Ocular Melanosis

Simon Petersen-Jones
Ocular Melanosis

- History
- Overview of Ocular Melanosis
- Signs to look for
- Treatment for Ocular Melanosis
- Current research in Ocular Melanosis
History of Ocular Melanosis Studies

• 1984: Described by Dr Covitz at a meeting of the American College of Veterinary Ophthalmologists
History of Ocular Melanosis Studies

• Royal (Dick) School of Veterinary Studies, University of Edinburgh.
History of Ocular Melanosis Studies
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History of Ocular Melanosis Studies

- 1988: Debbie & Vespa
- 1991: First journal article on ocular melanosis
- 1992: Presented at Eye Research Meeting (ARVO)
- 1998: Started investigations of OM in USA
  - Support from CTCA
History of Ocular Melanosis Studies

- 2005: Funding from NIH for one year graduate student
  - Lexi Mentzer
- 2005: Funding from CTCA
- 2005: Funding from MSU Purebred Dog Endowment Fund
- 2005: Some of work funded by AKC-CHF Acorn grant to UCDavis
Ocular Melanosis

- Inherited
- Cairn terriers (+ other breeds?)
- Both eyes deposition of pigmented cells in several parts of the eye
- Slowly progressive disease
- Leads to secondary glaucoma – intractable
- Age of onset/ rate of progression variable
Eye Cross Section
Aqueous Humor
Aqueous Drainage

→ iridocorneal angle
→ through trabecular meshwork in ciliary cleft
→ vacuolate into angular aqueous plexus
→ scleral venous plexus
→ blood stream
Gonioscopy

Examination of the opening into the ciliary cleft (drainage angle)
Assessment of Drainage Angle
Measurement of intraocular pressure (normal dog 12-25 mmHg)

- Schiotz tonometer
  - indentation of cornea
  - horizontal cornea
  - read scale reading
  - convert to IOP
  - add extra weights if IOP high
  - cheap
Measurement of intraocular pressure (normal dog 12-25 mmHg)

- **Tonopen**
  - applanation of cornea
  - portable
  - useful for large animals
  - more expensive
Features of Ocular Melanosis

• Pigment proliferation inside eye
• Pigmented cells in eye block fluid drainage pathways
• Eventually get an fluid accumulation inside eye
  – Increases pressure inside eye (intraocular pressure) = glaucoma
  – Sustained increased pressure causes pain and blindness
• Age that pigment develops – variable, from 4 years
• Age that glaucoma develops – between 7 yrs and into teens. Some slowly progressive cases may never develop glaucoma
Incidence of Glaucoma in Cairn Terriers

<table>
<thead>
<tr>
<th>% of Cairn terriers examined that had glaucoma</th>
<th>1974-1983</th>
<th>1994-2003</th>
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<tbody>
<tr>
<td></td>
<td>0.51%</td>
<td>1.82%</td>
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Rank for purebred dogs with glaucoma

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<th>23rd</th>
<th>9th</th>
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From: Veterinary Medical Database.

Stages of Ocular Melanosis

I. Donut-shaped thickening of iris root (dark-color)

II. Thickened iris root with appearance of small scleral pigment deposits

III. Thickened iris root with larger scleral pigment patches. Pigment visible within aqueous and coating ventral drainage angle

IV. Increased intraocular pressure. Iris atrophy. Secondary changes – staphyloma, phthisis bulbi.
Detailed Ultrasound of Eye

Pupil constricted

Pupil dilated
Normal

Ocular Melanosis

Pupil constricted

Pupil dilated
Stage 3. Ocular Melanosis
OM Pigment reaches back of Eye
17 Months apart
Stage IV. Ocular Melanosis
Ocular Melanosis - Treatment

• Preglaucoma
  – No drugs known to stop pigmented cell proliferation

• Once glaucoma has developed – use typical glaucoma management
  – When pressure is elevated needs immediate treatment

• DO NOT BREED FROM AFFECTED DOGS (CERF recommendation)
Ocular Melanosis - Treatment

• Antiglaucoma medications
• Surgical management of glaucoma
  – To reduce fluid formation in eye
  – To divert fluid from eye to tissues around the eye
• If eye is blind and painful – removal may be necessary
  – *Living With a Blind Dog*. Caroline Levin  (503)-631-3491
  – www.blinddogs.com
How to Recognize Ocular Melanosis

• Early stages – identified by veterinary ophthalmologist

• Later stages more obvious
  – Black patches on white of eye
  – Glaucoma causes irritation/pain
    • Rubbing eye
    • Blinking excessively
    • Keeping eye closed
Aims of Ocular Melanosis Research

- Identify the gene defect that causes ocular melanosis
- Develop a genetic test for ocular melanosis so the condition can be bred out of the breed
- Understand why the pigmented cells proliferate
Identification of Gene Mutation for Ocular Melanosis

• Genome-wide scan of genome to find genetic marker that is linked to ocular melanosis gene

• Understand process of disease development
  – May suggest Candidate genes to investigate
Canine Genome

- Genetic information held by DNA in nucleus of every cell
- DNA consists of 4 building blocks A, C, G & T
  - Arranged as two strands of DNA in double helix
Canine Genome

- Genetic information divided across 39 pairs of chromosomes
Canine Genome

• 2.5 Gb (2,500,000,000) base pairs of DNA
  – Chromosome 1 has 124,897,793 basepairs
• Disease causing mutation can be an alteration of one of those basepairs
• Dog genome sequenced
  – 35 million sequencing runs
Exchange of Genetic Material between Chromosomes
Genetic Mapping

- Uses naturally variations in DNA sequence that are inherited = markers
- Markers spread across the chromosomes
  - Look for version of marker linked to disease of interest
- Minimal marker set = 327 markers
Genome Wide Scan

- Needs good pedigree
  - Three generations
  - Dogs of known disease status
- Need DNA sample from dogs
- Check versions of each marker that dogs have
- Examine for linkage of a marker to the disease
Ocular Melanosis Pedigree
Problems with Genome Wide Scan

• Variable age of onset of ocular melanosis
  – At what age can we say a dog is truly unaffected?
• Difficulty in getting DNA samples from 3 generations of ocular melanosis families (with known disease status)
• Currently analysing results of microsatellite markers in 94 Cairn Terriers from ocular melanosis pedigrees
Candidate Gene

• Make educated guess as to which gene(s) if defective could cause disease

• How to educate ourselves
  – Examine affected eyes
  – Identify cell type proliferating
  – Try to culture proliferating cells to allow more detailed analysis
  – Look for similar diseases in other species
Results of Examination of Eyes

• Cell type is a melanocyte
  – Examined by electron microscopy
  – Examined by staining with different antibodies to further characterize cells
Other Similar Diseases

- Mice with hereditary glaucoma associated with pigmentation
  - Gene GNMB
  - Gene screened in Cairn Terriers – NOT the ocular melanosis gene

- Pigmentary glaucoma in humans
  - Appears different to the glaucoma in ocular melanosis
What is needed for OM research?

- More DNA samples from families with ocular melanosis
  - Affected dogs and relatives
  - Blood sample preferred
  - Cheek swab still usable
- Continuation of screening of dogs for OM
- Donation of eyes for histology and also for cell culture
Ocular Melanosis Screening Sessions

• Not a CERF examination
  – Just looking for OM
  – CERF screens for all eye diseases
• Dilation of the pupil not usually needed
  – OM can be diagnosed by looking at the front part of the eye
• Will want to collect a cheek swab
• Will need a copy of dog’s pedigree
Contact Information for Ocular Melanosis Research at Michigan State

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Ocular Melanosis - Summary

- Hereditary problem, increasing incidence
- Causes blindness and pain for dog in middle age
- Management of glaucoma not successful in long-term
- Considerable distress and expense for owner
- No early diagnostic test available
Questions?