

# Vitreous Hemorrhage as the Initial Sign of Renal Cell Carcinoma Metastasis

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Choroidal metastases generally appear as a solitary, yellow- or orange-colored mass in the macula or perimacular region of the eye. In an analysis of 520 eyes with uveal metastasis, the tumor appeared as a solitary mass (71%) with mean basal dimension of 9 mm and mean thickness of 3 mm.<sup>1</sup> In that analysis, associated findings included subretinal fluid (73%) and retinal pigment epithelial alterations (57%). Hemorrhage is an unusual finding with choroidal metastatic disease. Single case reports have highlighted this rare association. Vitreous hemorrhage has been described with uveal metastasis from occult lung cancer and hemorrhagic retinal detachment with metastatic renal cell carcinoma.<sup>2,3</sup> Herein, we describe a 79-year-old man with known renal cell carcinoma who developed sudden vitreous hemorrhage and was found to have an underlying choroidal mass that proved, upon needle biopsy, to represent renal cell carcinoma metastasis.

## CASE DESCRIPTION

A 79-year-old man with a 3-week history of floaters and photopsia noted decreasing visual acuity in the left eye. Examination disclosed vitreous hemorrhage. The patient was referred to us for evaluation, with concern for malignant melanoma. The ocular history was unremarkable, specifically with no evidence of trauma or retinal vascular disease. General medical history revealed renal carcinoma of the left kidney treated with nephrectomy 8 years previously, with no known systemic metastases. Additionally, the patient had a 40-year history of tobacco use.

On examination, visual acuity (VA) was 20/20 in the right eye and hand motions in the left eye. Bilateral

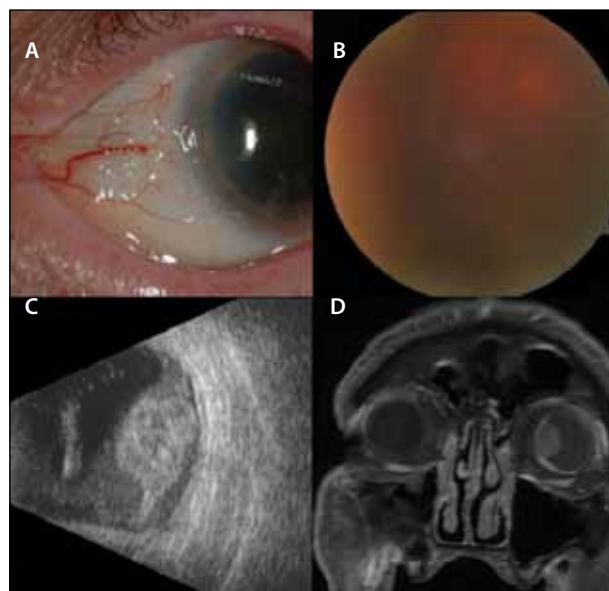


Figure 1. Prominent episcleral vessels raised suspicion of a ciliary body tumor such as melanoma (A). Dense vitreous hemorrhage complicated the fundus examination (B). Ocular ultrasonography demonstrated an oval-shaped cavitory lesion with high internal reflectivity, suggesting the presence of blood or necrotic debris. Vitreous opacities and debris were noted, consistent with hemorrhage (C). Coronal gadolinium-enhanced T1-weighted fat-suppressed magnetic resonance image of left eye showed an enhancing, dome-shaped tumor in the posterior nasal aspect of the globe (D).

advanced nuclear sclerosis was noted. The right eye was otherwise unremarkable. In the left eye, episcleral sentinel vessels were apparent nasally (Figure 1A). There

was dense vitreous hemorrhage precluding a view of the fundus (Figure 1B).

Ocular ultrasonography disclosed an intraocular mass with cavitation that measured 17 mm in basal diameter and 11 mm in thickness. The mass displayed signal variability suggestive of blood or necrosis (Figure 1C). Transillumination revealed a shadow in the nasal quadrant suggestive of an intraocular mass but without clear definition. Magnetic resonance imaging with gadolinium enhancement confirmed a solitary, well-defined, oval-shaped enhancing mass within the medial left globe (Figure 1D). Additionally there was hyperintense T1 signal consistent with intraocular hemorrhage. These features suggested a solid mass.

We performed fine-needle aspiration biopsy using the transcleral method into the tumor without direct visualization. Cytologic evaluation disclosed a scanty cellular specimen consisting of a few clusters of apparently malignant amelanotic cells with inadequate material for immunocytochemical stains. This cellular morphology, coupled with the patient's history with renal cell carcinoma, favored metastatic carcinoma over amelanotic choroidal malignant melanoma. We applied plaque radiotherapy to control the intraocular mass with apex dose of 7000 cGy over 5 days. Systemic evaluation revealed no other sites of metastatic disease. On follow-up, the tumor showed regression.

## DISCUSSION

Renal cell carcinoma arises from several cell types, including clear cell (75%), papillary types 1 and 2 (15%), chromophobe (5%), oncocytoma (5%), and collecting duct (<1%).<sup>4</sup> These different histological cell types result from distinct genetic abnormalities, each with a predictable clinical course. Renal cell carcinoma most often develops in patients between the ages of 50 and 70 years, and with a 1.5:1 male-to-female ratio. It is estimated that in the United States 31 900 new cases are discovered each year, resulting in more than 11 900 annual deaths.<sup>4</sup> Cigarette smoking has been found to be a risk factor, with a dose-response relationship. Approximately 30% of men with renal cell carcinoma are estimated to develop the malignancy from related tobacco use.<sup>4</sup> Our patient was a long-time smoker.

Renal cell carcinoma can be marked with the classic triad of flank pain, hematuria, and palpable flank mass. Still, although this triad is observed in only 9% of patients, it heralds advanced disease.<sup>4</sup> Metastases are evident at presentation in as many as 25% of patients, owing to potential growth in the retroperitoneal space before symptoms are manifest.<sup>5</sup> Tumor size is a significant predictor of metastatic potential. In a prospective

study of 187 patients, Ljungberg et al<sup>6</sup> found that 80% of metastatic cancers were diagnosed within 3 years of nephrectomy. In a comprehensive survey of 2691 patients with renal cell carcinoma, Thompson et al<sup>7</sup> found that the 3-year probability of metastasis was 0% for tumors less than 3 cm in size and 20% for those 7 cm or greater. Kunkle et al<sup>8</sup> found that for every 1-cm increase in tumor size, the risk of metastasis increased 22%. When present, renal cell carcinoma preferentially metastasizes to the lungs (75%), soft tissues (36%), bone (20%), liver (18%), central nervous system (8%), and cutaneous sites (8%).<sup>4</sup>

Renal cell carcinoma is a highly vascular tumor and is known to produce hemorrhagic metastases. Deregulation of the VEGF pathway results from abnormalities in pVHL, a tumor suppressor gene implicated in sporadic clear cell renal carcinoma and Von Hippel-Lindau syndrome.<sup>4</sup> This deregulation ultimately leads to unregulated angiogenesis, which explains the characteristic histologic findings of malignant clear cells enclosed by capillaries and vascular sinuses.<sup>5</sup> Hemorrhagic metastases from renal cell carcinoma to several tissue types have been described in the literature.<sup>9-12</sup> Vitreous hemorrhage, a presenting feature of other ocular neoplasms such as uveal melanoma, can also rarely be the initial manifestation of uveal metastasis, particularly renal cell carcinoma, as in our case.<sup>13</sup>

Metastatic renal cell carcinoma to the uvea comprises only 2% of uveal metastases according to a survey by Shields et al, and typically presents as a homogeneously orange-tinged mass.<sup>1,14</sup> Cases of metastatic renal cell carcinoma to the choroid, including those presenting years after nephrectomy and a rare case of apparently spontaneous remission, have been described in the literature.<sup>3,12,15</sup> This malignancy is recognized for its tendency to hemorrhage in the subretinal or subretinal pigment epithelial space.<sup>2,3</sup> Haimovici et al described a 77-year-old man with known renal cell carcinoma who presented with hemorrhagic retinal detachment from choroidal metastasis.<sup>3</sup> Other metastatic tumors to the eye, including those caused by breast cancer, can also produce hemorrhage. In an analysis of 264 patients with choroidal metastases from breast cancer, retinal hemorrhage was found in 2%, and there was no case of vitreous hemorrhage.<sup>16</sup>

## SUMMARY

Renal cell carcinoma is a highly vascular tumor that can present with hemorrhagic features. This can be explained by the molecular defects in pVHL that occur with sporadic renal cell carcinoma, deregulating VEGF activity and increasing angiogenesis. This case dem-

onstrates that although vitreous hemorrhage is a rare presentation of choroidal metastasis, it may be the first clinical sign of metastatic renal cell carcinoma. ■

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