

Uveal Melanoma in Solid Organ Transplant Recipients

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Introduction

Uveal melanoma is a rare malignancy with a complex aetiology and its occurrence in solid organ transplant recipients is even rarer. It is primarily found in the Caucasian population and is the most common primary intraocular tumor in adults with a mean age-adjusted incidence of 5.1 cases per million per year¹. Tumors are located either in iris (4%), ciliary body (6%), or choroid (90%). The host susceptibility factors for uveal melanoma include fair skin, light eye colour, inability to tan, ocular or oculodermal melanocytosis, cutaneous or iris or choroidal nevus, and BRCA1-associated protein 1 mutation². Most patients with uveal melanoma present with painless loss or distortion of vision (metamorphopsia). Not infrequently, larger tumors will be associated with a serous (fluid) retinal detachment, which causes flashing or flickering of light (photopsia)³. In some cases, the patient will be entirely asymptomatic, and the tumour will be identified on routine ophthalmic screening⁴. Solid organ transplant recipients are at an increased risk of developing various malignancies due to long-term immunosuppressive therapy. The association between solid organ transplantation and cutaneous melanoma is well-established, however reports of uveal melanoma in transplant recipients are scarce. Here, we present a case series of two patients who developed uveal melanoma following kidney transplantation. These cases highlight the importance of close monitoring and heightened vigilance for unusual malignancies in transplant recipients, as well as the need to further elucidate underlying mechanisms and optimal management.

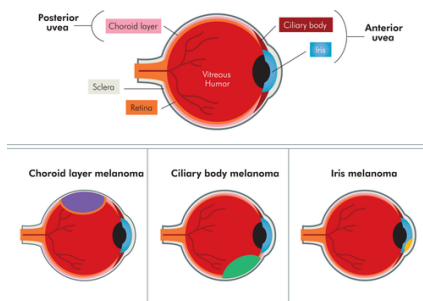


Figure 1. Illustration of the uveal tract.

Case 1

A 46-year-old male, status post kidney transplant thirteen years ago, presented with a decline in visual acuity. He presented in 2019 with a monitored left eye lesion since 2016, accompanied by declining visual acuity noted in early 2019. Clinical examination revealed subretinal fluid, position, and lipofuscin. The lesion size was too small for biopsy initially. By December 2019, the diagnosis was confirmed as left uveal melanoma (choroidal melanoma) located temporally, measuring 12.5 x 10.0 mm with a thickness of 5 mm. Treatment was commenced with photodynamic therapy in March and May 2019, followed by plaque brachytherapy in October 2019 due to insufficient reduction in lesion thickness post-photodynamic therapy. The patient underwent annual follow ups with no evidence of metastasis noted at the last review in December 2023. This case underscores the challenges of managing ocular melanoma in transplant recipients, emphasizing the importance of early detection, tailored treatment strategies, and long-term surveillance to optimize outcomes and prevent metastatic spread.

Case 2

A 64-year-old female, who underwent a renal transplant 24 years prior, presented with a lesion in her left eye that had been under surveillance for seven years, now exhibiting new asymptomatic growth. Her medical history includes cutaneous melanoma, autosomal dominant tubulointerstitial kidney disease (ADTKD) associated with the UMOD gene, and stage 5 chronic kidney disease (CKD). She is maintained on Tacrolimus as an immunosuppressant post-transplant. The lesion, monitored by her optometrist, showed asymptomatic growth. Ophthalmologic evaluation revealed lipofuscin with a thickness greater than 2 mm and subretinal fluid; however, the lesion was too small for a biopsy. She was diagnosed with left uveal melanoma – temporal choroidal melanoma measuring 8.5 mm x 10.5 mm with a thickness of 3 mm. She underwent plaque brachytherapy with favorable results to date, showing no evidence of metastasis at the latest review. She has regular six-month follow-up visits to monitor for disease progression or metastasis. It was determined that the uveal melanoma was not a metastasis of her cutaneous melanoma.

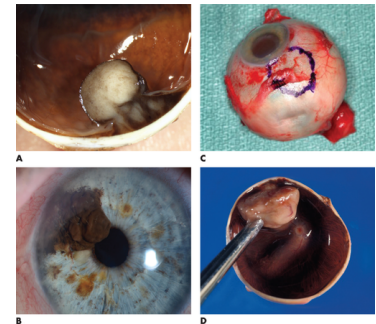


Figure 2. (A) Choroidal melanoma, (B) iris melanoma, (C) a ciliary body gross specimen for orientation, and (D) the same ciliary body melanoma in cross section are shown.²

Discussion

The development of uveal melanoma in solid organ transplant recipients is a rare but concerning phenomenon. The underlying mechanisms contributing to the increased risk of uveal melanoma in this population remain unclear. It is hypothesized that long-term immunosuppressive therapy may play a role in promoting melanoma development by impairing immune surveillance mechanisms. Additionally, the potential contribution of other factors such as viral infections and genetic predisposition warrants further investigation. Despite effective local treatment, the survival rate of uveal melanoma has not changed over a 25-year period⁵. This may well reflect an inability to prevent or treat metastatic disease. Uveal melanoma has a unique biomolecular signature which is quite distinct from that of cutaneous melanoma. While there have been significant improvements in molecular prognostic testing to sub-classify patients, to date, this has not translated into improvements in patient survival^{5,6}.

Outcome and Conclusion

We report two cases of uveal melanoma occurring in kidney transplant recipients, highlighting the need for increased awareness and vigilance for unusual malignancies in this population. Further research is needed to better understand the pathogenesis of uveal melanoma in solid organ transplant recipients and to develop optimal management strategies for these patients.

References

1. Kalki S, Shields CL. Uveal melanoma: relatively rare but deadly cancer. *Eye (Lond)*. 2017 Feb;31(2):241-257. doi: 10.1038/eye.2016.275. Epub 2016 Dec 2. PMID: 27911450; PMCID: PMC5306463.
2. Chattopadhyay C, Kim DW, Gombos DS, Oba J, Qin Y, Williams MD, Esmaili B, Grimm EA, Wargo JA, Woodman SE, Patel SP. Uveal melanoma: From diagnosis to treatment and the science in between. *Cancer*. 2016 Aug 1;121(15):2299-312. doi: 10.1002/encr.29727. Epub 2016 Mar 15. PMID: 26991400; PMCID: PMC567680.
3. Eskelin S, Kovita T. Mode of presentation and time to treatment of uveal melanoma in Finland. *Br J Ophthalmol*. 2002; 86: 333-338.
4. Eagle RC Jr, Grossniklaus HE, Syed N, Hogan RN, Lloyd WC 3rd, Folberg R. Inadvertent excision of eyes containing uveal melanoma. *Arch Ophthalmol*. 2009; 127: 141-145. doi: 10.1093/ptor/ktn031.
5. Curtin JA, Busam K, Pinkel D, Bastian BC. Somatic activation of KIT in distinct subtypes of melanoma. *J Clin Oncol*. 2006 Sep 10;24(26):4340-6. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/16998311>
6. Theraul J, Weitz JA, Hess J, Treiber N, Lissou C, Weisinger SE, et al. Checkpoint inhibition for advanced mucosal melanoma. *Eur J Dermatol*. 2017 Apr 1;27(1):160-165. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28174141>.