Choroidal Melanoma Mimicker: A Case of Metastatic Clear-Cell Renal Cell Carcinoma

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Established Facts

- Metastatic disease is the most common intraocular malignancy.
- Metastatic renal cell carcinoma exhibits high mortality with a median survival of less than 3 years.

Novel Insights

- Renal cell carcinoma may have a similar clinical appearance to uveal melanoma.
- Surgical resection of delayed-onset choroidal metastasis from renal cell carcinoma may achieve total remission.

Keywords

Choroidal melanoma · Melanoma · Metastasis · Uveal melanoma · Renal cell carcinoma · Clear-cell renal cell carcinoma

Abstract

Choroidal melanoma is the most common primary intraocular malignancy, yet metastatic disease remains the most common malignancy of the eye. Differentiating these entities is essential as treatment, systemic associations, and prognosis vary dramatically between the two. Established diagnostic criteria are accurate for the diagnosis of uveal melanoma. Yet, metastatic disease may be misdiagnosed as a uveal melanoma in rare cases. We report a case of metastatic clear-cell renal cell carcinoma masquerading as uveal

melanoma. A 73-year-old Caucasian man with a history of renal cell carcinoma presented with a 15 × 12 × 7 mm homogenous, pigmented, and acoustically hollow mass without hemorrhage or exudation. The patient was initially treated with plaque radiotherapy with good tumor regression. However, the patient developed pain and vision loss due to total exudative retinal detachment. Subsequent enucleation allowed histopathologic confirmation of clear-cell renal cell carcinoma. Nine years following enucleation, the patient remains in complete remission without evidence of other systemic metastases. Renal cell carcinoma should be considered when evaluating patients with probable uveal melanoma. Delayed-onset ocular metastasis from renal cell carcinoma exhibits an atypical clinical course with the possibility of durable remission following enucleation.

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Introduction

While choroidal melanoma is the most common primary ocular malignancy, metastatic disease represents the most common malignancy of the uveal tract. The most common primary locations of cancers with uveal metastasis are breast and lung, representing 47 and 21% of metastases, respectively [1]. Additional less common sites are gastrointestinal tract, kidney, skin, and prostate [1]. The differentiation of uveal melanoma from metastasis is often achieved without tissue biopsy via clinical criteria, which has up to 99% accuracy [2]. Even so, rare tumors occasionally provide diagnostic dilemmas and must be considered when evaluating choroidal masses [3].

Kidney and renal pelvis cancer accounts for 3.7% of all new cancer diagnoses with a median age of diagnosis of 64 and a 2:1 male predominance [4, 5]. The most common form of renal cancer is clear-cell renal cell carcinoma, accounting for 70–80% of cases [5]. Metastases develop in 33% of cases, most commonly to lungs, liver, bone, and brain, with rarer involvement of the pancreas, gastrointestinal tract, or adrenal and parotid glands [6]. Intraocular and orbital metastases from renal cell carcinoma are rare with only 32 cases published in the English literature since 1934 [7]. Here, we report a case of metastatic clear-cell renal cell carcinoma masquerading as uveal melanoma.

Case Report

A 73-year-old Caucasian male presented to the eye center with a 2-month history of left eye redness and progressively blurred vision. The patient reported a history of renal cell carcinoma treated with a nephrectomy 4 years prior. He claimed no known recurrence and was without evidence of systemic disease at the time of presentation.

On initial exam, the patient's visual acuity was 20/70 in the right eye and 20/100 in the left eye. Anterior segment exam revealed atypical sentinel vessels penetrating the sclera nasally in the left eye (Fig. 1a) and 3+ nuclear sclerotic cataracts in each eye. A pigmented ciliochoroidal mass without exudation, hemorrhage, or subretinal fluid was seen nasally in the left eye through the dilated pupil (Fig. 1b). Transillumination approximated the extent of the lesion (Fig. 1c). Dilated exam showed the pigmented mass nasally in the left eye, but the retina appeared otherwise unremarkable and without subretinal fluid. B-scan ultrasound revealed a 15 × 12 × 7 mm solid homogenous mass (Fig. 1d), and standardized A-scan showed medium internal reflectivity. Metastatic workup included a computed tomography (CT) scan of the abdomen and pelvis, liver function testing, and chest X-ray. The CT scan revealed scarring from a right nephrectomy with no hepatic lesions or mesenteric adenopathy. Hepatic enzymes and chest X-ray were normal.

The patient was treated with an I¹²⁵ plaque, which delivered 9,000 cGy to the tumor apex. At 3 months, tumor thickness had decreased from 7.0 to 5.5 mm with stable visual acuity. Despite continued regression of the tumor, 2 months later the patient's vision decreased to light perception secondary to a total exudative retinal detachment. The patient elected to undergo enucleation at this time. Hematoxylin and eosin stain demonstrated polygonal cells with clear cytoplasm (Fig. 2a). Immunohistochemistry was negative for S-100, Melan-A, tyrosinase, HMB-45, and neuron-specific enolase (Fig. 2b). There was positive staining for CD-10 and EMA (Fig. 2c). This histopathology is consistent with the diagnosis of metastatic clear-cell renal cell carcinoma. Nine years following enucleation, there remains no evidence of additional metastatic disease on positron emission tomography, total body CT, and bone scan.

Discussion

Many carcinomas and adenocarcinomas exhibit clear-cell morphology. Further, there are histologic subtypes of uveal melanoma that exhibit clear cytoplasm, which includes balloon-cell degeneration and clear-cell melanoma. Balloon cells may be observed in choroidal melanoma post radiation and represent degraded melanosomes [8]. Clear-cell melanoma comprises a distinct subtype of uveal melanoma identified in 2 of the 1,493 eyes enucleated and reviewed in the Collaborative Ocular Melanoma Study [9]. Immunohistochemistry aids differentiation of these entities from clear-cell metastases. Clear-cell uveal melanomas demonstrate positive staining with the melanocytic markers S-100 and HMB-45 [9]. The tumor in this case was negative for melanocytic markers, which included S-100, Melan-A, tyrosinase, and HMB-45, making it unlikely to represent one of these uveal melanoma variants.

Ocular metastasis from renal cell carcinoma most commonly involves the choroid (62.5% of reported cases), and less commonly the iris and ciliary body (25 and 12.5%, respectively) [7]. Metastatic renal cell carcinomas within the choroid are typically dome-shaped, yellow lesions and have a mean thickness of 4 mm. Some appear red or orange, which is thought to be secondary to the tumor's high vascularity and tendency to hemorrhage. However, there was substantial clinical variability with one previous case of a pigmented, acoustically hollow lesion that was initially diagnosed as uveal melanoma [10]. Thus, the tumor presented in this report further illustrates the importance of considering renal cell carcinoma when evaluating a patient with probable uveal melanoma. In patients with a known history of renal cell carcinoma, there should be a high index of suspicion for metastases

Fig. 1. External photographs and ultrasound images. **a** Nasal atypical sentinel vessels explaining chief complaint of a red eye. **b** Visible mass of the ciliary body through the dilated pupil. **c** Transillumination reveals a well-circumscribed pigmented mass. **d** A- and B-scan show a dome-shaped homogenous mass.

Fig. 2. Histopathology of ciliary body mass consistent with a diagnosis of metastatic clear-cell renal cell carcinoma. **a** Hematoxylin and eosin stain with characteristic clear-cell appearance. **b** Negative staining of pan-melanoma cocktail. **c** Positive staining of CD10, consistent with clear-cell renal cell carcinoma.

when presenting with choroidal masses, even if clinical signs suggest uveal melanoma.

Metastatic renal cell carcinoma has a high mortality with a 5-year survival rate of 11.7% [4] and a median survival of 27 months [11]. This patient has reached 9 years of disease-free survival since presenting with an ocular metastasis, remaining in total remission 13 years after his initial treatment with nephrectomy. Thus, this case represents a rare example of durable remission following plaque radiotherapy and subsequent enucleation. Interestingly, renal cell carcinoma may develop delayed-onset solitary metastasis, more than 10 years af-

ter nephrectomy, in 4.7–11% of patients that survive 10 years following nephrectomy [12, 13]. These metastases appear more indolent than the earlier manifestation of this disease. A recent review of late-onset intracranial metastases from renal cell carcinoma demonstrated total remission after surgical resection of the metastases, further illustrating the atypical clinical course observed in this group of patients [14]. As the choroidal metastasis in this case presented 4 years after nephrectomy, it may not qualify as delayed-onset, but the patient's clinical course supports its similarity to the delayed phenotype. Further, the presentation with sentinel vessels and

visual symptoms likely led to early diagnosis and treatment that may not have been possible with metastasis in other locations. Providing hope for patients with a poor prognosis remains a delicate aspect of ocular oncology, especially in patients with metastatic disease. While the struggle to balance optimism with clear prognostication remains challenging, delayed-onset ocular metastasis from renal cell carcinoma may be effectively treated with surgical resection.

Statement of Ethics

This case report complies with the guidelines for human studies as published by ICMJE, the rules regarding informed consent, and the policies of the institutional review board. No animal experiments were performed in this study.

Disclosure Statement

The authors have no financial interest in this study.

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