metastatic breast CA

Clinical Exam Findings

- DVA cc OD 20/50 ph 20/30  OS 20/40  ph NI
- Pupils: (-) APD noted
- External: chemotic conjunctiva OS with obvious proptosis, downward displacement of left orbit. Peri-orbital edema of LUL
  - Hertel exophthalmometry: 15mm OD  22mm OS b101

- See Photos

External finds
What’s wrong with this picture?
Now what’s wrong with this picture?

Cosmo says, Thank You and Drive Safely!