You Can’t Afford To Miss This!

Understanding Posterior Ocular Tumors

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Tumor Definition

tumor /tu·mor/ (too´mer)
also called neoplasm. a new growth of tissue characterized by progressive, uncontrolled proliferation of cells. The tumor may be localized or invasive, benign or malignant. A tumor may be named for its location, for its cellular makeup, or for the person who first identified it.

Ocular Tumors

- Eyelid Tumors
- Iris / Ciliary Body / Choroidal Tumors
  - Retina / ONH and Pigment Epithelium
- Conjunctival Tumors
Lecture Outline

- Choroidal Nevus
- Choroidal Melanoma
- Congenital Hypertrophy of the RPE
- Choroidal Metastasis
- Melanocytoma
- Combined Hamartoma of the Retina & RPE
- Choroidal Hemangioma
- Choroidal Osteoma
- Retinal Astrocytic Hamartoma
- Retinoblastoma

Ocular Anatomy
Retinal Anatomy

- NFL: Nerve Fiber Layer
- ILM: Inner Limiting Membrane
- GCL: Ganglion Cell Layer
- IPL: Inner Plexiform Layer
- INL: Inner Nuclear Layer
- OPL: Outer Plexiform Layer
- ONL: Outer Nuclear Layer
- ELM: External limiting membrane
- IS: Photoreceptor Inner Segment
- IS/OS: Junction of inner and outer photoreceptor segments
- OS: Photoreceptor Outer Segment
- RPE: Retinal Pigment Epithelium
- Choroid

Cirrus HD-OCT Healthy Macula
Population by Race for the US: 2000

RACE

Total population ............. 281,421,906  100.0%

White ....................... 211,460,626  75.1%

Source: U.S. Census Bureau, Census 2000 Redistricting (Public Law 94-171) Summary
CHOROIDAL NEVUS

• Most common tumor
• Proliferation of choroidal melanocytes
• Present in ~ 7.9% of Caucasians
• Growth is rare after puberty ????

Choroidal Nevus
As we age:

- Nevi increase in number and thickness
- Pigment changes
- Metaplasia
- Drusen / lipofuscin

**Choroidal Nevus**

- Nevi are less than 2mm in thickness
- No known relationship to sunlight exposure
- Have indistinct borders
- May undergo malignant change into melanoma

**Choroidal Nevus**
Clinical Findings

- Typically do not cause visual symptoms
- Signs of Suspicion
  - Vision changes
  - > 2 mm in thickness
  - Orange pigment
  - Proximity to optic disc
  - Subretinal fluid

1 in 8845 transform into melanoma

Nevoma
To Find Small Ocular Melanoma

- T= thickness
- F= subretinal fluid
- S= symptoms
- O= orange pigment
- M= tumor margin touches disk

DOCUMENTED GROWTH - MEANS EVERYTHING

Using Helpful Hints = Ultrasound hollow, Halo

Nevoma
Nevus vs Melanoma?
Special Testing

- OCT
  - Can detect retinal edema, subretinal fluid, retinal thinning and RPE detachment
  - Helpful in determining presence of drusen

- FA
  - Findings depend on the amount of pigment within nevus and the overlying RPE
  - Hypofluorescence due to blockage of choroidal filling
  - Hyperfluorescence of surface drusen

Treatment & Management

- Baseline fundus photography
- Consider OCT if location permits
- Consider B-Scan if suspicious
- Yearly dilated fundus examination
CHOROIDAL MELANOMA

- Accounts for 90% of all uveal melanomas
- Cells undergo neoplasia, reproducing at a faster rate than usual
- Typically large
  - Although 30% are less than 3 mm thick

Choroidal Melanoma
Clinical Findings

- Orange pigment
- May be amelanotic
- Look for subretinal fluid
  - 91% vs 14% of nevi
  - Intermittent blurred vision or flashes secondary to fluid shift
- Fluid = significant risk of metastasis

Choroidal Melanoma
Choroidal Melanoma
Retinal Arterial Macroaneurysm

Presentation of Melanoma

Asymptomatic
Systemically well
Flashes
Pain is rare
Scotoma
Vitreous hemorrhage
VF defect
- Caucasian ethnicity
- Light colored eyes (blue)
- Fair skin
- Propensity to burn when exposed to UV light
- Cutaneous nevi or freckles
- Iris nevi

Risk Factors of Melanoma

Quadrant Uveal Melanoma in 8100 patients

Shields CL, et al. Uveal melanoma analyses in 8100 consecutive patients. Report #1
Special Testing

**OCT**
- Can detect sub-retinal fluid
- Has been shown to detect early seeding
- Helpful in monitoring response to treatment

**B Scan**
- Classic mushroom appearance
- Acoustically hollow
- Choroidal excavation with orbital shadowing
- Can identify extraocular extension

**FA**
- No pathognomonic pattern
- Typically, mottled fluorescence during arteriovenous phase, followed by leakage and staining

## Melanoma
Collaborative Ocular Melanoma Study

- Organized and funded in 1985 to address issues related to the management of choroidal melanoma. > 4000 patients. 65% pts eligible
- Primarily to study the overall survival of patient following treatment
  - Small melanomas: < 2.5 mm in height
  - Medium melanomas: 2.5 – 10.0 mm in height
  - Large melanomas: > 10.0 mm in height
- Secondary outcomes = metastasis-free survival, years of useful vision

Treatment & Management

- Enucleation
- Radioactive plaques
- Proton beam radiotherapy

Most widely accepted

Less common

Treatment depends on...
1. state of other eye
2. location
3. extent of tumor
4. size
5. health
6. age of pt
Risk factors for metastasis

• Thickness > 2 mm
• Symptoms: Flashes, floaters, loss of vision
• Proximity to the optic nerve
• Documented growth

Uveal Melanoma


10 year mortality for uveal melanoma
• Large 50%
• Medium 25%
• Small 12%

Pattern of metastasis
• Uveal: hematogenous
• Cutaneous: lymphatic

Most common sites of metastasis for uveal melanoma
• Liver 89%
• Lung 29%
• Bone 17%
• Skin / Subcutaneous 12%

Median survival after dx of metastasis - 6 months

Choroidal Melanoma
Using fluorescence in situ hybridization and molecular assay techniques, several genetic abnormalities in uveal melanoma were found on chromosomes 1, 3, 6, and 8.

- Monosomy 3
  - Found in up to 50% of uveal melanomas
  - Imparts a worse prognosis.
  - In small melanoma it provokes the argument for earlier treatment than observation.

Role of Cytogenetics

CONGENITAL HYPERTROPHY OF THE RETINAL PIGMENT EPITHELIUM
Congenital Hypertrophy of the Retinal Pigment Epithelium

- Common benign lesion
- Focal area in which the RPE cells are taller and more densely packed with melanosomes

Clinical Findings

- Discrete margins, typically near the equator
- Lacunae are common
- Multiple lesions may be confined to one sector of the fundus – bear tracks
These lesions are not true tumors
- No growth
- No subretinal fluid
- Ultrasound will show flat lesion
- No intrinsic vessels

Congenital Hypertrophy RPE

Familial Adenomatous Polyposis (FAP)
- AD inheritance
- Adenomatous polyps throughout rectum & colon
- Starts to develop in adolescence (15-40 yrs)
- If untreated – all pts will develop colorectal cancer

Systemic Association

>80% of patients with FAP have atypical CHRPE lesions
Treatment & Management

- Typically remains stationary
- May occasionally increase in diameter or spawn an elevated nodule that may represent adenoma or adenocarcinoma

CHOROIDAL METASTASIS
Choroidal Metastasis

Most common site for uveal metastases - 90%

Estimated incidence of 30,000 cases/year

Choroidal melanoma 2,500 cases per year

Primary site
- Breast (women)
- Lung (men)

Clinical Findings

Creamy-white, placoid choroidal lesion

Fast growing

Usually found in posterior pole

Exudative RD common

Tumors may metastasize elsewhere
Lung Metastasis

Choroidal Metastasis

Breast Metastasis

Choroidal Metastasis
Metastatic Prostate Cancer

Metastatic Breast Cancer
**Special Testing**

- **OCT**
  - Dome shaped elevation of retina and RPE with adjacent subretinal fluid
  - Can detect retinal edema, RPE thickening and RPE detachment

- **B Scan**
  - Shows diffuse choroidal thickening
  - Moderately high internal acoustic reflectivity

- **FA**
  - Shows early hypofluorescence and diffuse late staining

**Treatment & Management**

- Observation
- Radiotherapy
- TTT
- Systemic therapy
- Enucleation
Ocular metastases are the most common ocular malignancies. Estimated incidence of 30,000 cases per year. Choroidal melanoma 2,500 cases per year.

**Choroidal Metastasis**

Breast cancer is the most common tumor to metastasize to the eye - followed by lung cancer. 85% of patients with breast cancer metastases will have a known history of breast cancer. Breast cancer metastases tend to be bilateral and multiple. 40% of these patients have a brain metastasis.

**Metastatic Tumors**
Breast cancer in 2010
- (< 1%) new cancers in men
- 192,400 (27%) new cancers in women

Metastasis from breast cancer occurs in 25% of women at a median of 5 years.
3 years if ocular metastasis

The most common location is the lung, bone, lymph nodes and liver

Metastatic Tumors
http://www.nationalbreastcancer.org/metastatic-breast-cancer

Lung cancer metastasis rarely bilateral and multifocal
They often produce pain
Lung cancer metastasis 70% of patients don’t know they have cancer
Chest x-ray very important

Metastatic Tumors
MELANOCYTOMA

- Benign melanocytic uveal tumor
- Composed of large, plump magnocular nevus cells that are heavily pigmented
- Can present in all age groups and races
  - African-Americans
  - Females

Melanocytoma
Clinical Findings

- Patients are usually asymptomatic
- Adjacent to or within the optic nerve
- Black in color with feathery margins
- Visual field defect may be present
- APD may be present

Melanocytoma
Special Testing

- OCT
  - Disruption of the internal limiting membrane
  - Disorganization of involved retina
  - Visualization of subretinal surface

- FA
  - Shows hypofluorescence of deep vessels due to blockage
  - The disc margin may stain in late phases

Treatment & Management

- No systemic association
- Typically stationary
- 2% of cases develop into melanoma
- No treatment is recommended
Combined Hamartoma of the Retina & RPE

- Rare, benign tumor
- Likely congenital
- Involves retina, RPE and overlying vitreous
- Typically presents in late childhood or early adulthood
  - Strabismus
  - Blurred vision
  - Metamorphopsia
  - Loss of vision

Can be Asymptomatic
Clinical Findings

- Grey pigmentation with superficial gliosis
- Secondary retinal wrinkling and vessel tortuosity
- Lesions can be
  - Juxtapapillary
  - Peripapillary
  - Within posterior pole

Systemic Association

- Neurofibromatosis
  - Type 1
    - Café-au-late spots
    - Neurofibromas
    - Lisch nodules
    - Short stature
    - Scoliosis
  - Neurofibromatosis
    - Type 2
    - Acoustic neuromas
    - Hearing loss
    - Balance problems
    - Cataracts
**OCT**
- Shows retinal disorganization and elevation with overlying ERM
- Ability to monitor macular changes 2° to traction

**B Scan**
- Can be used to rule out compressive lesions
- May be unable to pick up depth of hamartoma
- Findings not characteristic

**FA**
- Rarely diagnostically important
- Findings are characteristic

### Special Testing

### Treatment & Management

- Patients are monitored annually for
  - Growth of lesion
  - Vision changes secondary to macular traction
- Consider annual OCT of macula
- Ask pertinent history questions in regards to NF-1 and NF-2
- Refer for vitrectomy with membrane peel in cases where vision is significantly affected
CHOROIDAL HEMANGIOMA

- Mass of vascular channels within choroid
- Circumscribed vs. Diffuse [Sturge-Weber]
- Symptoms in adulthood secondary to RD

Choroidal Hemangioma
**Choroidal Hemangioma**

- **CIRCUMSCRIBED**
  - Orange/red mass with indistinct margins
  - Usually peripapillary
  - Acoustically solid lesion
  - Subretinal fluid or macular edema

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**Choroidal Hemangioma**

Dr. Aaron Gold
**Choroidal Hemangioma**

- Affects over $\frac{1}{2}$ the choroid
- Enlarges slowly
- Deep-red colored fundus
- Found exclusively in patients with Sturge-Weber Syndrome

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**Sturge-Weber Syndrome**

- Congenital hamartomatous malformations
- May affect
  - Eye
  - Skin
  - CNS
- Motor seizures – 85%
- Mental retardation – 60%
- Facial cutaneous venous dilation (port-wine stain) present in 96%

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**Systemic Association**
Special Testing

**OCT**
- Acute leakage shows subretinal fluid with intact photoreceptor layer and normal retinal thickness
- Chronic leakage shows loss of photoreceptors, retinoschisis, and retinal edema

**B Scan**
- Acoustically solid lesion
- High internal reflectivity

**FA**
- Rapid spotty hyperfluorescence in the early arterial phase
- Diffuse intense late hyperfluorescence

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**Choroidal Osteoma**

- Benign ossifying tumor of the choroid
- Composed of mature bone
- Young females
- Benign – may grow
- VA < 20/200 in 56-58% after 10 yrs
Clinical Findings

- Orange-yellow lesion
- Typically unilateral
- Well-defined
- Usually juxtapapillary

- Vision loss 2° to
  - Subretinal Fluid
  - Neovascularization
  - Photoreceptor loss

Special Testing

- **OCT**
  - Inner retina preserved

- **B Scan**
  - Highly reflective anterior surface
  - Orbital shadowing

- **FA**
  - Irregular, diffuse mottled hyperfluorescence in the early and late phases
  - Neovascularization may be present.
• No systemic association

• No malignant potential

• CNVM may develop

Treatment & Management

RETINAL ASTROCYTIC HAMARTOMA
Retinal Astrocytic Hamartoma

- Vascular and glial tumor of the retina
- Rare and benign
- No threat to vision
- Frequently seen in tuberous sclerosis

Clinical Findings

- May be multiple or bilateral
- Can be calcified
- Can be
  - Endophytic
  - Vitreous
  - Exophytic
  - Subretinal
Systemic Association

- Solitary lesions may be found in normal individuals

- Tuberous Sclerosis
  - 50% of patients have astrocytomas
  - Multiple/bilateral
  - Rare genetic disease
  - Benign tumors grow on skin, brain, kidneys, and heart

Special Testing

**OCT**
- Inner retinal thickening and disorganization with a gradual transition to normal retina
- Retinal traction (27%)
- Intratumoral cysts (67%)
- Adjacent edema (47%)

**FA**
- Hyperfluorescence without leakage
Retinoblastoma

- The most common primary, intraocular malignancy in childhood
- Results from malignant transformation of primitive retinal cells before final differentiation.
- Seldom seen after age 3
Retinoblastoma

Retinoblastoma – life threatening disease

Most common intraocular malignancy in children / dx=18 month
300 new cases of retinoblastoma diagnosed each year in the US
Initial Features:

- Leukocoria 70%
- Strabismus 25%
- Other (VA) 5%

~15% will present with iris neovascularization
Hyphema may also be present

Retinoblastoma

Leukocoria

- Retinoblastoma
- Coats disease
- Congenital Cataract
- Coloboma
- Toxocariasis
- ROP
- PPHV
- Retinal Detachment

Retinoblastoma
In 75% of cases - enucleation is performed

In 25% of cases - conservative treatment is administered

Special Testing

Treatment & Management
Retinoblastoma Treatment

Intravenous chemoreduction (carboplatin, etoposide, vincristine)
Subconjunctival carboplatin
Transpupillary thermotherapy
Cryotherapy
Laser photocoagulation
Plaque radiotherapy
External beam radiotherapy

International Classification of Retinoblastoma

<table>
<thead>
<tr>
<th>Group</th>
<th>Description</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>A</td>
<td>Small RB &lt; 3 mm size</td>
<td>Plaque, TTT</td>
</tr>
<tr>
<td>B</td>
<td>Larger RB &gt; 3 mm size</td>
<td>Chemoreduction W / WO EBRT</td>
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<tr>
<td>C</td>
<td>Contained seeds</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>Diffuse seeds</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>Extensive &gt; 50% globe, NVI, Opaque media</td>
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Recurrences = within 1st year
choroidal nevus
choroidal melanoma
retinoblastoma
choroidal osteoma
choroidal hemangioma
astrocytic hamartoma
choroidal metastasis
choroidal hemangioma
retinoblastoma
choroidal melanoma
choroidal osteoma
lymphoid tumor
References


The End!

Any Questions ????