


Ocular Melanoma



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March 8, 2019

Uveal Melanoma

- Melanoma of the iris ciliary body and choroid
- Diagnostic and metastatic evaluation
- Major treatment modalities
- Fine needle aspirate biopsies

Uveal Melanoma

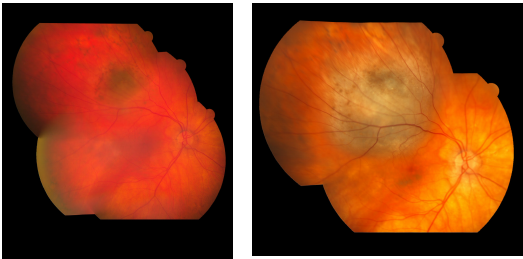
A brief review

The uveal tract

Iris
Ciliary body
Choroid



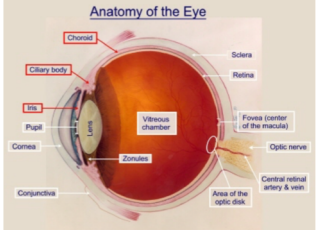
Malignant Transformation



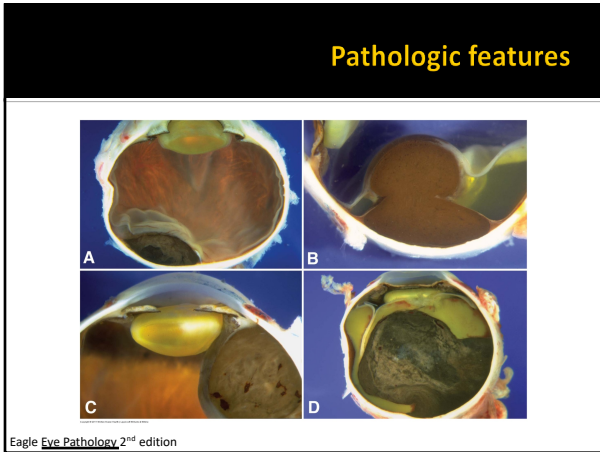
11/2010 8/2012

Ocular Melanoma Basics

- Ocular Melanoma
 - Uveal Melanoma
 - Arise from melanocytes in uveal tract
 - Anterior Uveal Melanoma
 - Iris Melanoma 5%
 - Posterior Uveal Melanoma
 - Ciliary body melanoma 5%
 - Choroidal melanoma 90%



Uveitis.org



Uveal Melanoma

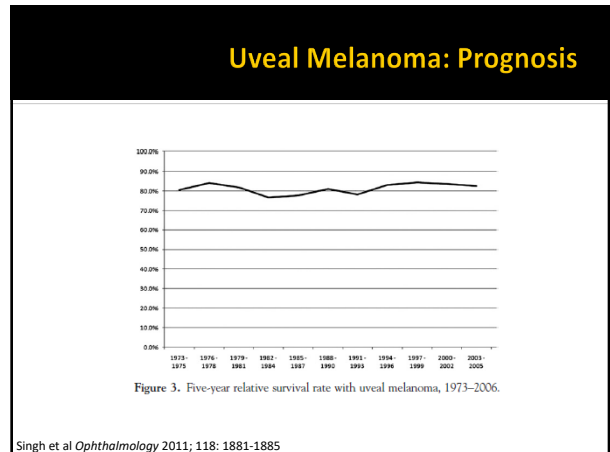
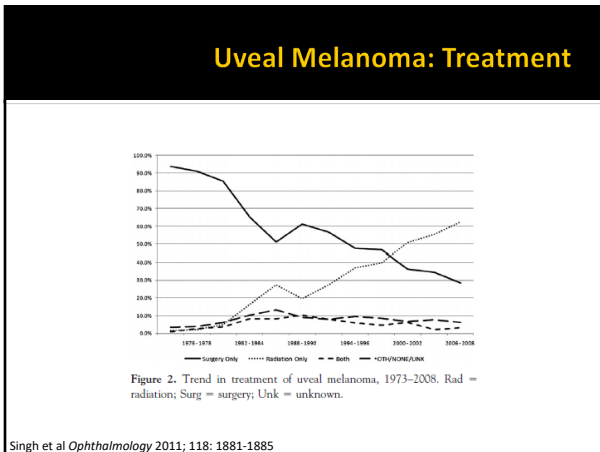
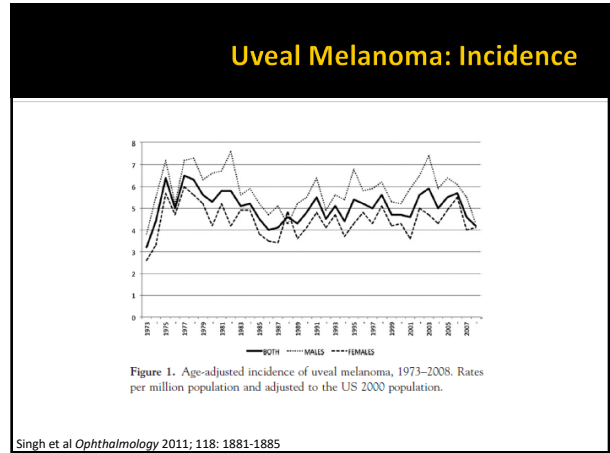
- Most common primary intraocular malignancy in adults
- 5-10% of all melanoma
- A **distinct disease**
- Poorer prognosis than cutaneous melanoma
- Most patients have no known family history
- Metastasis
 - Liver 93%
 - Lung 24%
 - Bone 16%

National Cancer Institute Surveillance, Epidemiology, and End Results Database

Current State of Affairs

- Review of Surveillance, Epidemiology, and End Results (SEER) program database in the US from 1973-2008
- Evaluate trends in incidence, treatment and 5-year relative survival rates.

Singh et al *Ophthalmology* 2011; 118: 1881-1885



Uveal Melanoma: Prognosis

- Metastasis evident in <3% at initial Dx
 - Can occur more than 20 years after local treatment
- Currently no curative therapy for metastatic disease
 - Median survival after mets: 9 months
- Benefit of early detection debated
 - Variable surveillance recommendations

Kath et al 1993

Uveal Melanoma: DDX

- Choroidal nevus
- Metastasis
- Hemangioma
- Choroidal hemorrhage

Uveal Melanoma: DDX

- Choroidal nevus
 - Common benign pigmented lesion of uveal tract
 - Present in 10%



Aao.org

Uveal Melanoma: Epidemiology

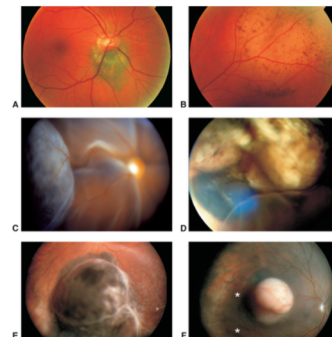
- Age
 - Increases with age, peaks at 60
- Race
 - Rare in non white races
- Genetics
 - Most cases are sporadic
- Risk Factors
 - Fair skin, blue iris color
 - Congenital ocular melanocytosis, neurofibromatosis

Uveal Melanoma: Diagnosis

- Clinical diagnosis
 - Fundoscopic exam
 - Thickness, fluid, symptoms, orange pigment, margin
 - To Find Small Ocular Melanoma
- Ultrasound
 - Shape, acoustic hollowness, vascularity
- Fluorescein angiography
 - Vascularity

Kath et al 1993

Uveal Melanoma Clinical Exam



BCSC 2018-19

Uveal Melanoma: Iris

BCSC 2018-19

Uveal Melanoma: Management

- Observation
- Enucleation
- Brachytherapy
- Proton Beam irradiation
- Surgical resection
- Thermal laser treatment

Kath et al 1993

Enucleation

D

Radiation

©ECN

PBRT

- MRI orbits
- Tantalum marker clip placement in the OR
- CT scan with clips in place
- PRBT given in Seattle
 - Seattle Cancer Care Alliance

Uveal Melanoma: Metastasis Risk Factors

- Tumor size
- Tumor location
- Cell type (spindle vs. epithelioid)
- Vascular patterns
- Patient age
- Tumor genetics

Fine Needle Aspirate Biopsy

Why do we perform biopsies?

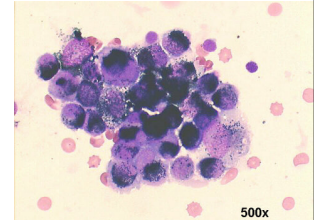
- Diagnosis
- Prognosis

Diagnostic Biopsy

- Cases in which diagnosis is unclear
- Can assist in determining appropriate therapy
- Not performed very frequently
- Sample is used for cytology
 - often referred to as the "wet" specimen

Cytology

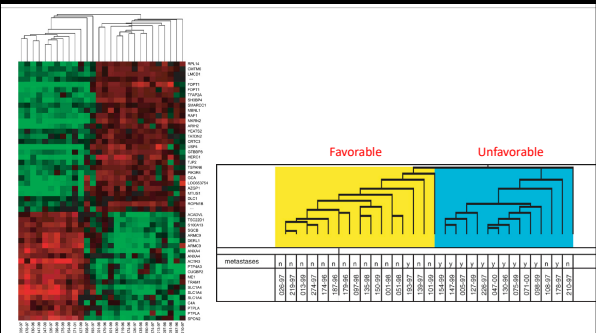
- Purpose is to evaluate cells under microscope
- Specimens should go directly to the cytology lab in anatomic pathology



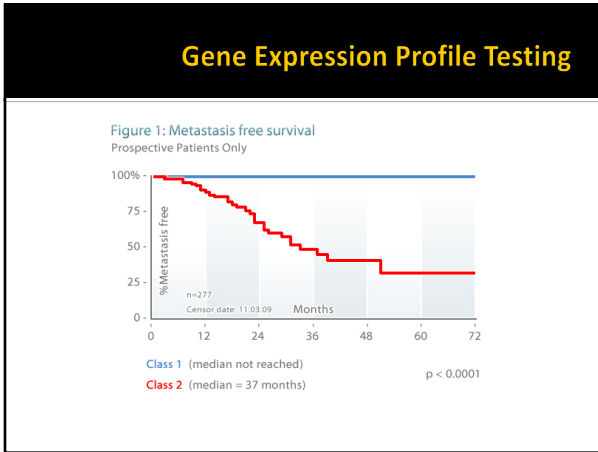
Prognostic Biopsy: Gene Expression Profile (GEP) Testing

- Commercially available
- Predicts with great accuracy which patients will develop metastatic disease
- Currently no curative therapy available
- Sample is used for RNA testing
 - often referred to as the "dry" specimen in the OR

Microarray Studies: two tumor types



Petrausch, U et al, Eye (2008) 22, 997-1007



Clinical Scenario: Prognosis

RESULTS

DecisionDX-UM Class = 2

Discriminant Value = 1.14

Patients with a Class 2 molecular signature have a high risk of experiencing near term (within 5 years) clinical metastasis. A discriminant value ≥ 0.100 is reported with normal confidence.

Test Results should be interpreted using the Clinical Experience information contained in this report which is derived from clinical studies involving patient populations with specific clinical features as noted in section titled Clinical Experience. These results have not been validated in patients with clinical features different from those described. The discriminant value relates to Class 1 vs 2. See page 2 of initial report for discussion on discriminant value confidence.

CLINICAL EXPERIENCE FOR CLASS 1A, 1B AND 2

The DecisionDX-UM assay has been evaluated in over 700 patients with uveal melanoma to date. The majority of these patients participated in a prospective, multi-center study to validate the predictive accuracy of this gene expression-based molecular assay. Outcomes are collected and the ability of the molecular signature to predict metastasis is being evaluated at regular intervals. The most recent censor date (June 9, 2011) of the prospective study included 514 patients with follow-up data available for analysis. The censor date for this subpopulation is June 9, 2011. The actual outcomes for metastasis of the predicted low-risk (Class 1A), intermediate-risk (Class 1B), and the high-risk (Class 2) molecular signatures are shown below.

Molecular Signature Class	Percent Metastasis Free at 3 Years	Percent Metastasis Free at 5 Years
Class 1A	99%	98%
Class 1B	93%	79%
Class 2	50%	28%

n=514, Log-rank (Mantel-Cox) test, p<0.0001

- ### FNAB methods for intraocular tumors
- Trans-corneal
 - Trans-scleral
 - Trans-vitreous

Trans-corneal biopsy

- For iris tumors/iridociliary tumors
- Clear cornea incision
- Pupil not dilated
 - May use preop pilocarpine or Miochol intraoperatively
- AC must be maintained
 - Injection of BSS
 - Healon

Finger et al, BJO 2005

Trans-scleral biopsy

- Scleral flap created
- Attention to good hemostasis
- Immediate plaque or cryotherapy to bx site
- Flap sutured
- Decrease risk of seeding
 - Change suture/instruments after biopsy

Singh et al, ARVO 2011

Trans-vitreous biopsy

- 2 Sclerotomies made
 - 25 gauge trochars
- Light pipe and 27g needle
- AVI lens
- Decrease risk of seeding
 - Cryo port
 - Suture ports

Carl Greenewald

Singh et al, ARVO 2011

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