

CASE REPORT

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Multimodal imaging of tumour-related lipid exudation and exudative retinal detachment following brachytherapy in choroidal melanoma

Elena Ros-Sanchez^{1*}, David Oliver-Gutierrez^{1,2}, Paul Buck¹, Tetiana Goncharova-Simón¹, Marta Garrido-Marín¹, Miguel Ángel Zapata-Victori¹ and Anna Boixadera¹

Abstract

Background Choroidal melanoma is the most common primary intraocular malignancy, accounting for 90% of all uveal melanomas. Although radiation therapy (brachytherapy, proton beam and gamma knife) is a standard and effective treatment for choroidal melanomas, it carries a risk of vision-threatening complications such as cataract, optic neuropathy, and radiation retinopathy. A lesser-known complication is tumor-related lipid exudation (TRLE), characterized by subretinal and intraretinal lipid accumulation following radiotherapy, potentially resulting from radiation-induced vasculopathy and increased vascular permeability.

Case report We report a case of a 61-year-old man with a long-standing choroidal nevus under observation for 15 years. Due to signs of growth and subretinal fluid detected on OCT, malignancy was suspected, and Ruthenium-106 brachytherapy was performed. One-month post-treatment, the patient developed progressive exudative retinal detachment with lipid exudation, despite preserved visual acuity. At the nine-month follow-up, worsening exudation and tumor growth were observed, prompting a second brachytherapy session and intravitreal aflibercept injections every eight weeks, leading to complete resolution of lipid exudation and restoration of retinal anatomy. Six months post-treatment, the tumor remained flat, and visual acuity improved to 20/20.

Conclusions TRLE is an underrecognized complication of radiation therapy for choroidal melanoma, with risk factors including pre-radiotherapy subretinal fluid, increased tumour thickness, and Bruch's membrane rupture. Studies suggest that anti-VEGF therapy may help mitigate exudative complications; however, its efficacy remains uncertain. This case highlights the importance of recognizing TRLE as a potential complication of brachytherapy and underscores the critical role of multimodal imaging in early diagnosis and monitoring, ensuring optimal treatment outcomes for patients with choroidal melanoma.

Keywords Choroidal melanoma, Multimodal imaging, Radiotherapy, Brachytherapy, Tumor-related lipid exudation, Case report

*Correspondence:
Elena Ros-Sanchez
elena.rs9@gmail.com

¹Ophthalmology, Hospital Universitari Vall d'Hebron, Passeig de la Vall d'Hebron 129, Barcelona 08035, Spain

²Ophthalmology, Innova Ocular Verte Barcelona, Barcelona, Spain



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Background

Choroidal melanoma is a life-threatening malignancy, comprising 90% of all uveal melanomas. It predominantly affects Caucasians, with a mean age at diagnosis of 60 years. Major risk factors include fair skin, light-coloured eyes, and intermittent ultraviolet exposure [1, 2]. A choroidal nevus, present in 4% of Caucasians, is a significant precursor. DeSimone et al. identified several predictive features of malignant transformation, summarized in the mnemonic “To Find Small Ocular Melanoma Doing Imaging,” including tumour thickness > 2 mm, subretinal fluid, symptoms, orange pigment, melanoma hollow, and diameter > 5 mm [3].

Treatment is tailored to tumour characteristics and patient factors, with radiotherapy being a standard approach for posterior uveal melanomas. Although effective, all forms of radiation, including brachytherapy, proton beam and gamma knife, are associated with potentially sight-threatening complications. These include anterior segment pathology, radiation-induced cataract (8–83% at 5 years), optic neuropathy (16%), and radiation retinopathy (10–63%, mean onset 25.6 months) [4, 5].

A lesser-known but clinically relevant complication of radiation therapy is ‘tumour-related lipid exudation’ (TRLE), characterized by intraretinal or subretinal lipid accumulation with variable degrees of fluid exudation from the irradiated tumour [6].

We present a case report of TRLE following brachytherapy for choroidal melanoma, emphasizing the critical role of multimodal imaging in diagnosing and managing this rare complication.

Case presentation

A 61-year-old man was referred to the Retina Department due to signs of growth and potential malignant transformation of a choroidal nevus into choroidal melanoma. He had been under follow-up for this nevus for the past 15 years. His systemic history included a colon neoplasm treated five years prior, with complete remission, and type 2 diabetes mellitus with good systemic control. His best-corrected visual acuity (BCVA) was 20/20 in both eyes. The patient was asymptomatic and attended routine check-ups.

On examination, the anterior segment was unremarkable. Right eye fundoscopy showed no abnormalities. Left eye fundoscopy revealed a superior-temporal amelanotic choroidal nevus measuring 7.5 × 5.2 in base and 2.5 mm in height. Optical coherence tomography (OCT) showed the presence of subretinal fluid (Fig. 1). Observation was decided. At the six month- follow-up visit, tumour growth was observed both on fundoscopy and B-scan ultrasonography, with new dimensions of 9 × 8.66 in base and 3.52 mm in height, with persistent subretinal fluid (Fig. 2). Given these findings suggestive of malignancy suspecting

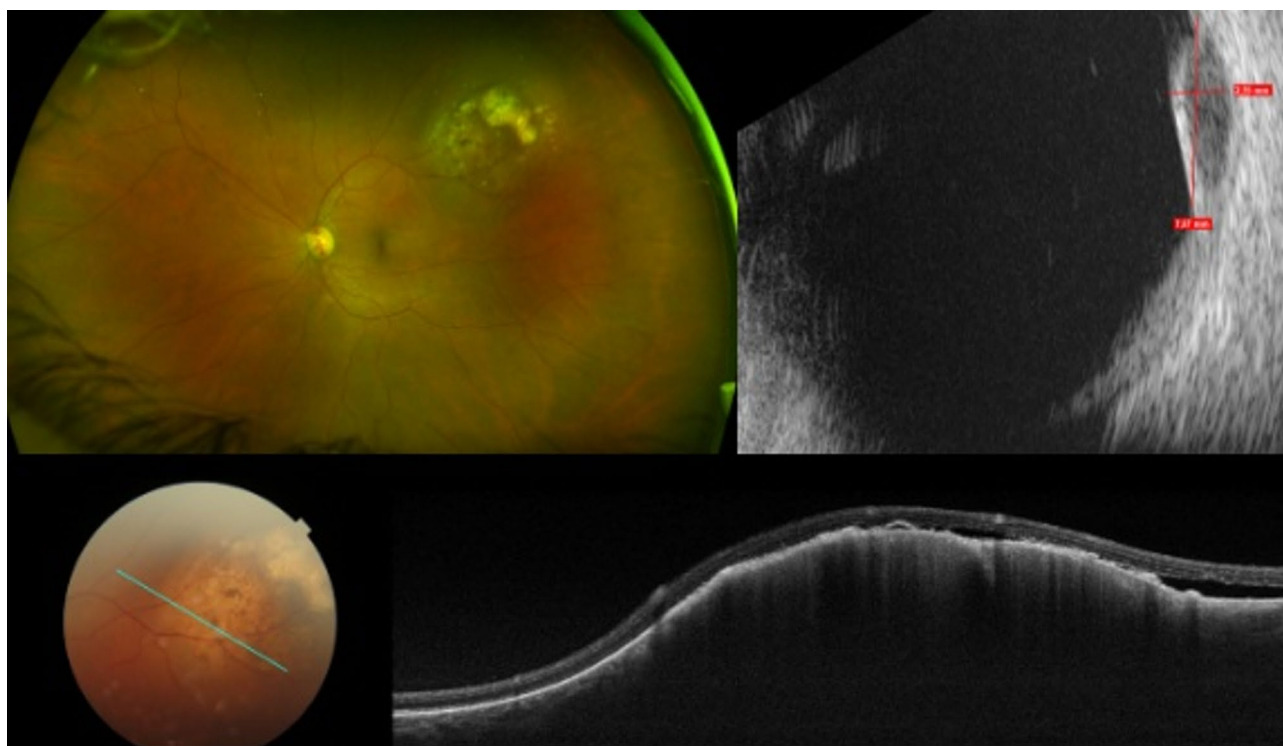


Fig. 1 Left eye retinography showing an amelanotic choroidal nevus in the supero-temporal region. Left eye ultrasound shows an extension of 7.67 × 5.2 mm in base and 2.55 mm in height with melanoma hollow. OCT shows the choroidal nevus with associated subretinal fluid at its base

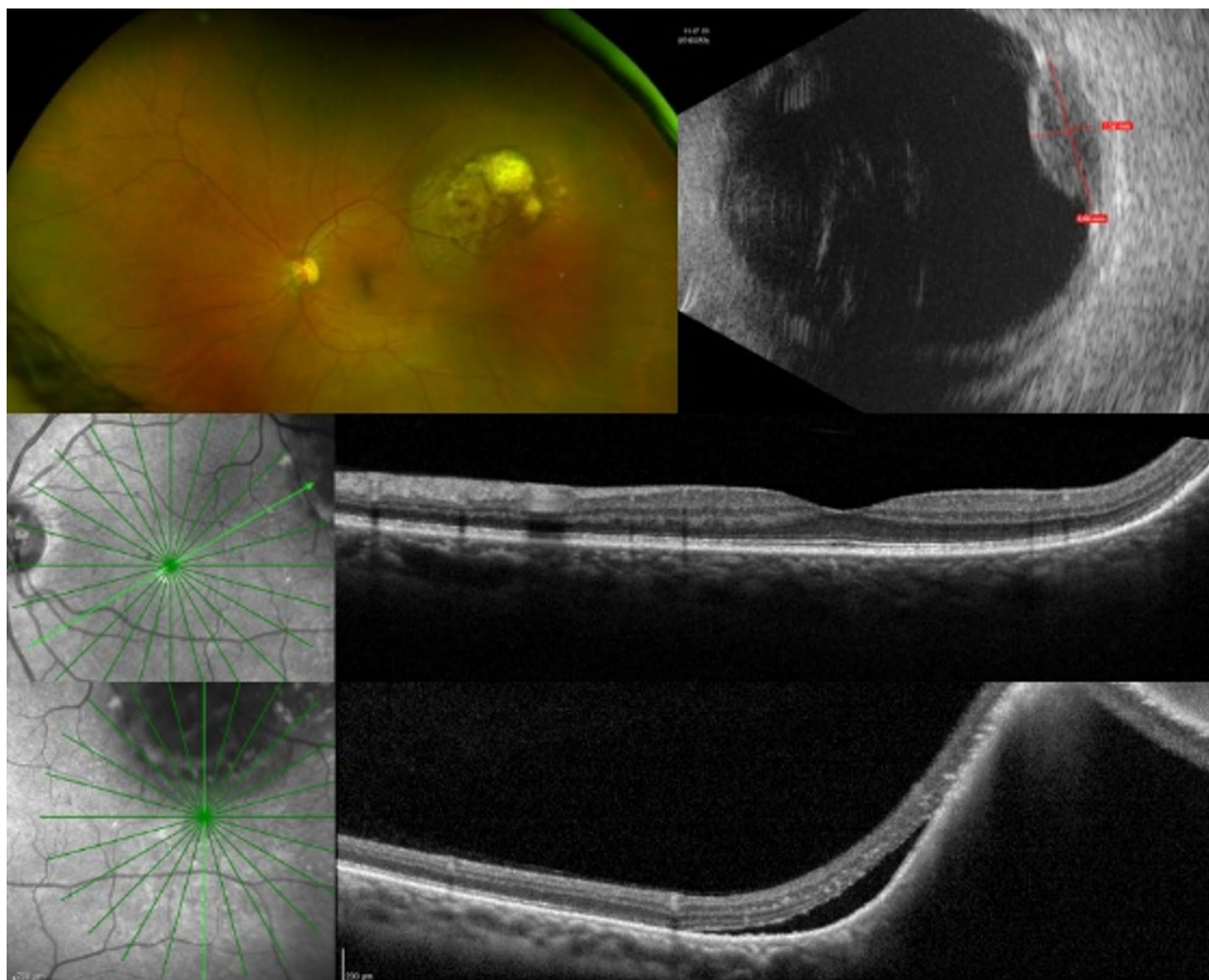


Fig. 2 Retinography of the left eye reveals an enlarging choroidal lesion in the supero-temporal region. Left eye ultrasound shows an extension of 9×8.66 mm in base and 3,52 mm in height. OCT shows no fluid in the macular region and an increase of the subretinal fluid at the base of the tumor

the evolution to a choroidal melanoma, Ruthenium-106 brachytherapy (80 Gy to the apex) was performed.

One month after the procedure, left eye BCVA remained 20/20. Fundoscopy showed a new Bruch's membrane rupture, an exudative retinal detachment inferior to the lesion, accompanied by subretinal haemorrhage. Two months post-brachytherapy, visual acuity remained unchanged. The serous retinal detachment continued to expand, with persistent subretinal haemorrhage. At the nine-month follow-up, further progression was noted, including an increase in lesion thickness on ultrasonography, greater exudative retinal detachment, and the appearance of extensive subretinal lipid exudation with BCVA decreasing to 20/40 (Fig. 3). Based on these findings, a second brachytherapy was scheduled, delivering 80 Gy to the apex, as it was deemed safe by the Radiation Oncology department in terms of the accumulated radiation dose to the sclera.

An intravitreal aflibercept injection was administered at the brachytherapy plaque removal, followed by additional intravitreal aflibercept injections every 8 weeks until subretinal exudation decreased and visual acuity improved. Six months after the second brachytherapy, left eye BCVA improved to 20/20. Fundoscopic examination revealed a flat, amelanotic tumour with a thickness of less than 1 mm, as confirmed by ultrasound, with no signs of exudative retinal detachment and complete resorption of the lipid exudation (Fig. 4). OCT confirmed the absence of subretinal fluid. As a result, intravitreal therapy was discontinued, and the patient was scheduled for routine follow-up.

Discussion and conclusions

Brachytherapy is an effective treatment modality for choroidal melanoma; however, like other forms of radiotherapy, it can lead to complications such as cataract, vitreous

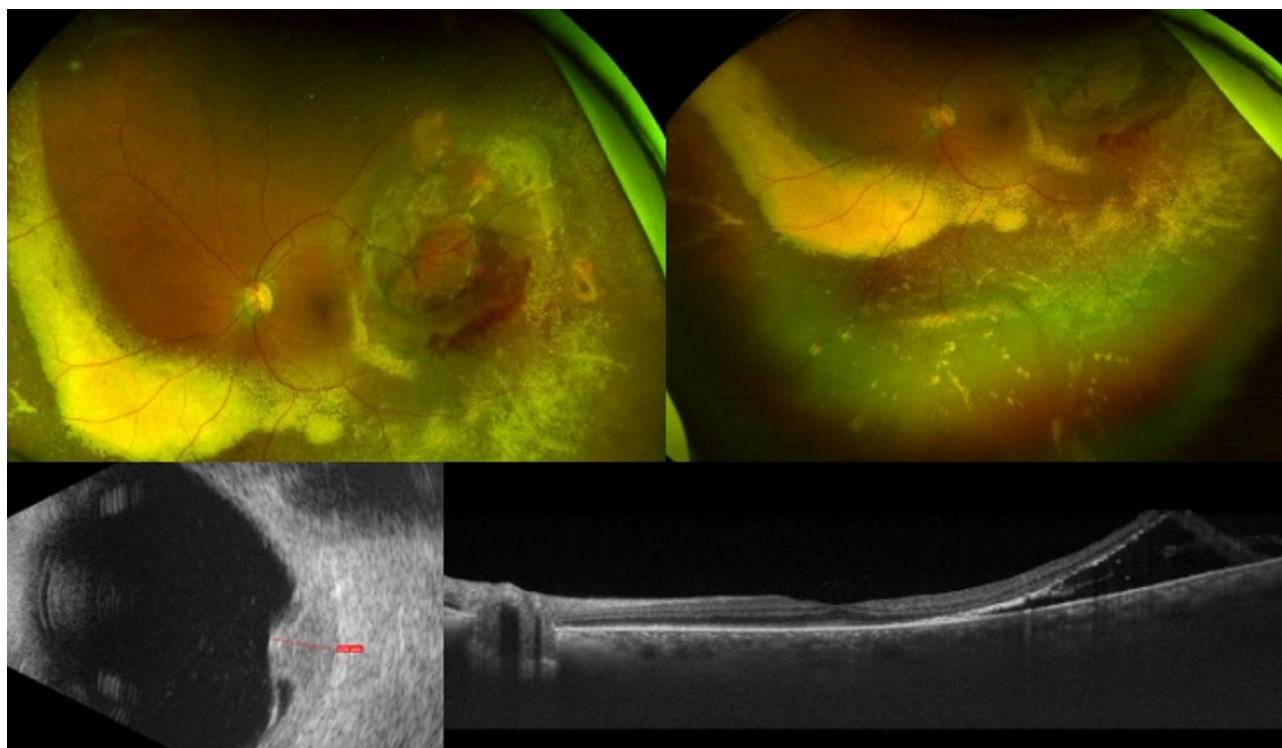


Fig. 3 Nine months after the first brachytherapy. Left eye retinography showing inferior exudative retinal detachment with an important lipid exudation surrounding the choroidal melanoma and extending to the inferior and nasal retinal periphery. OCT shows subretinal fluid approaching to the centre of the macula from the temporal posterior pole. Ultrasound shows an increase of tumour thickness to 4 mm and the Bruch's membrane rupture

haemorrhage, glaucoma, radiation retinopathy, maculopathy, and papillopathy [7]. A lesser-known complication of this treatment is TRLE, which may result from radiation-induced vasculopathy of the tumour vessels or the release of pro-angiogenic cytokines. This would lead to increased vascular permeability of the tumour vessels, allowing extravasated fluid and lipids to move through the Bruch's membrane and RPE into the subretinal space. The protective barrier of the Bruch's membrane and RPE would help explain why the incidence of lipid exudation from choroidal tumours is low [8].

Mills et al. investigated the associated risk factors for lipid exudation following plaque radiotherapy in uveal melanoma and found that 13% of cases treated with I-125 developed this complication, with an average onset of 10 months post-treatment. Young age, high serum low-density lipoproteins, low serum high-density lipoproteins, high tumour thickness and exudative retinal detachment in the preoperative period constituted the most important risk factors. Moreover, they observed that the occurrence of TRLE was associated with poorer visual outcomes and an increased risk of neovascular glaucoma [6]. Subsequently, in a case-control study, Mashayekhi et al. examined the systemic and tumour characteristics predictive of development of TRLE following plaque radiotherapy for posterior uveal melanoma. TRLE

developed in 8% of the treated eyes, with the primary risk factors identified as rupture of Bruch's membrane, posterior tumour location closer to the optic nerve or fovea, larger tumour base, with radiation dose to the tumour base correlating with the extent of lipid exudation. Additional factors included the absence of adjuvant therapy with transpupillary thermotherapy (TTT), and the presence of pre-radiotherapy serous retinal detachment, as well as a transient increase in serous retinal detachment in the first months following treatment [8].

Our case report involved a middle-aged man who presented risk factors associated with TRLE, including the presence of subretinal fluid prior to radiotherapy and its progression in the first months following treatment, along with a new rupture of the Bruch's membrane that appeared immediately after the first brachytherapy. Due to suspected tumour growth despite initial therapy, the patient underwent an additional treatment with Ruthenium-106 brachytherapy. Subsequently, intravitreal therapy with Aflibercept was administered to reduce both lipid exudation and exudative retinal detachment.

Anti-VEGF therapy has been studied as a treatment for the resolution of exudative retinal detachment secondary to choroidal melanoma, with published studies primarily using Bevacizumab. In a retrospective study, Houston et al. evaluated the efficacy of intravitreal Bevacizumab as

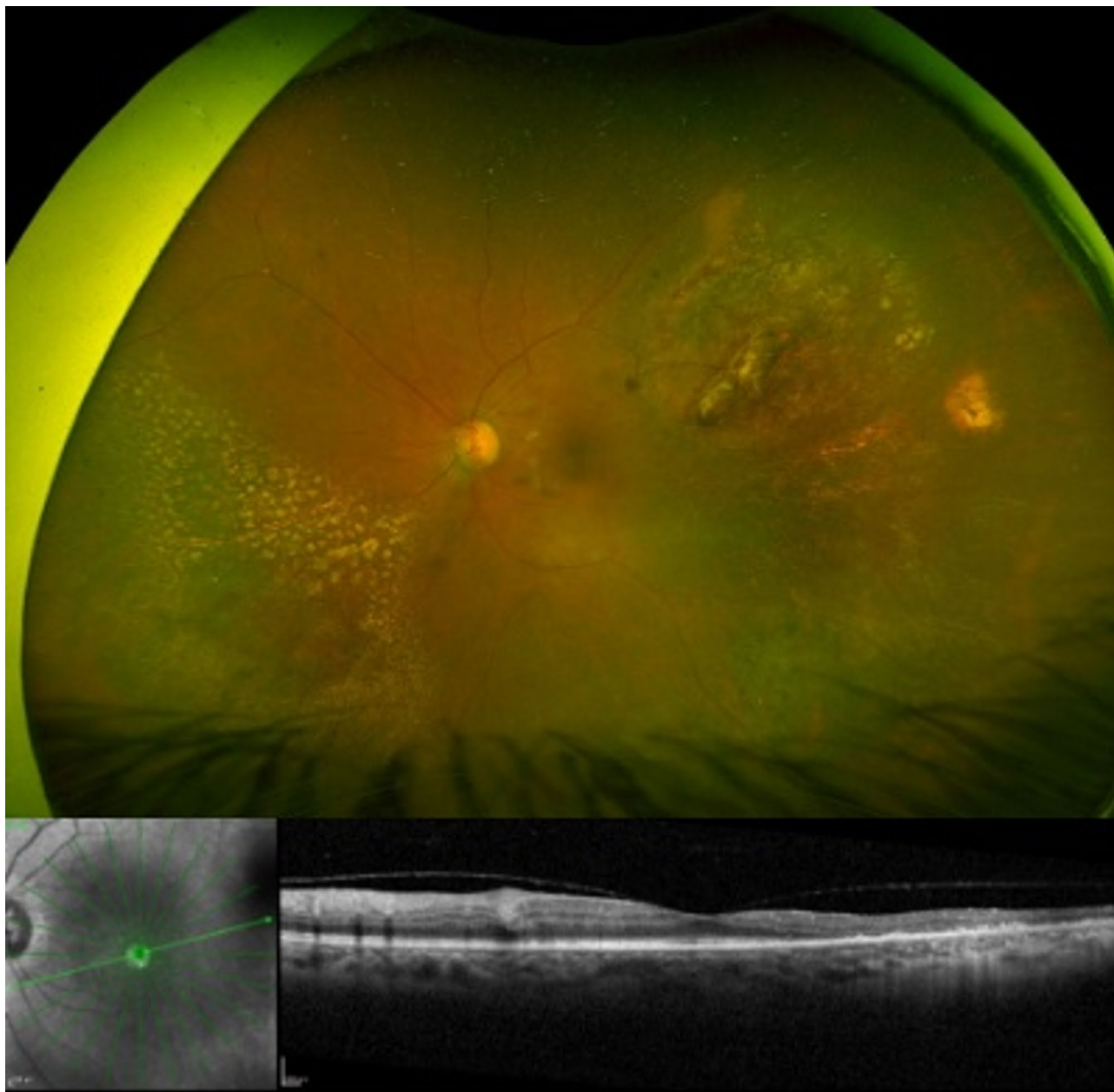


Fig. 4 Left eye retinography shows resolution of inferior exudative retinal detachment and reduction of the lipid exudation. OCT shows resolution of subretinal fluid with retinal atrophy temporal to the fovea secondary to the brachytherapy

an adjuvant therapy to plaque brachytherapy for choroidal melanoma, administering it immediately after plaque removal. They observed a 73% resolution rate in patients receiving combined therapy, with a mean resolution time of four months [9]. Additionally, a comparative study assessed the effectiveness of intravitreal triamcinolone versus intravitreal Bevacizumab for the treatment of large exudative retinal detachment secondary to uveal melanoma. The study found a higher regression rate of retinal detachment (69%) in patients treated with intravitreal

triamcinolone immediately after brachytherapy, with steroid-induced cataract being the most common complication [10].

In our case, the patient initially underwent brachytherapy; however, a second brachytherapy was required within the first year due to tumour growth and extensive subretinal detachment and lipid exudation, indicating insufficient local tumour control. Unlike previously reported cases, no immediate intravitreal anti-VEGF or triamcinolone treatment was administered, making

it uncertain whether such an approach could have prevented the subsequent progression and significant exudation observed in the following months.

After the second brachytherapy, intravitreal anti-VEGF therapy with aflibercept was initiated every eight weeks. However, to date, no published studies have evaluated the use of aflibercept as an adjunctive therapy for the management of choroidal melanoma with associated exudative retinal detachment. Despite this, the patient showed a favourable response to aflibercept, with complete resolution of exudation. These findings suggest that aflibercept could be a potential adjunctive therapy in such cases, as its mechanism of action is similar to that of other anti-VEGF. While the resolution of exudation may be attributed largely to the anti-VEGF therapy, the fact that tumour growth occurred after the initial brachytherapy also suggests that the second brachytherapy may have contributed to improve local tumour control and, consequently, to the resolution of TRLE.

Regarding long-term vascular changes, some studies have assessed the effects of I-125 brachytherapy and TTT as primary treatments for choroidal melanoma. Pilotto et al. reported that retino-choroidal anastomoses developed in 11% of patients treated with TTT, while none were observed in those treated with brachytherapy. These findings were associated with an increased risk of tumour recurrence [11]. In our case, fluorescein angiography has not yet been performed; thus, we cannot confirm the presence or absence of vascular anastomoses involving the tumour. However, based on the aforementioned study, the risk would be expected to be relatively low.

In conclusion, this case underscores the importance of recognizing TRLE as a potential complication of brachytherapy for choroidal melanoma and highlights the crucial role of multimodal imaging in its early detection and monitoring. The successful resolution of the exudative retinal detachment following brachytherapy combined with intravitreal aflibercept suggests that the combined therapy may be a useful option in managing TRLE. However, further studies are needed to better define its role. Case reports like this contribute valuable insights that help refine clinical decision-making and optimize treatment approaches for choroidal melanoma.

Abbreviations

OCT	Optical coherence tomography
OCT-A	Optical coherence tomography – Angiography
TRLE	Tumour-related lipid exudation
BCVA	Best-corrected visual acuity
TTT	Transpupillary thermotherapy

Authors' contributions

AB, MZ and MG were in charge of the patient and did the follow-up, collected the data. ER and DO wrote the manuscript. PB and TGS revised and corrected the manuscript. All authors read and approved the final manuscript.

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Data availability

All data generated or analysed during this study are included in this published article.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report.

Competing interests

The authors declare no competing interests.

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