Eye Alert: Iris Pigmentation

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Pigment changes of the iris alert the owner or the clinician of a condition well worth concern. Differential diagnoses include iris freckle, nevus, cyst, and malignant melanoma.

Freckle
The most benign of the iris pigment changes is an iris freckle. It is caused by increased pigmentation of the anterior border layer melanocytes, without an increased number of melanocytes. There is no discrete mass or nodule on the iris surface (figures 1 and 2).

Nevus
An iris nevus results from an increased number of atypical but benign-appearing melanocytes in a discrete mass or nodule within the anterior border layer of the iris (figure 3). A diffuse nevus of the iris is present in congenital melanocytosis (figure 4). An acquired diffuse nevus of the iris (figure 5) may be associated with unilateral heterochromia, peripheral anterior synechia, or iris nodule (localized inflammation). An iris nevus or freckle has a low malignant potential but a high anxiety potential for the pet owner and veterinarian who worry about the possibility of malignant melanoma.

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Figure 4 - A diffuse nevus of the iris or congenital melanocytosis may be within the iris stroma without causing a nodular or mass appearance.

Figure 5 - An acquired diffuse nevus occurred following uveitis. Note the misshapen pupil. Melanocytic reactions and macrophages laden with melanin granules account for the discoloration and irregularity of the iris surface. The inflammatory component of this iris will alter in appearance after months of treatment with anti-inflammatory medication.

Iris Cysts

Iris cysts vary in size but they are always spherically shaped and usually pigmented. The densely pigmented cysts can challenge your diagnostic capabilities. Utilizing procedures such as transillumination, ultrasound, and occasionally aspiration may be necessary to diagnose iris cysts.

The origin of iris cysts is poorly understood. Histologically, the cysts are generally a unilayered structure of mature pigmented cells. The cells can be free floating in the chambers or attached to the posterior iris surface or ciliary body. The lumen of the cyst is filled with unidentified fluid (probably of aqueous properties). If the cyst is small, its size should be monitored with periodic examinations. If the cyst is large and occurs in the primary pupillary axis, it can be deflated by anterior chamber paracentesis with a fine needle or by laser destruction (figures 6 and 7).
Malignant Melanomas

It is suspected that malignant melanoma of the feline iris constitutes a higher percentage of uveal melanomas than cited for humans (approximately 5 to 8%). Iris melanomas arise from the anterior border layer tissue of the iris, similar to nevi. Most, if not all, iris malignant melanomas arise from pre-existing nevi.

A geographic distribution of iris malignant melanomas in the feline has not been categorized into frequency of occurrence. However, the categories established in human medicine are inferior, temporal, nasal, and superior locations.

The clinical presentation of an iris melanoma may be as a discrete mass, a diffuse mass, a heterochromia, freckle or nevi, glaucoma, or chronic uveitis. The masses may be deeply pigmented, partially pigmented, or even nonpigmented. They frequently show neovascularization and a roughened surface. The mass may distort the pupil or the range of movement of the pupil. Gonioscopic examination of the iris surface and iridocorneal angle may help to classify the mass’ characteristics (figures 8 and 9).
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Figure 9 - Diffuse melanoma with variable pigment qualities. Iridocorneal angle invasion noted. Also note the pigment on the adjacent lid margin as well.

In humans, most iris malignant melanomas are composed of spindle cells that are usually benign. In cats, the composition is epithelioid or mixed (figures 10, 11, and 12). A recent article examined globes from 9 cats with localized to diffuse hyperpigmentation. A combination of cell types was found, leading the authors to speculate that this cell makeup may represent a progression of characteristics from iris freckle to diffuse melanoma.

A diffuse iris melanoma is a malignancy that can vary in hyperpigmentation from localized to multifocal to generalized. The globe may even become buphthalmic due to neoplastic cells infiltrating the iridocorneal angle, causing secondary glaucoma. Extension of the melanoma may be visible in portions of the conjunctiva and sclera. The above progression and threat of metastasis have stimulated debate among pathologists and ophthalmologists.

Figure 10 - Iris tip with melanosis of iris stroma and surface. Rapid color change caused concern, so the eye was enucleated (H. & E. stain 4X).

Figure 11 - Iris anterior surface showing normal feline iris pigment cells and the invading overgrowth of melanocytes (H. & E. stain 40X).

Early diagnosis of an iris melanoma with enucleation is recommended to prevent the neoplasia from metastasizing. All enucleated globes should be histologically evaluated to help understand the characteristics of malignancy more fully and predict the prognosis of the animal.

The debate over when an eye should be enucleated will always exist. For many owners it is hard to justify the loss of a cat’s visual eye because of a pigment change on the iris. Ophthalmologists generally agree that these pigmented spots, without thickening or distortion of the iris and no associated inflammation, should be serially monitored instead of enucleated. The evaluations should include measurement of the pigmented areas, photographs, biomicroscopic and gonioscopic examinations of the hyperpigmented areas every 3 to 6 months.
Baseline values of the cat’s general condition should be obtained. Tests can include a complete blood count, serum chemistry panel, and thoracic and abdominal radiographs. If the periodic evaluation documents a change in the iris pigmentation and character, a more definitive answer may be obtained by submitting an iris biopsy or cytology from a freckle by using the surface vacuum technique. Both techniques have positive and negative implications. An iris biopsy may result in enough trauma to release neoplastic cells for metastasis or cause hemorrhage. Although needle aspiration of the surface cells is a safer technique, it may not yield enough cells to determine the nature of the hyperpigmentation.

Many veterinarians, aware of these dilemmas, convince the owner that because of the potential of malignancy it is best to enucleate. Veterinary ophthalmologists are aware that most of the pigmented spots never develop into diffuse melanoma even if they slowly change in shape. However, the interval of transformation from freckle to nevi to melanoma is unknown.  

Defining the early clinical features is an important task of the veterinarian. Both the practitioner and the ophthalmologist should consider the long-term studies on 49 cats with anterior uveal melanoma that documents a known or suspected metastasis in 53 percent to 66 percent of the cats.  

The value of early enucleation to decrease the long-term rate of metastasis is unknown. A controlled prospective clinical study that compares the three- to five-year survival rates of cats receiving early and late enucleation will help answer the existing controversy. Additional studies of the clinical, histopathological, and cytological risk factors associated with metastasis of the feline iris melanoma are warranted.  

References


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Ultrasonographic Examination of the Thyroid Gland of Hyperthyroid Cats: Comparison to $^{99m}\text{TcO}_4$-Scintigraphy

High-resolution ultrasonography was evaluated by researchers at the University of California at Davis as an alternative to $^{99m}\text{TcO}_4$-scintigraphy for examining size and appearance of thyroid glands in hyperthyroid cats. Thyroid ultrasound examinations were performed on 6 normal and 14 hyperthyroid cats. Thyroid lobe volume was estimated from ultrasound images using the equation for a prolate ellipsoid, $\pi/6$ (length*height*width). Total thyroid volume was estimated by adding the volume estimations of the left and right lobes. Thyroid lobes of hyperthyroid cats were considered abnormal if estimated volume exceeded the 99 percent confidence interval for normal thyroid volume determined from the control group.

Scintigraphic examinations performed on hyperthyroid cats were evaluated for unilateral versus bilateral disease and for the presence of ectopic activity. Mean thyroid lobe volume and total thyroid volume for normal cats was 85 and 169 mm$^3$, respectively. Mean thyroid lobe volume and total thyroid volume for hyperthyroid cats was 578 and 889 mm$^3$. There was significant difference in mean estimated total thyroid volume of normal and hyperthyroid cats. Thyroid lobes with greater than normal $\text{TcO}_4$-uptake on scintigraphy were larger and had variable homogeneity, echogenicity, and margination on ultrasound examination. There also was an 85.7 percent agreement of scintigraphy and ultrasonography in differentiating normal from abnormal thyroid lobes. A fair correlation between estimated total thyroid volume of hyperthyroid cats and most recent pretherapy serum thyroxine values were also found.

This preliminary study indicates that thyroid ultrasound examination may provide information that is useful for diagnosis and treatment of feline hyperthyroidism. Although ultrasound provides accurate evaluation of the thyroid glands, it cannot replace $^{99m}\text{TcO}_4$-scintigraphy for screening of metastatic lesions and ectopic glands.—(Resource: Vet. Radiol. Ultrasound 35(1):53-58, 1994)

Feline Immunodeficiency Virus Predisposes Cats to Acute Generalized Toxoplasmosis

This North Carolina State University study examined the effects of a pre-existing, clinically asymptomatic feline immunodeficiency virus (FIV) infection on a primary challenge with Toxoplasma gondii. Parenteral challenge of FIV-infected cats with tachyzoites of the ME49 strain of T. gondii caused a precipitous drop in all lymphocytes (CD4+, CD8+, and B cells) and generalized severe toxoplasmosis. The predominant postmortem lesions included acute and often fatal interstitial pneumonia, dominated histologically by macrophages, and multifocal to coalescing hepatic necrosis. Immunohistochemistry revealed numerous T. gondii antigen and tachyzoites in macrophages and other cell types in the lung lesions. The proliferative response of peripheral blood mononuclear cells to specific (T. gondii antigen) and nonspecific (Concanavalin A) mitogens was defective in the dually infected cats, suggesting marked immunosuppression. In contrast to the dually infected cats, cats infected only with T. gondii developed a transient, mild clinical disease characterized by anorexia, lethargy, and multifocal chorioretnitis. Lymphocyte changes in T. gondii-infected cats included an early panlymphopenia followed by re-establishment of all lymphocyte subset profiles. These cats also showed

(continued on next page)
cats also showed a reduced proliferative response to Concavalin A at 1 week after challenge, but a measurable in vivo response to *T. gondii* antigens, as evidenced by in vitro lymphocyte proliferation in the absence of mitogenic stimulus.

These results show that infection of cats with FIV-NCSU1 markedly enhances their susceptibility to a primary *T. gondii* infection and provides a model to study the mechanisms of the underlying immunological defects(s) occurring early after HIV infection that may predispose individuals to development of acquired immunodeficiency syndrome and associated diseases.—(Resource: *Amer J Pathol* 143:1486-1497, 1993)

Evidence for Genetic Involvement in Feline Dilated Cardiomyopathy

Quantitative genetic evaluation of clinical dilated cardiomyopathy (DCM) was conducted in a large cattery with known history. Data showed that clinically affected cats were significantly more interrelated than randomly chosen case-control populations from the same colony. The results of this study suggest that quantitative inheritance, either interactive with or independent of nutrition or presently unknown factors, is involved in feline dilated cardiomyopathy.—(Resource: *J Vet Int Med* 7:383-387, 1993)

Radiology Case Review

Victor Rendano, V.M.D., M.S. and James Richards, D.V.M.

A five-year-old domestic longhair cat was presented because of weight loss and coughing. Physical examination revealed a thin animal with periodontal disease and a grade III/VI heart murmur. No mass lesions were palpable. A radiograph of the thorax (figure A) was obtained and blood was submitted for analysis. Significant clinicopathologic findings included a packed cell volume (PCV) of 18% and blood urea nitrogen (BUN) of 173.

What are your radiographic findings and your diagnosis?—See page 8 for interpretative comments.

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Figure A
Radiology
(continued from page 7)

Radiographic findings
- Mineralization of the aorta
- Prominence of the pericardial silhouette
- Increased peribronchial and interstitial tissue volume with focal areas of alveolar opacification.
- Prominence of the caudal vena cava

Comments
The mineralization of the aorta probably occurred secondary to renal failure. Multiple tissues can mineralize when an animal is uremic. The kidneys, gastric mucosa, lungs, vocal cords and aorta are organ systems that will show histologic and periodically radiographically detectable mineralization. Mineralization is the preferred term rather than calcification since the material deposited is a conglomerate containing more than just calcium.

Mineralization in conjunction with uremia was once termed “metastatic calcification”; however, the current preferred terminology is “dystrophic mineralization” since the deposition of the calcium salts is preceded by degeneration of tissues. Additionally, the term “metastatic” frequently conjures the image of neoplasia. The connective tissue is the target site for the deposition of the minerals, with elastic fibers being the initial location in the aorta. The etiology for the heart murmur was not determined. The changes in the lung parenchyma can occur secondary to uremia or pulmonary edema that is secondary to heart disease. The periodontal disease and the renal failure can be related.

Postscript
The animal became anorectic and weak. The owners chose to have the cat euthanatized; postmortem evaluation of the tissues was not permitted.

Correction—
In table 2 on page 4 of volume 9, number 2 issue of Feline Health Topics change "excessive pancreatic insufficiency" to "exocrine pancreatic insufficiency."