Case Report

Taiwan J Ophthalmol 2023;13: 548-551

Access this article online

Quick Response Code:

Website: http://journals.lww.com/TJOP

DOI: 10.4103/2211-5056.360046

Sympathetic ophthalmia following radiation-induced scleral necrosis in choroidal melanoma

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Abstract:

Sympathetic ophthalmia (SO) is a bilateral granulomatous panuveitis. We report a rare case of SO presenting after scleral necrosis as a late complication of Gamma Knife radiotherapy for choroidal melanoma. A 55-year-old woman presented with primary choroidal melanoma in the right eye and has been treated with Gamma Knife radiotherapy with stable tumor size. Five years after radiotherapy, a pigmented protrusive uveal mass was visibly noted over the superior sclera of the same eye, corresponding to periocular soft tissue enhancement on computed tomography. Biopsies of the pigmented mass showed the absence of malignancy. One month later, acute blurred vision with signs of sympathetic ophthalmia developed in the left eye. The patient received high-dose systemic corticosteroids and immunomodulatory therapy. The intraocular inflammation in the left eye subsided with improving vision, and the uveal mass in the right eye flattened after the anti-inflammatory therapy. Scleral necrosis is a rare complication following radiotherapy for choroidal melanoma and may incite sympathetic ophthalmia, for which prompt and aggressive treatment is important to save vision, especially for the fellow eye.

Keywords:

Choroidal melanoma, Gamma Knife radiotherapy, orbital, radiation-induced scleral necrosis, sympathetic ophthalmia, tumor

Introduction

Sympathetic ophthalmia (SO) is a rare bilateral granulomatous panuveitis characterized by autoimmune hypersensitivity directed against the antigen of uveal or retinal tissue, which usually follows penetrating ocular injury or intraocular surgery.[1,2] Primary choroidal melanoma rarely initiates SO.[3,4] Although enucleation is the conventional treatment and has been preferred for large choroidal melanoma, many eyeball-conserving therapies including local excision, radiotherapy (e.g., Gamma Knife, charged-particle external beam radiation, and plaque radiation therapy), photocoagulation, and transpupillary thermotherapy have been reported to treat median-to-small–sized lesions.[5] Several case reports have indicated the uncommon association between SO and radiotherapy for choroidal melanoma.[6-8]

Herein, we report a case of SO presenting 5 years after radiotherapy for choroidal melanoma. Orbital pseudotumor, also termed nonspecific orbital inflammation, was present in the eye with choroidal melanoma postradiotherapy. Scleral necrosis underneath the presumed orbital pseudotumor developed and subsequently incited SO. Written permission was obtained from the reported subject for granting consent to share her information and ophthalmic images for publication.

Case Presentation

A 55-year-old woman experienced progressive blurred vision and black shadow in the right

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Submission: 16-06-2022
Accepted: 24-08-2022
Published: 31-10-2022

How to cite this article: Chen YC, Chao YJ, Tsai CC, Chen SJ, Hwang DK. Sympathetic ophthalmia following radiation-induced scleral necrosis in choroidal melanoma. Taiwan J Ophthalmol 2023;13:548-51.

eye. A blackish bulging mass beneath the temporal retina with serous retinal detachment was observed. B-scan ultrasonography showed an intraretinal tumor with high internal echogenicity, measuring 21 mm × 12 mm in size [Figure 1a], which, on contrast-enhanced magnetic resonance imaging (MRI), presented as a heterogenous hyperintense orbital mass originating from the ocular wall, extending into ocular cavity [Figure 1b]. Primary choroidal melanoma was then diagnosed. After serious discussion with the patient and family, regional Gamma Knife radiotherapy was performed to treat melanoma. Hyphema and serous retinal detachment developed after radiotherapy, so multiple times of intravitreal injection of anti-vascular endothelial growth factor agents were given. Although vision in the right eye has gradually declined to no-light perception due to persistent hyphema and diffuse atrophy of the outer retina, the size of the melanoma has shrunk without any recurrence or local orbital complication.

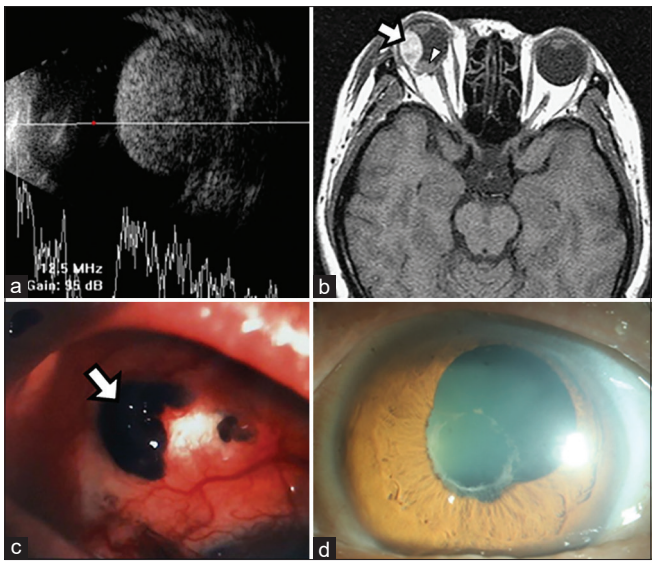

Figure 1: A 55-year-old woman with sympathetic ophthalmia initially presented as an orbital pseudotumor and radiation-induced scleral necrosis after Gamma Knife radiotherapy for choroidal melanoma. Initial presentation of the choroidal melanoma as shown in (a) B-scan ultrasonography and (b) T1-weighted contrast-enhanced magnetic resonance imaging (arrow: the lesion of the choroidal melanoma; arrowhead: serous retinal detachment). (c) A dark, pigmented, and protrusive mass was seen over the right eye sclera 5 years after Gamma Knife radiotherapy for the choroidal melanoma (arrow). (d) Anterior chamber inflammation in the left eye abruptly occurred 1 month after appearance of the right scleral mass

Five years later, a pinkish elevated conjunctival mass was mentioned over superior-temporal quadrant of the right eye [Figure 2a], which correlated with the hyperintense orbital soft tissue mass measuring 18 mm in diameter and 6 mm in thickness on computed tomography (CT) without intraocular melanoma recurrence [Figure 3a]. Under close monitoring, the patient reported mild right orbital pain, and a dark, irregular, pigmented, protrusive mass was noticed at the previous superior-temporal elevated conjunctiva of the right eye 4 months later [Figures 1c and 2b]. Although it gradually enlarged and protruded, two sequential incisional biopsies of the pigmented mass showed epithelioid melanocytes in conjunctival tissue, melanin pigments admixed with granulation tissues and inflammatory cells, and negative staining of HMB-45 and melan-A, excluding the possibility of extraocular melanoma extension [Figure 4]. Whole-body positron emission tomography/CT scan did not show any distant metastasis of the melanoma.

Unfortunately, acute onset of blurred vision in the left eye developed 1 month after the appearance of the right pigmented mass. The vision was 6/8.6 in the left eye. Examination of the left eye showed congested conjunctiva, corneal edema, 1+ of anterior chamber cells and 1+ of flares, posterior synechiae of the iris, 1+ of anterior vitreous cells, absence of keratic precipitates [Figure 1d], and grade 0.5

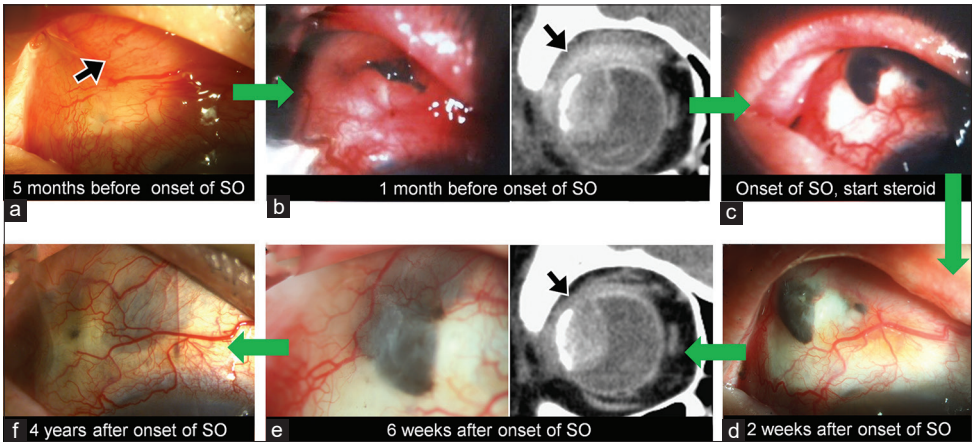

Figure 2: Serial changes of the right orbital pseudotumor and protrusive uveal mass before and after systemic steroid pulse therapy for sympathetic ophthalmia. (a) An extensive pinkish elevated mass was seen at superior-temporal quadrant of the conjunctiva five months before the onset of sympathetic ophthalmia (black arrow). (b) Scleral necrosis with uveal tissue protrusion developed at the thinned sclera, while the computed tomographic scan showed a more extensive orbital pseudotumor (black arrow). (c) With more bulging of the uveal mass, sympathetic ophthalmia was incited in both eyes. (d) After high-dose steroid therapy, the uveal mass flattened with conjunctival tissue growing over its surface. (e) Six weeks after onset of sympathetic ophthalmia, the computed tomographic scan showed shrinking orbital pseudotumor (black arrow) and a silent, smooth uveal tissue beneath the thinned sclera was seen. (f) Four years later, conjunctival epithelialization and vessels growth were noticed over the previous scleral perforation site

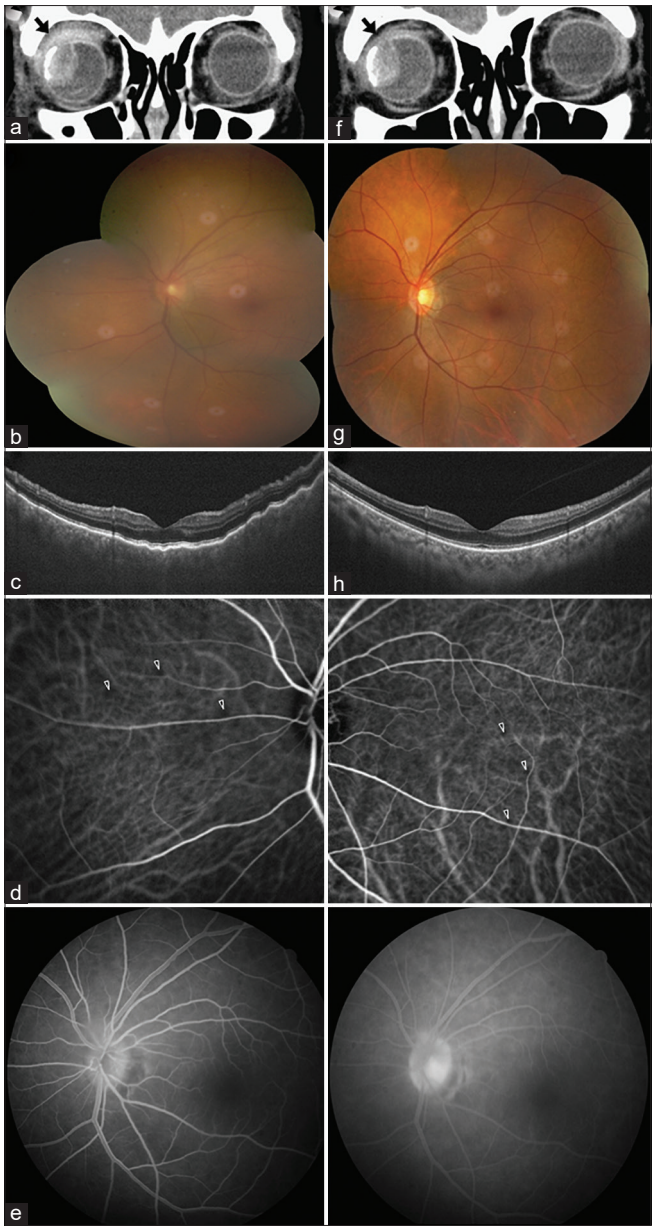

Figure 3: Changes of fundus and orbital tumor size before and after treatment of sympathetic ophthalmia. (a) Contrast-enhanced computed tomography revealed a hyperintense orbital mass (black arrow). In addition, the right eye choroidal melanoma with intraocular extension and calcification was shown, which remained unchanged in size after radiotherapy. (b) Sympathetic ophthalmia of the left eye presented with vitreous haze, choroidal thickening, and folding (c) 4 months after the onset of the right orbital mass. (d) The early signs of sympathetic ophthalmia were multiple areas of hypofluorescence (arrowheads; left image: area nasal to the disc, right image: area temporal to the disc) on indocyanine green angiography, while fluorescein angiography (e) showed disc staining without significant pinpoint leakage of the left eye (left image: early phase; right image: late phase). (f) The soft tissue enhancement of the right orbital mass markedly regressed after high-dose steroids therapy (black arrow), accompanied with resolution of signs of sympathetic ophthalmia (g and h), and the final vision of the left eye was 6/6

of vitreous haze without significant chorioretinitis lesion [Figure 3b], while the pigmented mass of the right eye protruded more extensively [Figure 2c]. Optical coherent tomography (OCT) of the left macula disclosed choroidal folding and thickening without

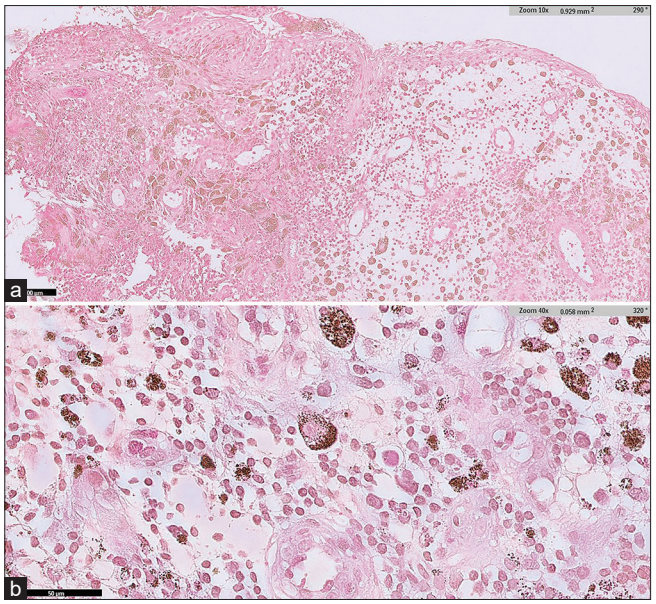

Figure 4: The histologic examination of the dark, pigmented, protrusive mass. (a) Bleach section showed epithelioid melanocytes with nucleoli in conjunctival tissue. (b) Abundant melanin pigments admixed with inflammatory cells and granulation tissues were shown in a high-power magnification view (×40). The histologic images exclude the possibility of local melanoma recurrence

intraretinal edema or subretinal fluid [Figure 3c]. Fluorescein angiography and indocyanine green angiography (ICG) showed dye leakage from optic disc and multiple hypofluorescent dark spots, respectively, but there was no significant retinal vessel leakage or dye pooling [Figure 3d and e]. The laboratory workups were all negative for systemic rheumatic or infectious diseases (e.g., sarcoidosis, syphilis, or tuberculosis).

SO was diagnosed based on the clinical presentations in its early stage (i.e., no significant vessel leakage and subretinal fluid), and intravenous steroid pulse therapy (methylprednisolone 1 g/day) had been administered for 3 days, followed by oral prednisolone in a gradually tapering schedule. Methotrexate 12.5 mg per week was also prescribed. The right orbital hyperintense soft tissue mass on CT scan markedly decreased in size [Figure 3f], and the pigmented mass also flattened at the slit lamp [Figure 2d-f] after systemic anti-inflammatory therapy. All signs of intraocular inflammation in the left eye subsided with choroidal contour and thickness returning normal on OCT [Figure 3g and h]. Vision in the left eye recovered to 6/6. The systemic corticosteroids and immunomodulatory therapy were tapered and discontinued 10 months after the onset of SO. No recurrence of uveitis or choroidal/orbital mass was noticed in both eyes during the last 4-year follow-up.

Discussion

In this case report, we present a case of SO with the initial presentation of orbital pseudotumor and

radiation-induced scleral necrosis (RISN). We believed that the exposed orbital melanin-containing mass in the right eye was actually the protrusive uveal tissue as a late complication of focal sclera perforation after Gamma Knife radiotherapy due to the absence of malignant cells noticed by biopsies. The protrusive uveal tissue, which originated from the weakest point of scleral thinning underneath the more extensive distribution of the orbital pseudotumor, incited SO in the left eye. Choroidal inflammation, thickening, and effusion presumably caused the uveal tissue in the right eye to enlarge and protrude even more from the sclera defect. Both vision and inflammatory signs improved in the left eye with SO after intensive steroids, in addition to flattening of the right uveal tissue and shrinking right orbital lesion on CT scan.

Choroidal melanoma may incite SO by extraocular tumor extension, intraocular surgery involving melanoma excision, or an undetected ocular penetrating wound.[3,4,9] Radiation-induced uveal tissue disruption after proton beam, helium ion irradiation, or ruthenium plaque brachytherapy, leading to autosensitization against uveal or retinal antigens, could rarely cause SO.[6-8,10] RISN is a rare and usually asymptomatic complication following radiation for choroidal melanoma, which may be caused by the local destructive effect of cytotoxic elements released from adjacent melanoma after radiation, and is characterized as fibrocyte reduction, collagen bundle swelling, and sclera melting.[11,12] To minimize the risk of tumor seeding, incisional biopsies of the protrusive uveal tissue were undertaken by cutting small pieces of the mass without disturbing its structural integrity. Therefore, RISN was a clinical diagnosis in this case and presumably led to SO.

Although the eyeball was preserved with Gamma Knife radiotherapy, the vision still cannot be maintained due to the early complications, such as hyphema and serous retinal detachment. The patient subsequently suffered from SO which affected the fellow eye 5 years after radiotherapy. Classical signs of SO include active anterior chamber inflammation, mutton fat keratic precipitates, and vitreous inflammation. Other fundus findings such as choroiditis, optic disc swelling, serous retinal detachment, and Dalen–Fuchs nodules may be present. Due to the frequent follow-ups and close monitoring of the right orbital pseudotumor and RISN, the onset of SO was detected early in the course of the disease, with the presentation of the mild-to-moderate anterior chamber and vitreous inflammation, choroiditis, hypofluorescent dark spots on ICG, and mildly decreased vision of the left eye.

We believe that all benefits and risks of each therapeutic option for melanoma should be discussed before making treatment decisions. Besides, clinicians should pay attention to this rare but vision-threatening complication in patients with any type of ocular or intraocular tumor after regional radiotherapy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Data availability statement

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Financial support and sponsorship

Nil.

Conflicts of interest

Prof. Chieh-Chih Tsai, Prof. Shih-Jen Chen and Prof. De-Kuang Hwang, an editorial board members at *Taiwan Journal of Ophthalmology*, had no roles in the peer review process of or decision to publish this article. The other authors declared no conflicts of interest in writing this paper.

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