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"Retinal Vasculitis" With Bilateral Retinal Detachments

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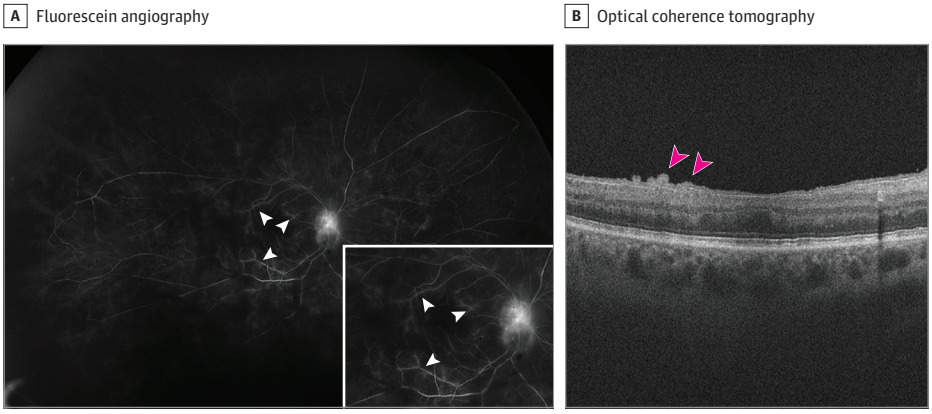

Figure 1. Fluorescein angiography and optical coherence tomography on presentation demonstrate retinal vasculitis and vitritis (right eye results shown). A, Fluorescein angiography shows dense vitritis, predominantly arteriole leakage (arrowheads), and nonperfusion. Inset is a magnified view, with arrowheads pointing to arteriole leakage. B, Optical coherence tomography shows disorganization of the outer retina with debris at the vitreoretinal interface (arrowheads).

A 68-year-old man with a remote history of B-cell lymphoma and active renal cell carcinoma (RCC), receiving cabozantinib therapy, was referred for worsening hazy vision in the right eye after recent outside retinal detachment (RD) repair of the left eye, with pars plana vitrectomy and gas. The patient noted blurry vision started around the time of cabozantinib therapy initiation. Cabozantinib therapy was discontinued for surgery and resumed 3 days later. The referring retina specialist noted vitritis and vasculitis intraoperatively, but the result of vitreous biopsy cytology was negative for malignant cells.

At presentation to our institution, the patient was taking oral prednisone, 40 mg/d. His visual acuity was 20/500 OD and hand motions OS, with an intraocular pressure of 18 mm Hg in both eyes. Right eye slitlamp examination results showed pigmented cells in the anterior chamber and lens capsule; the left eye showed prolapsed pigmented vitreous at the pupillary margin. Right eye fundus examination results revealed sheets of pigmented cell and vascular sheathing with optic nerve pallor. The left eye had a poor view, with 90% gas fill. Fluorescein angiography illustrated disc and vessel leakage (predominantly arteriole), capillary dropout, and peripheral nonperfusion in the right eye (**Figure 1**A) with no view in the left eye. Optical coherence tomography revealed debris at the vitreoretinal interface (Figure 1B).

WHAT WOULD YOU DO NEXT?

A. Vitreous tap and inject intravitreal foscarnet, vancomycin, and ceftazidime

B. Stop prednisone and proceed with diagnostic vitrectomy

C. Stop cabozantinib and admit for intravenous solumedrol

D. Magnetic resonance imaging of the orbits followed by lumbar puncture

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Diagnosis

Renal cell carcinoma bilateral ocular metastasis

What to Do Next

B. Stop prednisone and proceed with diagnostic vitrectomy

Discussion

Given the patient's history of B-cell lymphoma and active RCC, recurrent lymphoma or metastatic RCC must be ruled out. Thus, prednisone therapy was stopped, and the patient underwent diagnostic vitrectomy (choice B). Renal cell carcinoma is an uncommon tumor from the renal cortex, accounting for approximately 2% of systemic malignant tumors.[1] Renal cell carcinoma most commonly metastasizes to the lung, bone, liver, and brain,[2] and it rarely metastasizes to orbital or intraocular tissue, with fewer than 80 cases reported in the literature.[1]

Cabozantinib is a tyrosine kinase inhibitor approved for the treatment of metastatic RCC. There have been 3 case reports of cabozantinib causing cutaneous vasculitis but no reported ocular adverse effects.[3-5] Tyrosine kinase inhibitor–associated retinal vasculitis

would be a diagnosis of exclusion. If a subsequent biopsy result is negative, then it is appropriate to stop cabozantinib therapy and consider intravenous corticosteroids (choice C). The patient's examination findings and clinical history (no hypopyon, lack of pain, and nonseptic appearance) make infectious endophthalmitis less likely (choice A). If ocular metastasis is diagnosed, obtaining a magnetic resonance image of the orbit followed by a lumbar puncture (choice D) may be a necessary next step to evaluate for brain metastasis.

The most common cause of malignant intraocular tumors in adults is metastases from systemic malignant tumors. Choroidal metastases of RCC are typically dome shaped and yellow on examination, although some RCC metastases may appear reddish orange due to the high vascularity. In a review of 68 cases of ocular metastases of RCC, 50% had extraocular involvement and 50% were intraocular.[1] The most frequently involved site was the orbit (36.8%), followed by the choroid (29.4%), and RCC metastases were predominantly unilateral, with only 4 bilateral reported cases.[1] There is a single report in the literature of unilateral RCC ocular metastasis presenting as vitritis with no retinal or choroidal mass,[6] although retinal metastasis presenting as retinal vascular sheathing and retinitis has been reported previously in other solid organ tumors.[7]

Patient Outcome

The patient's diagnostic vitrectomy confirmed RCC metastasis in the vitreous. The patient then developed an RD in the right eye and a redetached left eye. He underwent bilateral sequential RD repair and subsequent diagnostic vitrectomy, with aqueous and retinal biopsy of the left eye. The biopsy results demonstrated malignant cells positive for RCC (**Figure 2**). The patient underwent palliative radiotherapy to the orbits, but due to continued disease progression, he passed away shortly thereafter.

To our knowledge, this is the first reported case of RCC ocular metastases with aqueous and retinal biopsies and positive bilateral vitreous biopsy results. The patient initially presented with "retinal vasculitis" and panuveitis after RD repair; however, it is possible that the sclerotic vessels were a result of metastatic cellular intravascular deposits causing occlusive disease and severe nonperfusion.

Figure 2. Full-thickness retinal biopsy specimen from the left eye, with immunohistochemistry positive for CK7 (pictured with arrowheads) and PAX8 and negative for CK20 and TTF1, pointing to renal cell carcinoma metastasis (arrowheads).

Metastatic RCC is a highly vascular tumor type—due to both the overproduction of vascular endothelial growth factor and other proangiogenic cytokines[6] and alterations in the von Hippel–Lindau tumor suppressor gene.[8] Renal cell carcinoma is metastatic in 30% of patients,[9] and it portends a poor prognosis, with a median survival of approximately 13 months and a 5-year survival of less than 10%.[10]

ARTICLE INFORMATION

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