ROSENBERG SCHOOL of OPTOMETRY

Optometric Clinical Practice

Volume 3 | Issue 2

2021

Choroidal Melanoma: Screening for metastasis and frequency of incidental second primary cancer diagnosis.

Ethan Leyda OD
The Ohio State University College of Optometry, Cleveland Veterans Affairs Medical Center,
ethan.leyda@va.gov

Recommended Citation

Leyda E. Choroidal Melanoma: Screening for metastasis and frequency of incidental second primary cancer diagnosis.. *Optometric Clinical Practice*. 2021; 3(2):19. doi: 10.37685/uiwlibraries.2575-7717.3.2.1023. https://doi.org/10.37685/uiwlibraries.2575-7717.3.2.1023

Choroidal Melanoma: Screening for metastasis and frequency of incidental second primary cancer diagnosis.

Abstract

Background: Choroidal melanoma is the most common primary intraocular malignancy in adults. This case report reviews clinical diagnostic features, imaging techniques, treatment, prognosis, and systemic work-up of choroidal melanomas. It also addresses choroidal melanoma metastasis and the incidental finding of second primary cancers through whole-body screening.

Case Report: A 71-year-old white male reported to the Cleveland VA Medical Center optometry retina clinic for a second opinion exam of an asymptomatic choroidal lesion in the right eye. The lesion was a 6 mm gray choroidal mass in the inferior peripheral fundus, with orange pigmentation, retinal pigmented epithelial hypertrophy along the superior border, and drusen. B-scan ultrasound showed a mass that was elevated by 2.5 mm with moderate reflectivity, suggestive of choroidal melanoma.

Conclusion: Early diagnosis of choroidal melanoma is important due to improved survival rates in those diagnosed when the choroidal melanoma is small. In addition to the clinical assessment, diagnosis may be aided by ancillary imaging such as OCT. Prognosis generally is poor due to late diagnosis and is dependent on choroidal melanoma size, genetic profile, and presence of metastasis. Whole-body screening for metastasis leads to the discovery of additional primary tumors at a rate nearly equal to that of metastasis.

Keywords

Choroidal Melanoma, Ocular Coherence Tomography (OCT), metastasis, second, primary cancer

INTRODUCTION

Choroidal melanoma is the most common primary intraocular malignancy in adults. Diagnosis of a choroidal melanoma is primarily made from observation of classic clinical features, including a pigmented dome-shaped tumor with subretinal fluid, orange pigment, and thickness greater than 2 mm. Larger choroidal melanoma size is related to a lower survival rate. Conversely, early diagnosis leads to early treatment and greater chance of patient survival. Incidence of metastasis is 25% and 34% at five and ten years respectively, while an additional primary cancer is discovered in about 10% of patients.[1] This case report reviews clinical diagnostic features, imaging techniques, treatment, prognosis, and systemic work-up of choroidal melanomas.

CASE REPORT

A 71-year-old white male reported to the Cleveland VA Medical Center optometry retina clinic for a second opinion of an asymptomatic choroidal lesion in the right eye. The patient's ocular history was significant for phototoxic maculopathy in the right eye secondary to welding, a low-risk glaucoma suspect, and allergic conjunctivitis. Best-corrected visual acuities were stable from baseline at 20/40 in the right eye and 20/20 in the left eye. The anterior segment evaluation was remarkable for trace papillae of the inferior palpebral conjunctiva. Dilated fundus examination revealed unremarkable findings for all structures in the left eye. The right eye revealed a stable macular scar and a 6 mm gray choroidal mass of the peripheral fundus inferiorly with orange pigmentation, retinal pigmented epithelial hypertrophy along the superior border, and drusen. B-scan ultrasound (Figure 1) was performed and showed a mass that was elevated by 2.5 mm with moderate reflectivity.

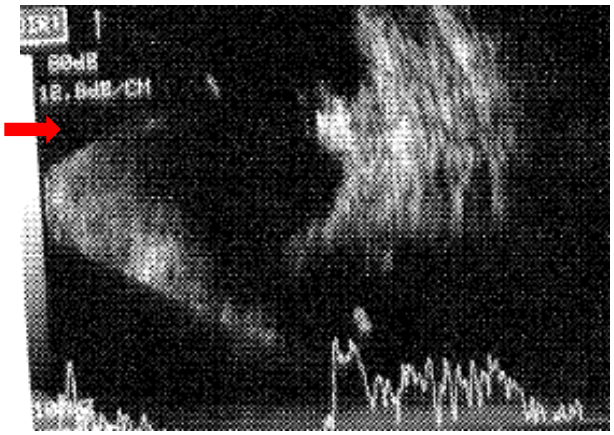

Figure 1: B-scan ultrasound of the patient's choroidal melanoma showing the elevated choroidal mass with medium reflectivity.

Ocular coherence tomography (OCT) revealed a peripheral elevated choroidal lesion via line scan. Because the mass was in the peripheral fundus, OCT with raster scanning and enhanced depth imaging, as well as autofluorescence, were difficult to obtain (Figure 2).

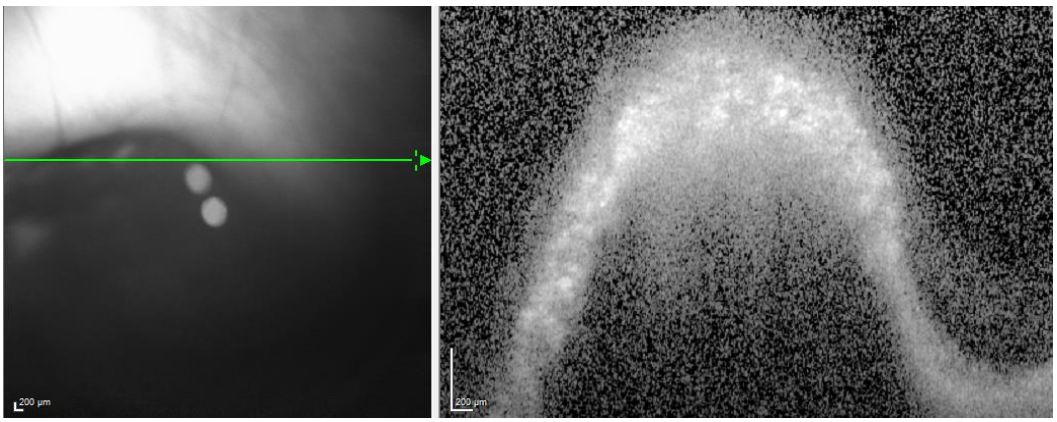

Figure 2: Spectralis OCT line scan showing the peripheral elevated choroidal melanoma.

The diagnosis of choroidal melanoma was made, and the patient was referred to an ocular oncologist at the Cleveland Clinic Foundation Cole Eye Institute. The ocular oncologist confirmed the diagnosis of choroidal melanoma, which was 7.5 x 6.5 x 2.5 mm in size with mild vascularity and medium internal reflectivity. Biopsy of the lesion confirmed a choroidal melanoma. Treatment was initiated with

a radioactive plaque that was sutured into place and delivered radiation for over seventy hours before removal.

Same-day CT scan of the chest/abdomen/pelvis was performed at the Cole Eye Institute. The report from urology stated, "suspicion of metastatic disease through the presence of a heterogeneously enhancing prostate with possible extracapsular extension, two adrenal nodules, and retro-peritoneal, retro-aortic, and pelvic lymphadenopathy." Care was then coordinated with the Cleveland VA urology service. Biopsy of the prostate revealed stage 3 adenocarcinoma of the prostate with perineural invasion. The patient was then initiated on hormone therapy. Treatment options were discussed with the patient, including resection and radiation.

The patient was seen four months after the initial diagnosis at the Cleveland VAMC optometry retina clinic. A large area of scarring and chorioretinal atrophy with retinal hemorrhages was seen in the area of the treated melanoma and an overall improvement in the lesion from the initial encounter was observed. The patient was scheduled to follow up again in 3 months.

DISCUSSION

Choroidal melanomas are uncommon, with an incidence of about 6 in 1 million in the United States, with 98% of those cases occurring in Caucasians. The median age of diagnosis is about 55 years and there is a slight predilection for men in almost all age groups.[1]

The diagnosis of choroidal melanoma is primarily based on ophthalmoscopic findings. Differential diagnoses must include choroidal nevus, congenital hypertrophy of the retinal pigment epithelium (CHRPE), subretinal blood, choroidal detachment, hemangiomas, metastatic carcinoma, and lymphoma. The classic appearance of choroidal melanoma is a pigmented dome-shaped tumor with an exudative retinal detachment. Typically, choroidal melanomas are pigmented but can also be amelanotic.[1] Choroidal melanomas are gray-green, brown, or yellowish in color and are characterized by subretinal fluid, thickness greater than or equal to 2 mm, areas of orange pigment (lipofuscin), presence of congested blood vessels, and growth.[2] Absence of drusen and a halo can also be used to differentiate the lesion. Autofluorescence of the tumor can be used to determine if one of the hallmark signs is present: hyperautofluorescence in the retinal pigment epithelium (RPE) that correlates with orange pigment accumulation.[3]

OCT has become the gold standard imaging technique for differentiating between benign and malignant choroidal lesions. OCT instruments have the ability to measure retinal lesions within 1µm. Small choroidal melanomas are defined as 1.5-2.4 mm in height and 5-16 mm in diameter, medium melanomas as 2.5-10 mm height and less than 16 mm diameter, and large melanomas as greater than 10 mm in height and greater than 16 mm in diameter.[4] The challenge to early detection of choroidal melanoma is its clinical similarities to benign choroidal nevus. Particularly in the case of small melanomas, the addition of OCT in diagnostic testing can be very beneficial. In a study comparing small choroidal melanomas versus similar-sized choroidal nevi, enhanced depth imaging optical coherence tomography (EDI-OCT) showed abnormalities at all levels of the retina, RPE, Bruch's membrane, and choroid. The small choroidal melanomas more often showed increased tumor thickness, subretinal fluid, lipofuscin deposition, and RPE atrophy. In addition to the clinical characteristics that were previously established, EDI-OCT of small choroidal melanomas more often showed the presence of shaggy photoreceptors, loss of external limiting membrane, loss of inner-outer segment junction, irregularity of inner plexiform and ganglion cell layers, and intraretinal edema.[3]

Although EDI-OCT and autofluorescence are newer ancillary testing modalities to help diagnose and manage patients with choroidal melanoma, ultrasound is still quite useful, especially in lesions in the extreme periphery where the OCT laser cannot reach. Combined A-mode and B-mode ultrasonography are used to image and measure the size of the tumor. Classic features of choroidal melanoma with B-scan are low-moderate internal reflectivity, choroidal excavation, and shadowing in the orbit.[1] Secondary tumors that metastasize to the eye typically have high internal reflectivity on B-scan.

Intra-venous fluorescein angiography (IVFA) can also be used in patients where the OCT laser cannot reach lesions in the extreme periphery. IVFA may detect the presence of intrinsic tumor circulation present in larger tumors, extensive leakage with progressive fluorescence, late staining and multiple pinpoint hot spots at the RPE.[1]

The choice of treatment for a choroidal melanoma is dependent on several factors including visual acuity, tumor size, and location, ocular structures involved, and metastasis. Radioactive plaque brachytherapy and proton beam radiation therapy

(PBRT) are primarily used in the treatment of small choroidal melanoma. Plaque radiation, PBRT, and enucleation are used primarily in the treatment of medium and large melanomas.[1] The Collaborative Ocular Melanoma Study (COMS) compared the effectiveness of brachytherapy to enucleation for treatment of medium sized choroidal melanomas, and the effectiveness of enucleation with and without pre-operative external beam radiotherapy for large choroidal melanomas.[4] The COMS found there was no difference in five year mortality rate for either treatment group in both the medium and large melanoma arms of the study. PBRT has become the "gold standard" treatment for choroidal melanomas due to the high level of tumor control and higher eye preservation rates without a reduction in efficacy. However, PBRT is less accessible because there are limited treatment centers with the required equipment and clinical expertise to administer it.[5]

Coordination of care with other specialties by the eye care team is crucial after the diagnosis of a choroidal melanoma. Genetic profiling, imaging for metastasis, and the determination of the cancer stage are performed. Screening for metastatic disease may vary but generally includes lung and liver imaging, along with liver function tests and physical examination. Positron emission tomography/computed tomography (PET/CT) is often used. Staging of the malignancy is based on the American Joint Committee on Cancer tumor, node, metastasis (TNM) staging system.[6] Staging and genetic profiling are important because they guide the treatment plan, determine the patient's prognosis, and help identify the appropriate treatment. TNM stages the cancer by tumor size using the thickness and largest basal diameter. Tumors are assigned to subgroups based on ciliary body involvement or extraocular extension. Tumors are then divided into groups by the presence or absence of metastasis and further divided based on the largest diameter of the largest metastasis. Gene expression profiling (GEP) divides uveal melanomas into classes 1A, 1B, and 2. Class 1 uveal melanomas are associated with low risk of metastasis and class 2 has the highest risk of metastasis.[7] In general, choroidal melanomas with a largest basal diameter more than 12 mm and class 2 GEP have the worst prognosis.[7] It is hypothesized that larger tumors have been present longer and, therefore, have had more time to metastasize, and/or larger tumors are an indicator of increased tumor malignancy and a greater growth rate.[8]

At the time of diagnosis, about 1.8% of patients are found to have metastasis.[9] After the development of metastatic disease, the median survival is about 13.4 months, with only 8% survival in 2 years.[10] The most common site for choroidal

melanoma metastasis is the liver (80-90%). Other potential systemic locations include the lungs, bone, and skin. Rates of metastasis observed in the COMS study after 5 and 10 years were 25% and 34% respectively.[1] Patients with metastasis to non-liver organ sites were found to have a longer median survival rate than those with metastasis to the liver. Patients with hepatic metastasis had a median survival rate of only 6 months.[11] Metastasis of choroidal melanoma can occur long after the primary tumor was definitively treated. Metastasis has been discovered up to 40 years after initial diagnosis, arising from metastatic cells in apparent dormancy.[12] Long-term follow-up studies have found up to 49% of choroidal melanoma patients die from metastatic melanoma.[9,10,12]

Whole-body screening after the diagnosis of choroidal melanoma can also discover second primary or synchronous cancers. In a study of 333 patients diagnosed with choroidal melanoma and subsequently screened with PET/CT, 10% were diagnosed with a second primary cancer, nearly equal to the percentage found to have metastasis in that study.[6] Multiple primary neoplasms have been reported to account for 13-16% of all malignancies and are considered to be the sixth most common presentation of cancer. In a long-term follow-up study, 6% of patients with uveal melanoma died of a second primary malignancy.[12] In another study of patients with uveal melanoma, PET/CT provided early detection of second primary cancers in 4.3% of patients. None of these patients reported symptoms that would have indicated a second primary cancer.[13] Radiation from PET/CT screening poses a second cancer risk. One report indicated the risk to be 0.2%-0.5% per year.[14] Therefore, the risk-benefit analysis should be considered when choosing PET/CT over other imaging techniques. The COMS study concluded there was no correlation between the treatment of choroidal melanoma and the occurrence of a second primary tumor.[15]

In general, second primary cancers are not as uncommon as thought. Cancer patients have approximately twice the risk of development of a second primary cancer compared to cancer-free patients of the same sex and age. There has been a rise in the number of second primary cancers, likely due to improvements in cancer treatment that allow patients to live longer. There are many potential causes of second primary malignancies, including environmental risk factors, lifestyle risk factors, genetic predisposition, polymorphisms for metabolizing enzymes, and radiation therapy.[16]

Conclusion

Early diagnosis of choroidal melanoma is important due to the improved survival rates for patients who are diagnosed when the choroidal melanoma is small. In addition to the clinical assessment, diagnosis may be aided by ancillary imaging such as OCT. The prognosis is generally poor due to late diagnosis being common, and is dependent on choroidal melanoma size, genetic profile, and presence of metastasis. As demonstrated by this case, whole-body screening for metastasis can lead to the discovery of second primary tumors. Detection of second primary tumors occurs at a rate nearly equal to that of metastasis.

References

1. Singh P, Singh A. Choroidal melanoma. *Oman J Ophthalmol*. 2012;5(1):3-9. doi:10.4103/0974-620X.94718
2. Bagheri, N. *The Wills Eye Manual: Office and Emergency Room Diagnosis and Treatment of Eye Disease*. 6th ed. Wolters Kluwer; 2017.
3. Shields CL, Kaliki S, Rojanaporn D, Ferenczy SR, Shields JA. Enhanced depth imaging optical coherence tomography of small choroidal melanoma: comparison with choroidal nevus. *Arch Ophthalmol*. 2012;130(7):850-856. doi:10.1001/archophthalmol.2012.1135
4. Margo CE. The Collaborative Ocular Melanoma Study: an overview. *Cancer Control.* 2004;11(5):304–309. doi: 10.1177/107327480401100504
5. Mishra KK, Daftari IK. Proton therapy for the management of uveal melanoma and other ocular tumors. *Chin Clin Oncol*. 2016;5(4):50. doi:10.21037/cco.2016.07.06
6. Freton A, Chin KJ, Raut R, Tena LB, Kivelä T, Finger PT. Initial PET/CT staging for choroidal melanoma: AJCC correlation and second nonocular primaries in 333 patients. *Eur J Ophthalmol*. 2012;22(2):236-243. doi:10.5301/ejo.5000049
7. Demirci H, Niziol LM, Ozkurt Z, et al. Do Largest Basal Tumor Diameter and the American Joint Committee on Cancer's Cancer Staging Influence Prognostication by Gene Expression Profiling in Choroidal Melanoma. *Am J Ophthalmol*. 2018;195:83-92. doi:10.1016/j.ajo.2018.07.033
8. Damato BE, Heimann H, Kalirai H, Coupland SE. Age, survival predictors, and metastatic death in patients with choroidal melanoma: tentative evidence of a therapeutic effect on survival. *JAMA Ophthalmol.* 2014;132(5):605–613. doi:10.1001/jamaophthalmol.2014.77
9. Lane AM, Kim IK, Gragoudas ES. Survival rates in patients after treatment for metastasis from uveal melanoma. *JAMA Ophthalmol.* 2018;136(9):981–986. doi:10.1001/jamaophthalmol.2018.2466

10. Krantz BA, Dave N, Komatsubara KM, Marr BP, Carvajal RD.. Uveal melanoma: epidemiology, etiology, and treatment of primary disease. *Clin ophthalmol*. 2017;11:279-289. doi:10.2147/OPTH.S89591
11. Kath R, Hayungs J, Bornfeld N, Sauerwein W, Höffken K, Seeber S. Prognosis and treatment of disseminated uveal melanoma. *Cancer*. 1993;72(7):2219-2223. doi:10.1002/1097-0142(19931001)72:7<2219::aid-cncr2820720725>3.0.co;2-j
12. Kujala E, Mäkitie T, Kivelä T; Very long-term prognosis of patients with malignant uveal melanoma. *Invest Ophthalmol Vis Sci*. 2003;44(11):4651-4659. doi: 10.1167/iovs.03-0538.
13. Chin K, Finger PT, Kurli M, Tena LB, Reddy S. Second cancers discovered by (18)FDG PET/CT imaging for choroidal melanoma. *Optometry*. 2007;78(8):396-401. doi:10.1016/j.optm.2007.03.013
14. Huang B, Law MW, Khong PL. Whole-body PET/CT scanning: estimation of radiation dose and cancer risk. *Radiology*. 2009;251(1):166-174. doi:10.1148/radiol.2511081300
15. Diener-West M, Reynolds SM, Agugliaro DJ, et al. Second primary cancers after enrollment in the COMS trials for treatment of choroidal melanoma: COMS Report No. 25. *Arch Ophthalmol*. 2005;123(5):601-604. doi:10.1001/archopht.123.5.601
16. Rheingold SR, Neugut AI, Meadows AT. Secondary cancers: incidence, risk factors, and management. In: Kufe DW, Pollock RE, Weichselbaum RR, et al., eds. *Holland-Frei Cancer Medicine*. 6th ed. BC Decker; 2003:chap 159. https://www.ncbi.nlm.nih.gov/books/NBK12712/