Case Reports in Ophthalmology

Case Rep Ophthalmol 2025;16:261–267
DOI: 10.1159/000544879
Received: November 14, 2024
Accepted: February 3, 2025
Published online: March 24, 2025

Case Report

Presumed Choroidal Metastasis of Primary Cutaneous Melanoma: A Case Report

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Keywords

Choroidal metastasis · Cutaneous melanoma · Case report · Ocular oncology

Abstract

Introduction: Choroidal metastases most often originate from breast tumors in females and lung cancer in males. Primary cutaneous tumors rarely metastasize to the uveal tract. ***Case Presentation:*** Here, we present a rare case of a 47-year-old female patient who was clinically diagnosed with a presumed choroidal metastasis of primary cutaneous melanoma. The patient presented with complaints of decreased vision in her right eye. Her best corrected visual acuity (BCVA) was 0.7 decimal in the right eye and 1.0 in the left eye. Examination revealed a pigmented choroidal lesion in the parafoveal region with a prominence of 2.9 mm, orange pigment on the surface, and subretinal fluid in its projection. She had no history of active malignancy, but at the age of 36, a localized stage IB cutaneous melanoma was removed from her back. Yearly follow-up visits at the dermatologist showed no evidence of active disease. Upon diagnosis of a choroidal tumor, the patient underwent brachytherapy with a ruthenium-106 plaque in the right eye. Follow-up at the oncologist revealed a widespread disease with metastases in distant lymph nodes, liver, lung, pancreas, and brain, an uncommon pattern for primary choroidal melanomas, resembling rather the metastasis pattern of primary cutaneous melanoma. The patient was started on systemic therapy against metastatic cutaneous melanoma. At 21 months after brachytherapy and 19 months after the initiation of systemic anticancer therapy, the patient's BCVA in the right eye returned to 1.0 decimal, the choroidal lesion reduced in size, and subretinal fluid receded. Two years after the initial presentation, all metastases were stable or decreased in size. ***Conclusion:*** This case highlights the possibility of a choroidal metastasis of cutaneous melanoma more than a decade after the first presentation of the disease and highlights the effectiveness of combined brachytherapy and systemic anticancer therapy in managing the disease.

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Introduction

The most frequent intraocular malignancy is uveal metastasis, detected postmortem in approx. 12% of patients with metastatic tumors [1, 2], followed by uveal melanoma, which is also the most common primary intraocular malignant lesion [3]. These two can be clinically distinguished by the presence of systemic malignancy and treatment response; however, in more complicated cases, the ultimate diagnosis can be made with molecular diagnostics. This paper describes a rare case of presumed choroidal metastasis of primary cutaneous melanoma, which was the first indication of systemic dissemination of the melanoma. The patient was diagnosed with a pigmented choroidal tumor after complaints of worsening eyesight in the right eye. Upon treatment with brachytherapy, follow-up with the oncologist led to the discovery of a metastatic disease process throughout the body with a metastasis pattern characteristic of primary cutaneous melanoma. Systemic cancer treatment with ipilimumab and nivolumab was started. The choroidal tumor and visual function have remained stable for 2 years, raising the question as to whether the lesion was a primary choroidal melanoma or a metastasis of primary cutaneous melanoma. Critical detection of this life- and sight-threatening disease allowed for prompt treatment and management and highlights the importance of collaboration between ophthalmologists and oncologists. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000544879).

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At the age of 36, the female patient was diagnosed with stage IB cutaneous melanoma, and the lesion was subsequently removed from her back. The lesion was histologically grade 2 with no ulceration. Lymph node scintigraphy and removal of 4 sentinel lymph nodes showed no lymphatic spread of the disease, and yearly follow-up visits at the dermato-oncologist showed no signs of disease relapse or recurrence. Positron emission tomography-computed tomography scan was performed when the patient was 41 years old, 5 years after the removal of the cutaneous melanoma, and it showed no pathological processes. Ultrasound scans of the axillary, abdominal, and pelvic areas were performed 9 and 11 years after the removal of the cutaneous lesion and were all unremarkable.

At the age of 47, the patient was referred to an ophthalmologist with complaints of worsening visual acuity in her right eye over the last 3 months. She had neither previous history of ophthalmological diseases nor any current systemic diseases. The patient's work involved mostly working with a computer. From family history, it was known that her father had died of prostate cancer at the age of 68, and her mother's father had had laryngeal cancer.

Upon presentation to our clinic, the patient's best corrected visual acuity was 0.7 decimal in her right eye and 1.0 decimal in her left eye. Examination of the right eye demonstrated an unremarkable anterior segment, lens, intraocular pressure, and vitreous. Fundoscopic examination revealed an elevated pigmented lesion in the supratemporal macula with the largest basal diameter of 7 mm and orange pigment on the surface (Fig. 1a). On a B-scan ultrasound, the lesion presented internal homogeneity and low reflectivity, with a prominence of 2.92 mm (Fig. 1b). Optical coherence tomography (OCT) showed subretinal fluid reaching the fovea (Fig. 1c). Given the lesion's characteristics, a clinical diagnosis of a malignant choroidal tumor was made. While fine needle aspiration biopsy would have been beneficial for ascertaining the diagnosis, the size of the lesion would have made it challenging, and the technique was not available in our center at that time. Based on clinical findings, which indicated a malignant process, prior experience, and considering that the patient had no active

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malignancy, a primary choroidal melanoma was suspected. Two weeks after the initial presentation, the patient underwent brachytherapy with a ruthenium-106 (Ru-106) plaque, which was placed fovea sparingly. The dose to tumor apex was 88.3 Gy and 189 Gy to the sclera.

The patient was thereafter referred to an oncologist for the assessment of systemic spread of the disease. A whole-body CT scan was undertaken, which revealed numerous metastases in the brain, liver, lung, and pancreas. There were 5 hyperdense lesions in the forebrain, the largest with a diameter of 1.2 cm and the other four less than 1 cm in size. One round 1-cm lesion characteristic of metastasis was found in the inferior lobe of the right lung. There were also three hypodense round lesions in the 4a and 4b segments of the liver, the larger one with dimensions of 1 × 1.3 cm. One small lesion was seen in the caudal pancreas. There were slightly enlarged lymph nodes in the region of the celiac trunk and the liver hilus, which were not definitively classified as metastases. No enlarged lymph nodes were detected elsewhere, and the rest of the CT scan was unremarkable.

To ascertain the primary origin of the metastases, a liver biopsy of a metastatic lesion was attempted. This was, however, unsuccessful because of the small size and difficult accessibility of the metastatic lesions. The patient was also referred to genetic testing and was screened for genes associated with a predisposition to malignancies. Two rare heterozygous mutations of melanocyte-inducing transcription factor (*MITF*) were found (c.666 + 5T>C and c.1462G>A), which have uncertain clinical significance to date.

Given the previous history of cutaneous melanoma as well as the pattern of metastatic spread, a primary cutaneous melanoma with metastatic spread was suspected (stage IV cutaneous melanoma). While the choroidal lesion was initially considered a primary choroidal process, these findings led us to suspect that it is, instead, a metastasis originating from the primary cutaneous melanoma. The oncologists started the patient on combined systemic therapy of ipilimumab and nivolumab, which works through the activation of T lymphocytes, and is considered the first-line treatment for primary cutaneous melanoma with asymptomatic brain metastases [4, 5]. A reduction in all metastatic lesions was seen after three treatment sessions administered at a 2-week interval, including lesions in the brain, liver, lung, and pancreas; the enlarged lymph nodes were smaller in size. However, before the fourth treatment session, the patient developed a fever, and the blood test showed elevated liver transaminases, which were attributed to immune-related hepatotoxicity. The fourth treatment session with ipilimumab and nivolumab was consequently postponed. She was started on per-oral dexamethasone on a tapering schedule, and after 4 weeks of treatment, the levels of liver transaminases had normalized. Anticancer monotherapy with nivolumab was restarted. Five months after the start of systemic therapy, the patient developed hypophysitis, characterized by fatigue, nausea, and loss of appetite, and she was started on replacement therapy with hydrocortisone. The patient currently receives monotherapy with nivolumab at 6-month intervals and hydrocortisone replacement therapy.

Regarding the ophthalmic findings, the choroidal lesion has reduced in size throughout the follow-up period (Table 1). Four months after brachytherapy (2 months after the initiation of systemic cancer therapy), the apical height of the lesion was 2.62 mm, 12 months after brachytherapy, it was 2.49 mm. Twenty-one months after brachytherapy, the patient had developed local retinopathy from the ionizing radiation around the tumor (Fig. 2a), but the best corrected visual acuity in the right eye had returned to 1.0 decimal (Table 1). Furthermore, there was no sign of subretinal exudation on the OCT scan (Fig. 2b). As the Ru-106 plaque had been positioned fovea sparingly for brachytherapy, the retinal layers of the right fovea were intact (Fig. 2b). 21 months after brachytherapy (21.5 months from initial presentation), her brain, liver, lung, pancreas, and lymph node lesions have shown no sign of enlargement, and she has developed no additional metastases.

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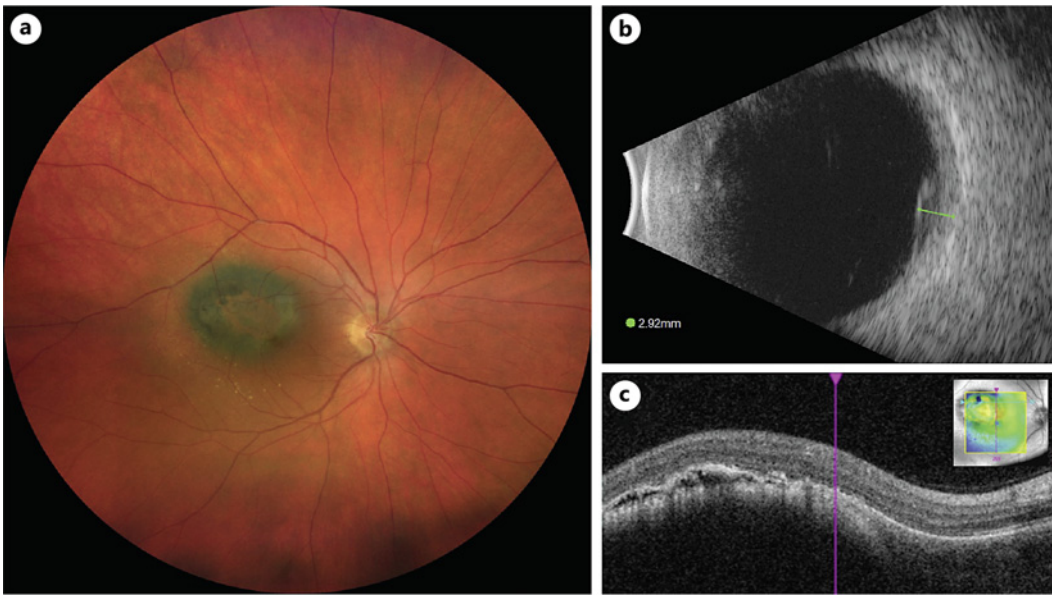

Fig. 1. Choroidal tumor in the right eye at presentation. **a** Fundus examination revealed a pigmented lesion with orange pigment in the supratemporal macula. **b** A B-scan ultrasound exam showed an apical height of 2.92 mm. **c** Subretinal fluid in the projection of the tumor was detected on OCT.

Table 1. Change of best corrected visual acuity and tumor prominence throughout the follow-up period

Time from brachytherapy	Best corrected visual acuity OD (decimal)	Tumor prominence
−2 weeks (presentation)	0.7	2.92 mm
2 months	0.1	
4 months	0.7	2.62 mm
7 months	0.1	
9 months	0.6	
12 months	0.6	2.49 mm
16 months	0.6	
18 months	0.8	
21 months	1.0	

Discussion

Here, we present a case of pigmented choroidal tumor in a patient with metastatic cutaneous melanoma. The case highlights the importance of careful planning of brachytherapy. While the choroidal tumor reached the fovea, the Ru-106 plaque was placed fovea sparingly. The dose to tumor apex was 88.2 Gy, which is less than the maximal dose of 150 Gy used in our ocular oncology center, as well as in some other centers [6]. The submaximal radiation dose was specifically chosen to avoid adverse damage to the fovea. Achieving a visual acuity of 1.0 decimal highlights the benefits of such an approach.

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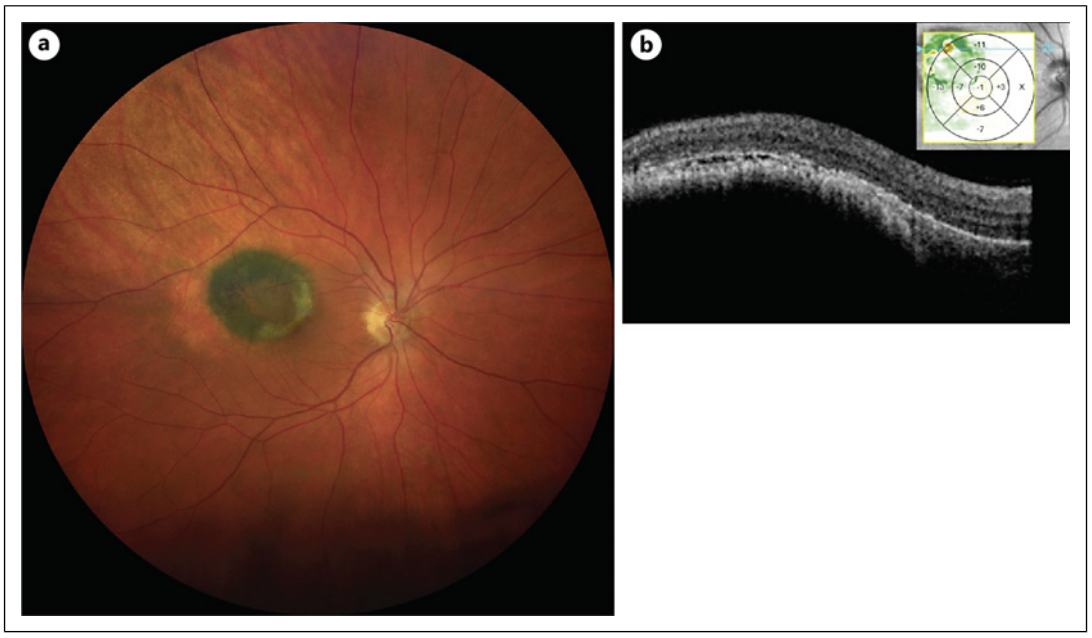

Fig. 2. Choroidal tumor 21 months after brachytherapy. **a** Fundus examination revealed local retinopathy around the tumor in the projection of the brachytherapy plaque. **b** There was no subretinal exudation on the OCT.

Whether the choroidal lesion was a primary uveal melanoma or metastasis of primary cutaneous melanoma remains unclear to date. A definitive answer could only be given if the molecular characteristics of the choroidal tumor were known, as cutaneous and uveal melanoma are molecularly distinct entities. More than 90% of uveal melanomas exhibit a mutation in *GNA11* or *GNAQ,* while mutations in *BRAF* and *NRAS* are most common in cutaneous melanomas [7]. Given the size of the tumor and the patient's complaints, the tumor could be effectively managed with brachytherapy, and no surgical intervention, which would allow investigation of the tumor's molecular profile, was warranted.

Although cutaneous melanoma accounts for only 3–5% of primary tumors metastatic to the eye [8], there are several indications that the lesion is a metastasis. Among those is the pattern of metastatic spread and survival rate. Cutaneous melanoma patients with tumor progression first develop regional lymph node metastases (50% of patients) [9]. However, regular follow-up visits to the dermato-oncologist showed no lymph node pathology in our patients. It is known that in patients with melanoma on the trunk, up to 35% develop direct distant metastases [10], which seem to be the case in our patient. The most common distant metastasis sites of cutaneous melanoma, diagnosed clinically or using imaging techniques, include the skin, subcutaneous tissue and distant lymph nodes (up to 59% of metastatic melanoma cases), lung (up to 36%), liver (up to 20%), central nervous system (up to 20%), pancreas (3%), and intestine (up to 8%) [9], which aligns with our patient's pattern of metastases. Conversely, 89% of metastatic uveal melanomas show metastases in the liver, 29% in the lungs, 11% in lymph nodes, and only 5% in the brain [11]. Metastatic choroidal melanoma is associated with a survival rate of 8% 2 years after diagnosis [11], while our patient has already been followed for 1 year and 9 months after the initial presentation.

Another factor supporting the patient's choroidal lesion as a metastasis of primary cutaneous melanoma is that cutaneous melanoma can have a late recurrence. A recurrence of later than 10 years after the initial presentation has been described in 6.9% of cutaneous

melanoma cases [12]. Although rare, several reports in the literature present cases of non-uveal melanomas with metastases to the uvea [13, 14].

There are also several factors speaking in favor of the choroidal lesion of our patient being a primary choroidal melanoma. It has been shown that individuals with primary cutaneous melanoma have a higher risk for uveal melanoma: a study of more than 150,000 patients with cutaneous melanoma showed a heightened occurrence of primary uveal melanoma in this population (odds ratio 1.99) [15]. In addition, both cutaneous and uveal melanomas are known to respond to immune therapy with ipilimumab and nivolumab [4, 16].

In conclusion, this is one of the few reported cases of presumed choroidal metastasis of cutaneous melanoma. This case demonstrates the successful management of the disease through combined brachytherapy and systemic immune therapy, and underscores the importance of collaboration between ophthalmologists and oncologists in treating such patients.

Statement of Ethics

This retrospective review of patient data does not require ethical approval in accordance with local and national guidelines. Written informed consent was obtained from the patient for publication of this case report and any accompanying images. All identifiable patient information is kept strictly confidential and not reported.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

No funding relevant to the published data was received.

Author Contributions

T.P. and A.K. contributed to writing, design, interpretation, and final approval of the manuscript and are accountable for the accuracy and integrity of the work.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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