



## UVEAL TUMORS

### Ring iris melanoma

[Article in Romanian]

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We are presenting a case of diffuse (ring) iris melanoma with secondary glaucoma, together with the differential diagnosis issues. The tumor extension and the high IOP imposed the enucleation of an eye that still had a good visual acuity. The pathology confirmed the diagnosis and showed the extension to the anterior chamber angle and the ciliary processes. The prognosis in this rare type of uveal melanoma is worse than in other iris melanomas.

### Iris cyst simulating melanoma

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Congenital cysts of the iris stroma are extremely uncommon and only a few cases have been reported. The vast majority of reported cases have been found in infants or children as a unilateral, translucent mass in the middle or peripheral third of the iris. 1-3 Although these cysts may remain dormant for years, they have a tendency to enlarge, causing corneal decompensation, secondary glaucoma, and eye pain. 2 Occasionally, they have been mistaken for iris melanomas leading to enucleation. 4,5 We describe a 14-year-old girl with a congenital cyst of the iris stroma, which over a period of 8 years enlarged, became opaque resembling melanoma, and required surgical excision.

### Cavernous hemangioma of the iris in an infant

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Iris hemangioma is a rare intraocular tumor which can present with spontaneous hyphema. Juvenile xanthogranuloma, malignant melanoma with proliferation of vessels or hemorrhages in the region of cystic degeneration, and inflammatory granulomas are frequently confused with the true hemangiomas. Some authors have even questioned the very existence of iris hemangioma. Clinical case reports of iris hemangiomas with histopathologic evidence and clinical course after surgery are uncommon. We could not find any reports of iris vascular tumors confirmed using immunohistochemical staining with vascular markers. We report a case of a cavernous hemangioma of the iris in a 3-month-old infant treated surgically, and the histopathological findings and immunohistochemical analysis with vascular markers (factor VIII and CD34) are also shown.

**Treatment of metastatic tumors of the choroid with proton beam irradiation**

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Ophthalmology. 2005 Feb;112(2):337-43

**OBJECTIVE:** To describe the clinical outcomes of patients treated by proton beam irradiation for choroidal metastatic tumors. **DESIGN:** Noncomparative case series.

**PARTICIPANTS:** A retrospective chart review was performed on a series of 63 patients (76 eyes) with choroidal metastases treated with proton beam therapy between December 1989 and September 2000.

**METHODS:** Patients were treated with 2 fractions of 14 cobalt gray equivalents (CGEs) (CGE = proton Gy x relative biological effectiveness 1.1), each using a nonoperative "light-field" technique. Ophthalmologic follow-up was available for 46 patients (55 eyes), with a mean follow-up time of 10 months. The medical record or the Social Security Death Index was used to obtain survival status, which was available in 94% of cases.

**MAIN OUTCOME MEASURES:** Tumor regression, recurrence, treatment-associated complications, and visual acuity were evaluated by ophthalmologic examination and ultrasonography. Eye retention and length of survival also were assessed.

**RESULTS:** At the time of ocular diagnosis, 49 patients reported a history of a primary cancer. Median survival time after ocular diagnosis was 16 months through May 2003. Most choroidal metastases were dome shaped (62%) and located at the posterior pole (95%). Mean tumor height was approximately 3.5 mm, and serous retinal detachment was seen in 63% of cases. Eighty-four percent of treated tumors regressed completely within 5 months of treatment, and none of these recurred. Retinal detachment resolved in 82% of patients within 3.8 months after treatment, and visual acuity was preserved or improved in 47% of the patients. Complications occurred in 56% of cases and included madarosis, keratitis, dry eye syndrome, cataract, neovascular glaucoma, chorioretinal atrophy, radiation papillopathy, and radiation maculopathy. None of the treated eyes required enucleation.

**CONCLUSIONS:** Proton beam irradiation is a useful therapeutic approach for choroidal metastases; it allows retention of the globe, achieves a high probability of local tumor control, and helps to avoid pain and visual loss. Although complications occur in most cases, many of these are minor and are not associated with a change in function. This modality is accurate and efficient, because it only entails 2 treatment fractions and does not require surgery for tumor localization.

**Systemic non-Hodgkin B-cell lymphoma encountered as a vanishing choroidal mass**

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**Case Reports****Transpupillary thermotherapy for subfoveal choroidal neovascularization associated with choroidal nevus**

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**PURPOSE:** To describe a patient with classic subfoveal choroidal neovascularization (CNV) associated with choroidal nevus, which was successfully treated using transpupillary thermotherapy.

**DESIGN:** Interventional case report.

**METHODS:** A 53-year-old woman underwent ophthalmologic evaluation, including fluorescein and indocyanine green angiography. Clinical and angiographic data were prospectively analyzed to evaluate visual acuity changes and angiographic evolution.

**RESULTS:** Three months after transpupillary thermotherapy, visual acuity had improved from 20/100 to 20/40. Fluorescein and indocyanine green angiograms showed absence of leakage from CNV. Final visual acuity was 20/32 after a 15-month follow-up.

**CONCLUSIONS:** Transpupillary thermotherapy may be a viable option for subfoveal CNV associated with CN, although further studies are needed to establish the correct setting.

### **The Collaborative Ocular Melanoma Study (COMS) randomized trial of pre-enucleation radiation of large choroidal melanoma: IV. Ten-year mortality findings and prognostic factors. COMS report number 24**

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**PURPOSE:** To report rates of death and related outcomes through 10 years after treatment of large choroidal melanoma and to evaluate characteristics of patients and tumors as predictors of relative treatment effectiveness and time to death.

**DESIGN:** Randomized multicenter clinical trial of pre-enucleation radiation vs enucleation alone conducted as part of the Collaborative Ocular Melanoma Study.

**METHODS:** Eligible patients were free of metastasis and other cancers at enrollment. All patients were followed for 5 years or longer at scheduled examinations and contacts for metastasis, another cancer, or death. Each decedent was classified as having histopathologically confirmed melanoma metastasis, suspected melanoma metastasis without histopathologic confirmation, another cancer but not melanoma metastasis, or no malignancy.

**RESULTS:** Within 10 years after enrollment, 576 of 1,003 patients died. Ten-year all-cause mortality rates were 61% for patients in both treatment arms. Ten-year rates of death with histopathologically confirmed melanoma metastasis were 45% in the pre-enucleation radiation arm and 40% in the enucleation alone arm. Older age and larger maximum basal tumor diameter were the primary predictors of time to death from all causes and death with melanoma metastasis. No differences in unadjusted or adjusted mortality rates were found between treatment arms. Of 448 patients eligible for 10 years of follow-up, 145 patients (32%) were alive and clinically cancer-free 10 years after treatment.

**CONCLUSIONS:** Longer follow-up confirmed the earlier report of no survival advantage attributable to pre-enucleation radiation. Mortality rates by baseline characteristics should facilitate counseling of patients who have large choroidal melanoma and no evidence of metastasis or another malignancy at diagnosis.

### **Primary extracutaneous malignant melanoma: a comprehensive review with emphasis on treatment**

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Onkologie. 2004 Oct;27(5):492-9

Extracutaneous malignant melanomas (EMM) require special consideration in the field of oncology due to their rareness and--depending on the localization—the frequency of late diagnosis with consecutive poor prognosis. Only 4-5% of all primary melanomas do not arise from the skin. Most frequently they originate from the mucous membranes lining the respiratory, digestive, and genitourinary tracts or in the eyes as well as in the cerebral meninges. Extracutaneous melanomas are considered to be biologically more aggressive than cutaneous melanomas. The Clark level and Breslow index used for evaluation of cutaneous melanomas are not applicable to EMM and, at present, there are no consistent, internationally accepted therapy standards for this form of the disease. For this reason, this review focuses primarily on the literature pertaining to therapeutic strategies as well as epidemiologic, biological, and diagnostic aspects of this disease. Publication Types:

### **Treatment options in the management of choroidal metastases**

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Ophthalmologica. 2004 Nov-Dec;218(6):372-7

We performed a retrospective study of 40 consecutive patients (50 eyes) treated for choroidal metastases of solid systemic malignancies in order to evaluate treatment results. Patients received either systemic or local therapy or a combination of both. The most common primary tumor was breast carcinoma (62.5%). Systemic chemotherapy alone was used in 13.3% of eyes, local therapy alone in 44.4%, and a combination of both in 42.2% of eyes. Local treatment modalities included brachytherapy, external beam irradiation, and laser photocoagulation. Complete regression of the choroidal metastases was seen in 57.8% of eyes, partial regression in 15.6 and no response in 4.4%; 22.2% were not available for re-evaluation. We have concluded that the treatment modality in patients with metastatic ocular disease should be individually tailored. When ocular metastases are concurrent with widespread metastatic disease, systemic chemotherapy alone or in combination with local therapy is reasonable. In patients manifesting metastases in the eyes alone, local therapy modalities may be safe, allowing conservation of visual functions with minimal systemic morbidity.

### **Identification of monosomy 3 in choroidal melanoma by chromosome in situ hybridisation**

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**BACKGROUND/AIMS:** In uveal melanoma monosomy 3 is emerging as a significant indicator of a poor prognosis. To date most cytogenetic studies of uveal melanoma have utilised fresh tissue or DNA extracted from tissue sections. In this study chromosome in situ hybridisation (CISH) was used to study monosomy 3 in tissue sections. The copy number of chromosome 3 was determined and related to patient survival.

**METHODS:** Archival glutaraldehyde or formalin fixed, paraffin embedded material was obtained from 30 metastasising and 26 non-metastasising choroidal melanomas. Hybridisations were performed using

centromere specific probes to chromosomes 3 and 18. Chromosome 18 was included as a control as previous abnormalities in uveal melanoma have not been described. Chromosomal imbalance was defined on the basis of changes in both chromosome index and signal distribution.

**RESULTS:** CISH was successfully performed on both glutaraldehyde and formalin fixed tissue. Four cases were unsuccessful because of extensive tumour necrosis. All cases were balanced for chromosome 18. Monosomy 3 was detected in 15 of the 26 cases of metastasising melanoma; the 26 non-metastasising tumours were all balanced for chromosome 3. Monosomy 3 was significantly associated with metastases related death.

**CONCLUSION:** CISH can successfully identify monosomy 3 in archival glutaraldehyde or formalin fixed, paraffin embedded tissue sections. Similar to previous studies monosomy 3 is a significant predictor of metastases related death.

### **Palladium 103 (103Pd) plaque radiation therapy for circumscribed choroidal hemangioma with retinal detachment**

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Arch Ophthalmol. 2004 Nov;122(11):1652-6.

**OBJECTIVE:** To describe clinical experience with palladium 103 ophthalmic plaque radiotherapy for choroidal hemangioma.

**METHODS:** One course of (103)Pd ophthalmic plaque radiotherapy was used in each of 5 patients with circumscribed choroidal hemangioma who had progressive loss of vision due to subretinal exudation. A mean apex dose of 2900 cGy (2900 rad) was delivered. Functional tests of outcome included best-corrected visual acuity. Anatomic results included changes in tumor height and subretinal fluid documented by ophthalmoscopy, fluorescein angiography, and ultrasonography.

**RESULTS:** All patients had complete resolution of subretinal fluid with reattachment of the retina. All tumors decreased in height (mean, 50%) after treatment. Three patients (60%) demonstrated improvement in visual acuity at the last follow-up, and in 1 patient vision remained stable with resolution of metamorphopsia. Twenty-four months after treatment, 1 patient whose visual acuity had recovered from 20/160 to 20/32 had a loss of vision to 20/160 because of radiation maculopathy. For all patients, a mean visual acuity improvement of 2 lines was documented (95% confidence interval, 0.23-0.88). Mean follow-up was 18.6 months (range, 6-29 months).

**CONCLUSIONS:** A single (103)Pd plaque radiation treatment was effective in decreasing tumor height, eliminating subretinal fluid, and improving visual acuity in patients with symptomatic circumscribed choroidal hemangiomas.

### **Choroidal and skin metastases from papillary thyroid cancer: case and a review of the literature**

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A patient with widely metastatic papillary thyroid cancer who had been previously treated with (131)I and external beam radiation presented with purple nodular lesions on his face and scalp. On biopsy, the nodules were papillary carcinoma with cells that stained for thyroglobulin. Subsequently he developed

decreased left eye visual acuity, and funduscopy revealed lesions typical of choroidal metastases. Dermal and choroidal metastases of papillary thyroid carcinoma are both rare. However, the significance of these clinical manifestations may be overlooked and ignored unless the diagnosis is considered. New skin nodules or visual acuity decline in a patient with papillary thyroid cancer may represent manifestations of distant metastatic disease and should prompt thorough evaluation with dermatological examination and funduscopy. Choroidal and skin metastases have almost always occurred in patients with advanced disease, but initial presentation with these lesions is possible, and in such instances a thorough search for additional sites of metastatic disease is recommended. Occasionally such metastases may respond to (131)I therapy or external beam radiation.

### **Transpupillary thermotherapy in the management of choroidal metastases**

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Eur J Ophthalmol. 2004 Sep-Oct;14(5):423-9

**PURPOSE:** To report the authors' experience in the use of infrared diode laser transpupillary thermotherapy in the management of selected posterior choroidal metastatic tumors.

**METHODS:** Seven eyes of seven patients were treated using 810 nm infrared diode laser. Spot sizes of 0.5 to 3 mm were selected, each lasting 1 minute. When necessary, the treatment was repeated at 8- to 10-week intervals. Disappearance of the tumor was the main outcome measure.

**RESULTS:** The primary sites of carcinomas were breast, prostate, and lungs. The largest basal diameters of ocular tumors varied between 5 mm and 10 mm and the thickness ranged between 2 mm and 4.5 mm. A mean power of 612 mW was used in one to four treatment sessions. In six eyes the tumors were reduced into flat scars whereas in one case the tumor continued to grow necessitating external beam radiotherapy. In three eyes the visual acuity decreased and in three eyes the vision became better. In one eye the vision was restored after external beam radiotherapy with the disappearance of extensive subretinal fluid. There were no immediate postoperative complications.

**CONCLUSIONS:** Transpupillary thermotherapy can be a reliable, convenient, and cost-cutting option in the management of small, solitary choroidal metastatic tumors with a thickness of less than 3.5 mm and which have minimal subretinal fluid. Although successful in terms of tumor control, treatment close to the fovea or optic nerve head may cause a permanent decrease in visual acuity.

### **Changing concepts in management of circumscribed choroidal hemangioma: the 2003 J. Howard Stokes Lecture, Part 1**

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Ophthalmic Surg Lasers Imaging. 2004 Sep-Oct;35(5):383-94

**BACKGROUND AND OBJECTIVE:** To review trends in the management of circumscribed choroidal hemangioma (CCH) and to propose treatment guidelines based on review of recent literature and the authors' personal experience with more than 250 cases.

**METHOD:** The English-language literature on the management of CCH was reviewed, with emphasis on changing concepts in recent years.

**RESULTS:** Xenon arc and argon laser photocoagulation and thermotherapy have been used to treat CCH with localized retinal detachment, but there has recently been enthusiasm for photodynamic therapy

(PDT) using fluorescein angiography and optical coherence tomography to monitor subretinal fluid and cystoid retinal edema before and after treatment. Tumors with extensive retinal detachment have been managed by surgical attempts at retinal reattachment followed by photocoagulation or cryotherapy, and more recently by radiotherapy. Management currently includes observation, argon laser photocoagulation, transpupillary thermotherapy, PDT, and radiotherapy. Enucleation may be necessary in rare cases. The goal of treatment should be to induce resolution of existing retinal detachment and to improve or stabilize visual loss.

**CONCLUSIONS:** There is increasing use of PDT for CCH with localized retinal detachment and radiotherapy for CCH with more extensive detachment. Although follow-up is short, current methods may achieve better tumor control and better visual outcome. However, caution is advised because long-term follow-up is still not available.

### **Photodynamic therapy of circumscribed choroidal haemangioma**

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Br J Ophthalmol. 2004 Nov;88(11):1414-8

**AIM:** To evaluate efficacy of verteporfin ocular photodynamic therapy (PDT) in treatment of 10 patients with a symptomatic circumscribed choroidal haemangioma. **DESIGN:** Prospective non-randomised, interventional case series and critical review of previously published studies.

**METHODS:** 10 consecutive patients (seven primary, two failed transpupillary thermotherapy (TTT), and one failed external beam radiotherapy) with symptomatic circumscribed choroidal haemangioma were treated using verteporfin 6 mg/m<sup>2</sup> given as an intravenous infusion over 10 minutes. Diode laser (690 nm) with an intensity of 600 mW/cm<sup>2</sup> for 83 seconds (50 J/cm<sup>2</sup>) was applied 5 minutes after completion of infusion. Single or multiple partially overlapping spots were applied based on the tumour basal dimensions. Periodic follow up with ophthalmoscopy, ultrasonography, and angiographic studies was performed.

**RESULTS:** All 10 patients showed evidence of regression with flattening of tumour, resolution of subretinal fluid, and reduction of choroidal vasculature on angiograms. The visual acuity either improved or remained stable in eight (80%) patients. Visual loss due to delayed choroidal atrophy was seen in two patients.

**CONCLUSIONS:** Although verteporfin PDT is an effective treatment for management of symptomatic circumscribed choroidal haemangioma, delayed treatment related effects can lead to visual loss.

### **Prognostic factors for survival after enucleation for choroidal and ciliary body Melanomas**

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Acta Ophthalmol Scand. 2004 Oct;82(5):517-25

**PURPOSE:** To evaluate prognostic factors for the survival of patients treated by enucleation for choroidal and ciliary body melanomas.

**METHODS:** The study included 293 consecutive patients (147 men and 146 women) treated by

enucleation for a choroidal or ciliary body melanoma during the period 1955-2000. The median age at treatment was 61 years (range 26-88 years). Clinical and histopathological findings, vital status at October 1st, 2002, and cause of death were registered. Prognostic factors for survival were evaluated by univariate and multivariate Cox proportional hazards analysis and by Kaplan-Meier survival analysis.

**RESULTS:** Follow-up was complete. The median follow-up time was 6.2 years (range 21 days to 43.4 years) and the median potential follow-up time was 25.7 years (range 1.9-47.7 years). In multivariate Cox proportional hazards analysis an increased risk of melanoma-related death was found for largest basal diameter ( $n = 264$ ,  $p < 0.001$ , mortality rate ratio (RR) = 1.09 for continuous parameter in mm), anterior tumour margin at the iris/ciliary body versus choroid ( $p < 0.001$ , RR = 2.22), and non-spindle cell type versus spindle cell ( $p = 0.047$ , RR = 1.45). An increased risk of death from all causes was found for men versus women ( $n = 266$ ,  $p = 0.02$ , RR = 1.41), high age ( $p < 0.001$ , RR = 1.41 for continuous parameter in 10-year age groups), largest basal diameter ( $p < 0.001$ , RR = 1.07), anterior tumour margin at the iris/ciliary body ( $p = 0.02$ , RR = 1.52), and non-spindle cell type ( $p = 0.04$ , RR = 1.34).

**CONCLUSION:** The risk of melanoma-related death after enucleation for a choroidal or ciliary body melanoma was high for tumours with large basal diameter, of non-spindle cell type and anterior location. Additional risk factors for death from all causes were male sex and high age.

### **Have choroidal and ciliary body melanomas changed during the period 1955-2000?**

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Acta Ophthalmol Scand. 2004 Oct;82(5):509-16

**PURPOSE:** To establish whether the presentation of choroidal and ciliary body melanomas and patient survival have changed during the period 1955-2000.

**METHOD:** The study included 209 unselected patients (97 men, 112 women) from Arhus County during the period 1955-2000. The median age at treatment was 64 years (range 26-88 years). The disease course from first symptom through clinical and histopathological findings to death was described in a historical follow-up design. Time trends were evaluated.

**RESULTS:** Treatment modality changed over time from enucleation to an almost equal distribution between enucleation and radiation brachytherapy. The age at treatment, or, alternatively, at diagnosis, increased significantly ( $p = 0.04$ ). No significant time trend was seen for largest basal tumour diameter ( $p = 0.08$ ) or tumour height ( $p = 0.27$ ). The clinical and histopathological findings did not show any consistent time trends. No significant time trend was found for melanoma-specific survival ( $p = 0.96$ ) or overall survival ( $p = 0.33$ ).

**CONCLUSION:** No consistent time trends were seen in clinical and histopathological tumour presentation and survival in patients with choroidal or ciliary body melanomas. The increase in age at treatment was in line with an increase in life expectancy in Denmark.