



Intraocular plasmacytoma: A case of iris involvement and a review of the literature

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ABSTRACT

Purpose: Describe a case of intraocular plasmacytoma in a patient with multiple myeloma successfully treated with photon irradiation.

Observations: A 61-year-old man with a history of relapsing/refractory multiple myeloma and left frontal bone plasmacytoma treated with monthly belantamab mafodotin salvage chemotherapy developed bilateral treatment-related corneal keratopathy. An iris mass was incidentally noted in the right eye during a follow-up examination. The mass was amelanotic with diffuse intrinsic vasculature involving the pupillary margin from 1:30 to 10:30. Fundus examination showed an irregularly shaped amelanotic superotemporal scleral lesion in the right eye and two smaller amelanotic scleral lesions in the left eye. Given known systemic multiple myeloma and history of left frontal bone plasmacytoma, a presumed diagnosis of iris and scleral plasmacytoma was made. Due to rapid progression of the iris plasmacytoma despite systemic chemotherapy, the patient was treated with 20 Gy photon irradiation to the anterior and posterior segments of both eyes. One month after photon irradiation, there was complete regression of the iris plasmacytoma, and the scleral lesions in both eyes also appeared to be regressing despite systemic progression of multiple myeloma.

Conclusions and importance: Intraocular plasmacytoma is rare and can occur in isolation but typically occurs as a manifestation of systemic multiple myeloma. Intraocular plasmacytoma can be successfully treated with photon irradiation in patients with multiple myeloma who progress on systemic chemotherapy.

1. Introduction

Plasma cell neoplasia is characterized by monoclonal proliferation of plasma cells.^{1,2} While the most common form is multiple myeloma with proliferation of plasma cells in the bone marrow, plasma cell neoplasia can also present as a localized plasmacytoma with extramedullary proliferation or as a combination of both bone marrow and extramedullary involvement.^{1,2} Solitary extramedullary plasmacytoma (SEMP) is a primary plasmacytoma that tends to be locally invasive and does not typically metastasize.¹⁻⁴ Secondary plasmacytoma occurs with multiple myeloma and tends to be more aggressive and prone to metastasis.¹⁻⁴ Plasmacytoma can occur in almost any organ or tissue, but involvement of the eye and its adnexa is rare.¹⁻⁴ Herein, we describe a case of multiple myeloma with secondary intraocular plasmacytoma that was

successfully treated with photon irradiation.

2. Case report

A 61-year-old white man with relapsing/refractory multiple myeloma and a left frontal bone plasmacytoma previously treated with daratumumab, cyclophosphamide, and selinexor started monthly belantamab mafodotin (an antibody-drug conjugate) salvage chemotherapy. Due to the high risk of keratopathy associated with belantamab mafodotin,⁵ the patient underwent regular ocular examinations. Before commencing belantamab mafodotin, best corrected visual acuity (BCVA) was 20/20 in both eyes. Other than pseudophakia bilaterally and a left cranial nerve VI palsy, which was being managed with a Bangerter filter to prevent diplopia, there were no other ocular findings.

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The patient received a total of six once-monthly infusions of belantamab mafodotin over the course of his treatment and developed bilateral belantamab mafodotin-associated keratopathy three weeks after the first infusion which required monitoring with frequent exams and adjustments to the belantamab mafodotin dosing schedule. At his four-month follow-up after commencement of belantamab mafodotin, in addition to keratopathy, an iris mass was noted in the right eye, which prompted referral to the ocular oncology service.

Examination revealed BCVA of 20/20 and 20/40 and intraocular pressures (IOP) of 9 mmHg and 10 mmHg in the right and left eyes, respectively. Slit lamp examination of the right eye showed an amelanotic iris mass with diffuse intrinsic vascularity involving the pupillary margin from 1:30 through 10:30 o'clock (Fig. 1a). By ultrasound biomicroscopy (UBM), the iris was thickened to 1.2 mm (Fig. 1b). Fundusoscopic examination of the right eye revealed an amelanotic, irregularly shaped scleral lesion along the superotemporal arcade measuring 6x4x0.8 mm (Fig. 2a). By optical coherence tomography (OCT), the lesion was deep to the choriocapillaris with a plateau-like contour (Fig. 2c). Given known systemic multiple myeloma and history of left

frontal bone plasmacytoma, the patient was diagnosed with presumed iris and scleral plasmacytoma in the right eye. The patient was asymptomatic other than ongoing photophobia from belantamab mafodotin-induced keratopathy. After discussion, he elected close observation for stability or improvement on systemic belantamab mafodotin.

Two months later, the iris plasmacytoma increased in size with dense amelanotic infiltration around the entire pupillary margin, numerous tortuous intrinsic vessels, and anterior chamber cells (Fig. 1c). Iris thickness by UBM had increased to 1.4 mm (Fig. 1d). The right scleral lesion remained stable but two new, small amelanotic scleral lesions were found in the left eye along the superotemporal arcade, measuring approximately 2x2x0.8 mm and 1x1x0.8 mm (Fig. 2b). By OCT, the lesions were dome-shaped and deep to the choriocapillaris (Fig. 2d). Repeat MRI of the brain and orbits was obtained, which showed near complete resolution of the left frontal bone plasmacytoma but new enhancing masses along the posterior lateral walls of the right and left maxillary sinuses suspicious for multiple myeloma. He was referred to radiation oncology and was treated with 20 Gy in 10 fractions using a 3D technique 6X photon irradiation with MRI image fusion. The treated

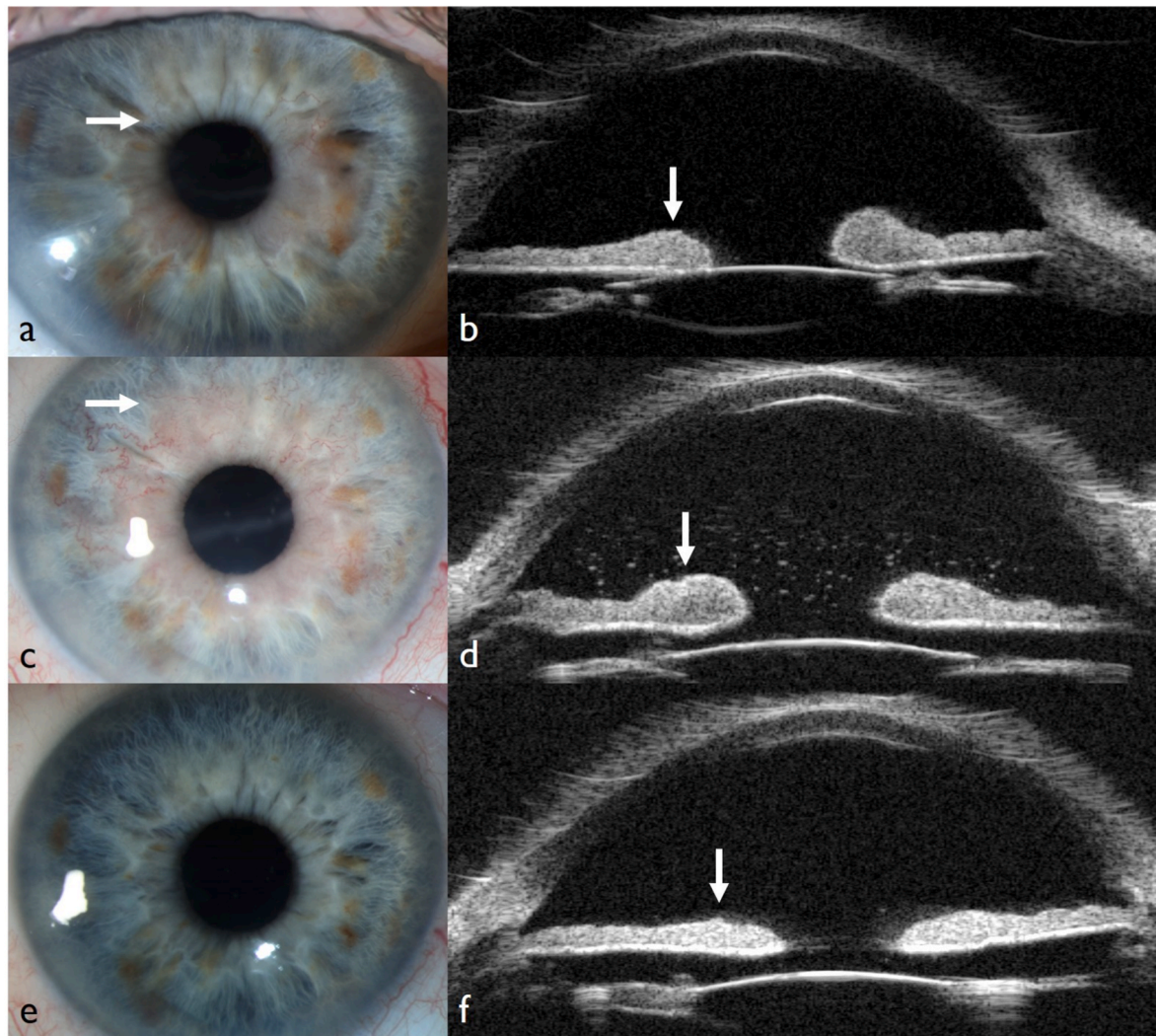


Fig. 1. Iris plasmacytoma managed with photon irradiation. A 61-year-old man presented with (a) amelanotic iris infiltration with diffuse intrinsic vascularity involving the pupillary margin from 1:30 to 10:30 (10:30 transition from tumor to normal iris denoted by white arrow), and (b) iris thickness of 1.2 mm by ultrasound biomicroscopy (UBM) (minimally involved 10:30 area denoted by white arrow). Despite systemic belantamab mafodotin therapy, the iris plasmacytoma progressed (c) to involve 360 degrees of the pupillary margin with numerous, tortuous intrinsic vessels and anterior chamber cellular infiltration (progression marked by white arrow). (d) Maximum iris thickness increased to 1.4 mm (white arrow) with anterior chamber cell visualized on UBM. One month after 20 Gy photon irradiation (e) there was complete regression of the iris plasmacytoma with resolution of anterior chamber cell and (f) return to normal iris thickness of 0.9 mm by UBM (white arrow).

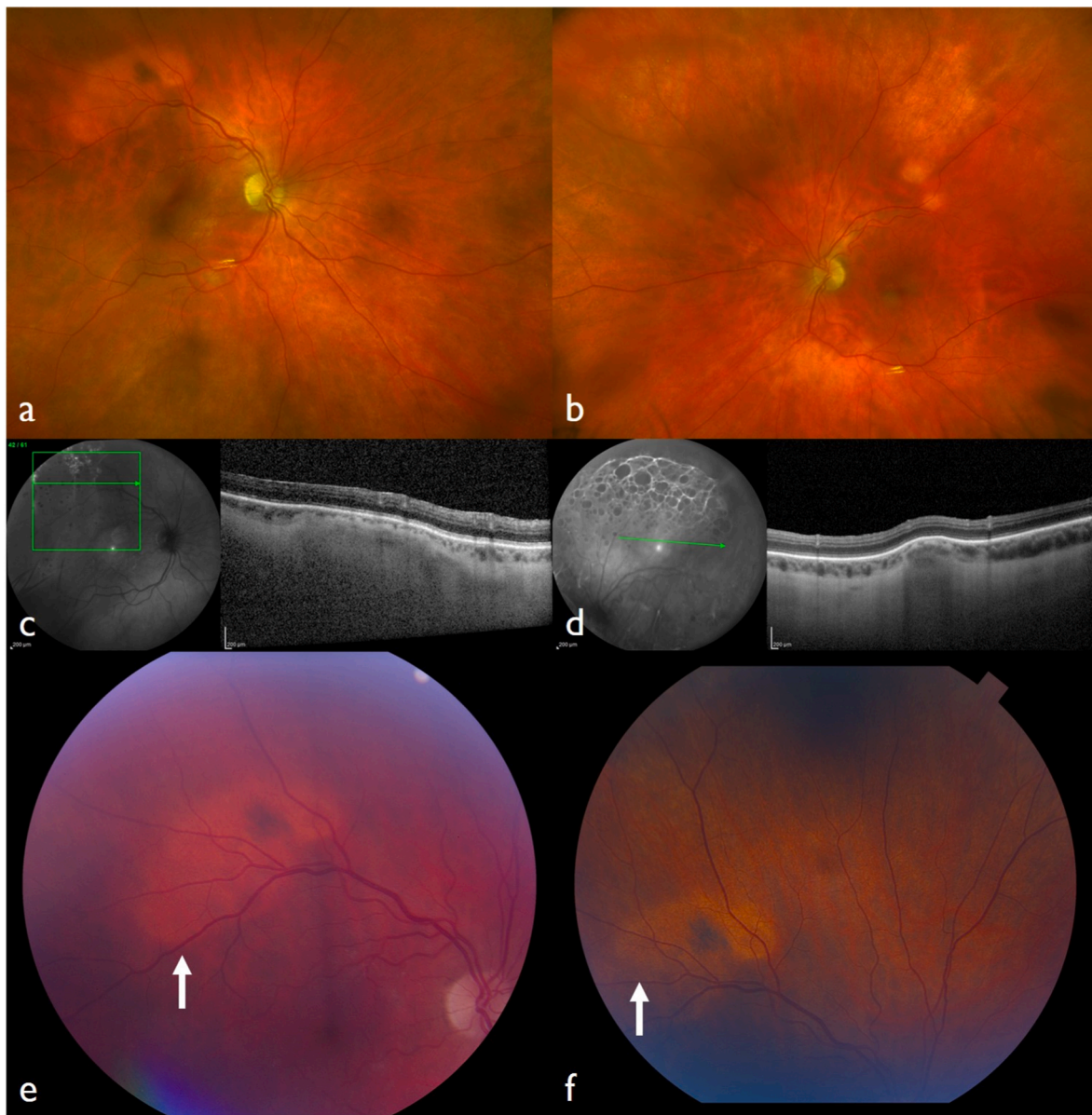


Fig. 2. Presumed scleral plasmacytoma. A 61-year-old male presented with (a) an amelanotic, irregularly shaped deep lesion along the superotemporal arcade in the right eye measuring 6x4x0.8 mm. Two months later (b) in the left eye there were two new, small amelanotic scleral lesions along the superotemporal arcade, measuring approximately 2x2x0.8 mm and 1x1x0.8 mm. By optical coherence tomography (OCT), the lesions in the (c) right and (d) left eyes were dome-shaped and deep to the choriocapillaris. Given known systemic multiple myeloma and systemic plasmacytoma, these lesions were suspicious for scleral plasmacytoma. Compared with (e) pretreatment color fundus photography, (f) three months after photon irradiation, the temporal margin of the scleral lesion in the right eye appeared to be regressing. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

volume encompassed the disease in the maxillary sinuses as well as the entirety of both globes to treat the iris and scleral lesions.

One month after photon irradiation, BCVA improved to 20/20 and 20/25 due to improved keratopathy, and IOP was 9 and 11 in the right and left eyes, respectively. The iris plasmacytoma had completely regressed (Fig. 1e) with normal iris thickness of 0.9 mm on UBM (Fig. 1f). The scleral lesions in both eyes also appeared to be regressing, with an early atrophic appearance and stable basal diameter. Three months after treatment, despite complete regression of iris plasmacytoma and partial regression of the scleral lesions (Fig. 2e and f), widespread systemic disease progression on belantamab mafodotin necessitated a change in therapy to liposomal pegylated doxorubicin.

3. Discussion

This case illustrates a patient with multiple myeloma diagnosed with presumed iris and scleral plasmacytoma successfully treated with photon irradiation. Plasmacytoma involving the eye, surrounding adnexa, and orbit is rare with few reported cases of intraocular plasmacytoma in the literature. A PubMed keyword search conducted July 2021 for plasmacytoma/multiple myeloma and iris, ciliary body, choroid, uvea, intraocular, or eye, revealed 16 cases of intraocular plasmacytoma (Table 1). Of all 17 cases, including the case reported here, mean patient age was 58 (range 35–82) years. Ten (59%) patients, including the patient presented here, had underlying systemic multiple myeloma with secondary plasmacytoma, and the other 7 (41%) patients had SEMP. Tumor involved the choroid only in 8 (47%) cases, iris and ciliary body in 3 (18%) cases, iris, ciliary body and choroid in 2 (12%)

Table 1
Literature review of intraocular plasmacytoma.

| Age | Sex (M/F) | Race (if known) | MM (Y/N) | Area(s) of intraocular involvement | Biopsy Proven (Y/N) | Ocular Treatment | Systemic Treatment | Follow up duration | Outcome |
|-------------------------------|-----------|-----------------|----------|--|---------------------|---|--|--------------------|--|
| ^a 61 | M | White | Y | Iris, Sclera | N | Photon irradiation (20 Gy) | Chemotherapy | 2 months | Ocular tumor regression. Systemic MM progression. |
| 59 ¹⁷ | M | N/A | N | Iris, Ciliary body | Y | Enucleation for secondary glaucoma | N/A | 3 years | Ocular tumor regression. No evidence of MM. |
| 45 ¹³ | M | White | Y | Choroid | Y | External beam radiation (20 Gy) | Chemotherapy, bone marrow transplant, radiotherapy | 8 months | Ocular tumor recurrence. Deceased from complications of MM. |
| 44 ¹² | F | White | N | Iris | Y | Ruthenium plaque radiotherapy (40 Gy) | N/A | 4 years | Ocular tumor regression. No evidence of MM. |
| 35 ¹⁴ | F | N/A | Y | Choroid | Y | Intravitreal chemotherapy | Chemotherapy, bone marrow transplant | 4 months | Ocular tumor regression. No reported follow up on systemic MM. |
| 59 ¹⁵ | F | N/A | Y | Iris, Ciliary body, Choroid | N | Intravitreal chemotherapy | Chemotherapy, bone marrow transplant | 7 months | Ocular tumor regression. Systemic improvement. |
| 61 ⁶ | F | N/A | N | Iris, Ciliary body, Choroid (collision tumor with ciliochoroidal melanoma) | Y | External beam radiation (53 Gy), secondary enucleation for neovascular glaucoma | N/A | 6 years | Ocular tumor regression. No evidence of MM. |
| 82 ⁷ | F | White | Y | Iris, Ciliary body | N | Palliative external beam radiation for secondary glaucoma (6 Gy) | No longer on systemic treatment | 1 month | Deceased from complications of MM. |
| 61 ¹⁰ | M | White | Y | Choroid | Y | External beam radiation (35 Gy) | Chemotherapy, bone marrow transplant, radiotherapy | N/A | Ocular tumor regression. Systemic improvement. |
| 55 ¹¹ | F | White | N | Iris, Ciliary body | Y | Custom plaque radiotherapy (40 Gy) | N/A | 3 years | Ocular tumor regression. No evidence of MM. |
| 44 ⁹ | F | N/A | Y | Choroid | N | Iodine plaque radiotherapy (80 Gy) | Oral dexamethasone | 2 months | Ocular tumor regression. Systemic improvement. |
| 76 ⁸ | F | N/A | N | Choroid | Y | External beam radiation (35 Gy) | N/A | 9 years | Ocular tumor regression. No evidence of MM. |
| 63 ¹⁶ | M | N/A | Y | Choroid | Y | N/A | Chemotherapy, radiotherapy | 1 month | Deceased from complications of MM. |
| 67 ⁴ | M | N/A | Y | Iris | Y | N/A | Chemotherapy | 6 months | Deceased from complications of MM. |
| ^b 57 ²² | M | White | Y | Choroid | Y | N/A | N/A | N/A | N/A |
| ^b 58 ²² | F | White | N | Ciliary body | Y | N/A | N/A | N/A | N/A |
| 54 ¹⁸ | M | N/A | N | Choroid | Y | Enucleation for secondary glaucoma | N/A | N/A | N/A |

Abbreviations: M = male, F = female, MM = multiple myeloma, Y = yes, N = no.

Plaque radiotherapy doses are given as the apex dose.

^a This is the case being reported.

^b Age at death.

cases, iris only in 2 (12%) cases, ciliary body only in 1 (6%) case, and iris with presumed scleral involvement in the 1 (6%) case detailed in this report. In one previously reported case, plasmacytoma was discovered as a collision tumor with plasmacytoma and ciliochoroidal melanoma occurring together in the iris, ciliary body, and choroid.⁶ Diagnosis was biopsy-proven in 13 (76%) cases and presumptive in 4 (24%) cases with underlying multiple myeloma, including the case presented here.

Patients were treated with radiotherapy in 9 (53%) cases using either plaque (n = 3), external beam (n = 5), or, in the present case, photon irradiation (n = 1), with concomitant systemic chemotherapy in 1 (6%) previously reported case.⁶⁻¹³ Of the 9 cases treated with radiotherapy, good local tumor regression was observed after radiotherapy without further treatment in 7 (77%) cases, including the case presented here.^{6,8-12} One of these cases was that of the collision tumor, which was originally irradiated for ciliochoroidal melanoma and required subsequent enucleation for neovascular glaucoma.⁶ In the case presented in this report, while our patient demonstrated ocular tumor regression on

follow-up, progression of systemic multiple myeloma necessitated a change in the systemic chemotherapy regimen. Two of the 9 (22%) cases did not demonstrate tumor regression after irradiation. Both patients died of multiple myeloma-associated complications shortly after treatment with one demonstrating ocular tumor recurrence after treatment and the other having external beam radiation as a palliative but not curative treatment for management of secondary glaucoma.^{7,13} The remaining patients were treated with intravitreal and systemic chemotherapy (n = 2, 12%),^{14,15} systemic chemotherapy alone (n = 2, 12%),^{4,16} or primary enucleation for secondary glaucoma (n = 2, 12%).^{17,18} The two patients that were treated with intravitreal and systemic chemotherapy demonstrated ocular tumor regression.^{14,15} The two patients that were treated with systemic chemotherapy alone expired within 6 months of ocular tumor detection from complications associated with multiple myeloma.^{4,16} For the 5 (29%) cases that presented with SEMP and had reported follow-up, there was no evidence of development of multiple myeloma after mean follow-up of 5 years

(range 3–9 years).^{6,8,11,12,17} For the 8 (47%) patients with multiple myeloma and reported follow-up, 4 (50%) patients died from multiple myeloma-associated complications, 3 (38%) patients had systemic disease improvement with treatment, and our case had systemic disease progression with local ocular tumor regression.^{4,7,9,10,13,15,16}

Approximately 7% of patients diagnosed with multiple myeloma have concomitant extramedullary plasmacytoma at presentation, with an additional 6% developing extramedullary plasmacytoma later in the course of their disease.^{19,20} Although ocular involvement is rare, a presumptive diagnosis can be made in cases with known multiple myeloma in the context of compatible clinical exam findings, typically amelanotic infiltration of the uveal tissue which can show intrinsic vascularity. In patients without known systemic multiple myeloma, biopsy is important to confirm the diagnosis of plasmacytoma, and subsequent workup should be undertaken to rule out concomitant systemic disease. In our patient with known multiple myeloma and a history of plasmacytoma, presumptive secondary intraocular plasmacytoma was discovered during required screening for belantamab mafodotin-associated corneal toxicity. Because intraocular plasmacytoma can be asymptomatic or other aspects of systemic disease may take priority, required corneal toxicity screening exams with this new class of medications could disclose a higher incidence of ocular involvement in multiple myeloma than has been previously recognized. Furthermore, in the setting of possible posterior segment involvement, a dilated eye examination may also be prudent at the time of initial belantamab screening and at subsequent visits if the patient develops new ocular symptoms.

While systemic chemotherapy is the mainstay of treatment for multiple myeloma, definitive radiation therapy may be curative in extramedullary plasmacytoma and is the standard treatment for solitary plasmacytoma according to international guidelines.²¹ Local radiotherapy is used in conjunction with systemic treatment for secondary plasmacytoma in patients with multiple myeloma. Our literature search found 9 patients, including the case presented here, with intraocular plasmacytoma managed with radiotherapy,^{6,8–12} of whom 7 had a favorable treatment response, including 3 cases in patients with underlying multiple myeloma. Compared with prior plaque or external beam radiotherapy, our case was uniquely managed with photon irradiation with prompt and complete ocular tumor regression.

In summary, we present a case of presumed iris and scleral plasmacytoma secondary to multiple myeloma, which was diagnosed during follow-up examination for belantamab mafodotin-associated keratopathy. Due to rapid tumor progression while on systemic chemotherapy, the patient was managed with local low dose photon irradiation with complete iris tumor regression. This case serves to illustrate that local radiotherapy can control extramedullary plasmacytoma in patients with multiple myeloma who progress on systemic chemotherapy. Clinicians should keep in mind that some patients with intraocular plasmacytoma may initially be asymptomatic, and future work should investigate whether required ophthalmology screening for new systemic multiple myeloma treatments discloses a higher incidence of secondary intraocular plasmacytoma by capturing asymptomatic cases.

Patient consent

The patient consented to publication of the case in writing.

CRediT author statement

Kafayat Oyemadé: Investigation, Writing – Original draft, Writing – Review & Editing. **Scott Stafford:** Writing – Review & Editing. **Morie Gertz:** Writing – Review & Editing. **Sanjay Patel:** Writing – Review & Editing. **Keith Baratz:** Writing – Review & Editing. **Lauren Dalvin:** Conceptualization, Methodology, Writing – Review & Editing.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

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