CASE REPORT

Vision Loss from Choroidal and Pituitary Metastases Secondary to Renal Cell Carcinoma: A Case Report

Laura D. Selby^a, Hillary C. Stiefel^{b,c}, Alison H. Skalet ^{b,d}, Molly S. Cardenal ^e, Kavita V. Bhavsar^{b,f}, and Kimberly M. Wings ^{b,f,g}

^aSchool of Medicine, Oregon Health & Science University, Portland, Oregon, USA; ^bCasey Eye Institute, Oregon Health & Science University, Portland, Oregon, USA; ^cOregon Eye Specialists, Newberg, Oregon, USA; ^dDepartment of Radiation Medicine, Oregon Health & Science University, Portland, Oregon, USA; ^eDepartment of Optometry, VA Portland Health Care System, Portland, Oregon, USA; ^fDepartment of Ophthalmology, VA Portland Health Care System, Portland, Oregon, USA; ^gDepartment of Neurology, Oregon Health & Science University, Portland, Oregon, USA

ABSTRACT

A 62-year-old male with a history of metastatic clear cell renal cell carcinoma (ccRCC) presented with decreased vision to 20/50 in the left eye. Fundus examination revealed an elevated, amelanotic mass lesion in the superotemporal macula, without involvement of the central macula by subretinal fluid or tumour. Given incongruity between the fundus findings and the degree of visual impairment, visual field testing was obtained, revealing a bitemporal hemianopia. Magnetic resonance imaging demonstrated optic chiasm compression by a pituitary mass, which had previously been overlooked on computed tomography imaging. Biopsy confirmed metastatic ccRCC to the pituitary, which presented simultaneously with the presumed choroidal metastasis.

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Introduction

Renal cell carcinoma (RCC) is the most common neoplasm of the kidney, accounting for 3.8% of all new cancer diagnoses made annually in the United States.¹ There are many different subtypes of RCC, with clear cell RCC (ccRCC) being the most common, occurring in 88% of over 4000 patients in a retrospective review.² Out of the top three most common RCC histological subtypes, patients with ccRCC have the worst prognosis with 5 year disease specific survival rates of 54.9–68.9%.^{3,4} While nephrectomy can be curative, there are several reports of metastases occurring decades after the primary tumour is removed.⁵ The most common metastatic locations include lung, bone, lymph nodes, liver, adrenal glands, and brain.⁶ Metastasis to the choroid or pituitary gland is rare. We present an unusual case of simultaneous choroidal and pituitary metastases in a patient with known metastatic RCC. This is the first reported case of simultaneous choroidal and pituitary metastases from RCC.

Case report

A 62-year-old male presented with 2 weeks of central vision loss in the left eye. His past medical history was significant for RCC. Twenty-one years previously, he had undergone left nephrectomy identifying ccRCC. He was subsequently followed for very slowly evolving pulmonary nodules, presumed to be related. Positron-emission tomography (PET)/computed tomography (CT) 2.5 years prior to presentation revealed new uptake in the right hilum and gastric fundus, as well as lytic bone lesions concerning for metastatic disease. Biopsy of the right hilar mass confirmed ccRCC. Additional staging workup at that time identified a 2.1 cm homogenously enhancing extra-axial frontal brain lesion most consistent with a meningioma (Figure 1). Neurosurgery was consulted and recommended surveillance of the lesion with serial CT scans, which were performed every 6 months. During this time, the patient underwent palliative radiotherapy for a pathologic compression fracture of the thoracic spine and chest wall.

CONTACT Kimberly M. Wings winges@ohsu.edu

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Figure 1. Frontal Meningioma. CT head with contrast coronal view, performed approximately 2 years prior to presentation, shows the suspected frontal meningioma under surveillance.

He stabilized on sunitinib therapy for 2 years prior to presentation to the eye clinic.

On initial presentation to optometry, the corrected visual acuity was 20/20 in the right eye and 20/50 in the left eye. Intraocular pressure was 14 mmHg in both eyes, pupils were round and reactive to light, no relative afferent pupillary defect (RAPD) was documented, and extraocular motility was full. Confrontation visual fields were notable for a superotemporal defect in the left eye. Dilated fundoscopic examination including optic nerve exam were normal in both eyes, except for a small, mildly elevated, amelanotic lesion in the superotemporal macula of the left eye (Figure 2A). He was referred to a medical retina specialist and macular optical coherence tomography (OCT) revealed a choroidal lesion with a small amount of subretinal fluid that did not extend to the fovea (Figure 2B and 2C). Ocular oncology was consulted, and B-scan of the left eye showed a minimally elevated choroidal lesion which measured 0.75 mm in thickness. The underlying sclera had an excavated-like appearance, but appeared intact. Fundus autofluorescence imaging showed an elevated mass just inferior to the superior temporal arcade with increased central autofluorescence, surrounded by a ring of relative hypofluorescence and an outer ring of hyperfluorescence. Given

the peripheral nature of the subretinal fluid, it was decided to carefully observe the choroidal lesion and continue systemic treatment with sunitinib.

The discrepancy between the location of the lesion with its associated subretinal fluid and the degree of the patient's visual impairment prompted formal Humphrey visual field 24-2 Sita Standard testing. The visual field revealed a bitemporal hemianopia respecting the vertical midline and showed a reduced foveal threshold with diffuse depression in the left eye only (Figure 3A). Formal neuro-ophthalmology exam 3 weeks after presentation revealed decreased vision to 20/30 in the right eye and 20/250 in the left eye, 0.3 log unit left RAPD and 1 mm anisocoria with left pupil larger than right, colour vision of 2/6 right eye and 0.5/6 left eye by Hardy-Rand-Rittler plates, normal cranial nerve exam bilaterally with small exophoria, and stable dilated fundus exam. OCT of the retinal nerve fibre (RNFL) and macular ganglion cell plus inner plexiform layers (GCIPL) were obtained, showing normal RNFL in all quadrants bilaterally, and normal GCIPL in the right eye. On the left, there was diffuse thinning of the GCIPL with far temporal macular subretinal fluid and choroidal elevation (Figure 4). Review of past head CT images displayed a suspicious mass arising from the pituitary gland, first appearing on CT several months before the discovery of the choroidal metastasis and showing growth over time (Figure 3B). Magnetic resonance imaging (MRI) of the sella with and without gadolinium was urgently obtained and confirmed a homogeneously enhancing sellar mass measuring 2.1×2.4 cm. The mass also involved the pituitary infundibulum and tented up the central optic chiasm, displacing the left optic nerve apex (Figure 5A–C).

The patient was referred urgently to neurosurgery and underwent transnasal transsphenoidal resection of the pituitary mass, with pathology confirming a diagnosis of metastatic ccRCC. Pre-operatively, pituitary hormones LH and FSH were found to be suppressed, but the remainder of the hypothalamic-pituitary axis was functional. Post-operatively, he was followed by endocrinology for panhypopituitarism with chronic adrenal insufficiency. Post-operatively, visual acuity improved markedly to 20/20 in the right eye and 20/25 in the left eye, but bitemporal hemianopia remained on visual field testing. The choroidal lesion was monitored closely and did not

Figure 2. Clinical imaging of the choroidal metastatic lesion in the left eye. Color fundus photos and optical coherence tomography images of the lesion are shown at the time of presentation (A–C) as well as 15 months later, in the absence of local therapy directed at the choroidal tumour (B–D). The appearance 3 months after full-fluence photodynamic therapy is shown in panels E–F.

demonstrate growth; however, the patient developed left hilar adenopathy and a small right adrenal metastasis one month after resection of the pituitary mass and was switched to nivolumab.

While on nivolumab, the patient's choroidal mass initially demonstrated minimal growth. However, significant growth was noted by 5 months postpituitary resection, with the lesion now measuring 1.7 mm in height and associated with subfoveal subretinal fluid. Concurrently, he developed worsening diplopia with new pupil-involving partial cranial nerve III and VI palsies of left eye. Vision was decreased to 20/60 in the right eye and 20/200 in the left eye with very narrow confrontation visual fields of both eyes. Central visual acuity decline in the left eye was attributed to subretinal fluid and peripheral vision loss to suspected worsening of his optic neuropathy. After a discussion of options including anti-vascular endothelial growth factor injection, photodynamic therapy (PDT), and external beam

radiotherapy, the patient elected for bevacizumab intravitreal injection in the left eye. This treatment was not associated with decreased subretinal fluid or improvement in vision. He was concurrently re-referred to neurosurgery, with MRI showing marked tumour growth and enlargement into the suprasellar cistern with over 1 cm upward deflection of the optic chiasm (Figure 5D and 5E). Decision was made for palliative re-resection of the pituitary mass. Within the 10 days between his eye exam and his second surgery, he reported a continued rapid decline of peripheral vision in both eyes with almost no remaining vision in the right eye. Intraoperatively, dissection into the arachnoid and cisternal spaces revealed a large, highly vascular tumour. It filled the prechiasmatic space and receded down into the sella and pituitary region, displacing the optic nerves and chiasm upwards in a severe fashion. Decompression was achieved with extensive devascularization of the tumour bed and successful relaxation of the

A. Visual Fields on Presentation **B. Review of Non-contrast CT Head**

Figure 3. Visual field on presentation and review of prior incidental neuroimaging. Humphrey Visual Field Testing (24–2 Sita Standard testing strategy) on presentation, showing a bitemporal hemianopia respecting the vertical midline in both eyes. Consistent with his eye exam, the left eye produced a more diffuse and dense pattern of depression (mean deviation of -12.93 dB left eye versus -6.90 dB right eye), as well as a reduced foveal threshold of 22 dB left eye versus 31 dB right eye (A). Review of historical CT head non-contrast revealed the pituitary lesion with growth over time on coronal views (B).

chiasm and optic nerve positions. While he sustained metabolic delirium and seizures immediately post-operatively, compromising his ability to do eye exams, the right eye was noted to be no light perception while the left eye improved markedly to 20/25- over the next few weeks. During this period, he received 30Gy of palliative radiation treatment in 10 fractions to the pituitary, which he tolerated well.

Progressive growth of the choroidal lesion in the left eye was observed in parallel with systemic disease progression over the next few months. The lesion now measured 2.4 mm in thickness and was associated with subretinal fluid extending to the fovea, threatening vision in the left eye, which still measured 20/25- (Figure 2D–F). Given his overall poor functional status, PDT was recommended over

external beam radiotherapy as a single treatment session can result in a sustained regression of small metastatic choroidal lesions and it was felt that this approach would be better tolerated.^{7–9} Following one session of full-fluence PDT, a reduction in subretinal fluid and a decrease in tumour thickness to 1.1 mm was achieved (Figure 2G–I). Vision improved subjectively and by a few letters in Snellen acuity, and visual field in his left eye remained stable on subsequent neuro-ophthalmic exams despite eventual development of moderate compressive optic nerve pallor and RNFL/GCIPL thinning from the pituitary tumour. Unfortunately, the patient succumbed to widespread recurrence of his ccRCC 5 months after PDT treatment, but he maintained excellent visual acuity of 20/25 in the left eye for the remainder of his life.

Figure 4. OCT of the retinal nerve fibre layer (RNFL) and macular ganglion cell plus inner plexiform layer (GCIPL) on presentation to neuro-ophthalmology. RNFL testing within 3 weeks of symptom onset displayed normal thickness in all quadrants and clockhours of both eyes, whereas diffuse thinning of the macular GCIPL was noted in the left eye only, with far temporal artefact from the subretinal fluid due to the concurrent choroidal mass.

Discussion

This is the first reported case of choroidal and pituitary metastasis of RCC occurring in the same patient simultaneously. Choroidal metastases are the most common malignant intraocular tumours in adults.¹⁰ The most common primary tumour locations in patients with choroidal metastases are the breast or lung, with less than 1% from primary RCC.^{10,11} Uveal metastases from RCC have been reported previously, but are rare, with 30 or fewer published cases in the current literature.¹² In a retrospective review performed by Shields et al., primary RCC was found in only 2% of 420 patients with uveal metastasis.¹³ In another large clinical series, there was only one case of metastatic RCC in 70 patients with cancer metastatic to the uvea.¹⁴ Ocular metastases from RCC are most likely to involve the choroid, iris, and ciliary body, although eyelid, conjunctival, and orbital metastases have previously been described.⁵ ccRCC

generally presents as amelanotic or lightly pigmented choroidal masses, thus a solitary metastatic lesion can be mistaken for amelanotic choroidal melanoma in a patient without a known primary tumour.¹⁵ They also tend to be highly vascular tumours, and A-scan ultrasonography often shows a higher internal reflectivity than that of melanoma.

Metastasis to the pituitary gland, regardless of tumour type, is also uncommon. It is a clinical complication typically seen in elderly patients or patients with diffuse malignant disease. In an autopsy series, the incidence of latent pituitary metastasis was approximately 5% in all cancer patients, occurring most commonly in those with neoplasms of the breast, lung, and gastrointestinal tract.^{16,17} Metastases to the pituitary from RCC, in particular, are extremely rare, with fewer than 30 cases reported.¹⁷ In a recent literature review, RCC was described as the primary tumour in only 2.6% of metastatic pituitary lesions in a series of 380 cases.¹⁶

MRI of the Sellar Mass on Presentation **MRI of the Sellar Mass Prior to Re-resection by Neurosurgery**

Figure 5. MRI of the pituitary mass on presentation. MRI Brain demonstrated a homogeneously enhancing mass measuring 2.1×2.4 cm in the sella also involving the pituitary infundibulum with mass effect on the optic chiasm. The sellar mass is shown on T2-weighted coronal MRI in panel A (tented chiasm, arrow) and T1 post-contrast sagittal views (B, arrow). Panel C shows the superior extent of the infundibular lesion on T1 post-contrast axial views, which exerted a mass effect on the left optic nerve apex (arrow) and was responsible for the left optic neuropathy on presentation. Five months after transsphenoidal decompression of the lesion, clinical recurrence with decreased right eye vision and pupil-involving partial cranial nerve III and VI palsies of the left eye prompted repeat MRI brain. T2 FLAIR coronal view in panel D is shown for comparison, revealing post-surgical changes along with a markedly enlarged lesion extending into both cavernous sinuses, as well as superior extension into the third ventricle more than 1 cm (T1 post-contrast FSE sagittal view, panel E).

The pituitary and choroidal metastatic sites have different implications for treatment. While lesions may be controlled with systemic chemotherapy or targeted therapies, choroidal metastases typically require focal treatment. Options include radiotherapy directed to the eye, laser therapy directed to the lesion(s), or enucleation. The treatment of choice depends upon the location and size of the metastatic lesions, the ocular co-morbidities, the tumour type, and the patient's general health and life expectancy. As RCC is a relatively radio-resistant tumour, doses higher than typical for other metastatic carcinomas are typically required for the treatment of choroidal lesions, and there is increased risk of radiation toxicity to the eye.¹⁸ PDT has been reported as

an effective alternative treatment of choroidal metastatic lesions, with the advantages of a localized, outpatient treatment of low duration.^{7,9,19,20} PDT involves the use of the photosensitive drug verteporfin to specifically target the tumour's vascular endothelial cells and create reactive oxygen singlets that lead to necrosis and infarction.²¹ In a recent case series by Ghodasra et al., PDT was found to provide complete resolution of subretinal fluid in 18 of 21 tumours (86%) and 9 eyes (69%) had stable or improved visual acuity after 12 months.²⁰ PDT shows promise as an effective therapeutic treatment option for choroidal metastases in the macula, and it allowed our patient to preserve vision in his only seeing eye for the remainder of his life with a single treatment.

With regard to pituitary metastases, radiotherapy or surgical resection is the treatments of choice. Local radiation therapy improves symptom control for pituitary metastases and survival of patients, but long-term control has typically been poor with surgical resection and radiation alone.²² Concerns about radiation optic neuropathy complicate the decision to undergo radiation treatment, and they must be balanced with the risks and recovery required of neurosurgical intervention.

With the advent of newer chemotherapeutic agents, systemic treatment of extra-CNS metastatic RCC has improved significantly. In particular, multi-kinase inhibitors like sorafenib and sunitinib have been effective in controlling the growth of RCC metastases in many patients.^{23,24} Nivolumab, a monoclonal antibody immune programmed death-1 checkpoint inhibitor, has also shown promise in survival of patients with advanced RCC.²⁵ Immune checkpoint inhibitors like nivolumab may have better blood brain barrier penetration than other targeted therapies such as everolimus (an inhibitor of mammalian target of rapamycin), but the effectiveness of these checkpoint inhibitors on CNS structures remains to be seen, and monitoring metastatic lesions can be complicated by immune-mediated expansion of tumours in the absence of true tumour growth.^{26–28}

In summary, this case demonstrates a unique presentation of ccRCC. Improvement in survival of patients with metastatic RCC may be associated with increased incidence of ocular and central nervous system metastases affecting vision. Therefore, they should be carefully monitored for visual symptoms and early signs of treatment failure.

In particular, this case highlights the importance of a comprehensive eye examination with visual fields in patients presenting with visual impairment not otherwise explained by metastatic lesions within the eye.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

ORCID

Alison H. Skalet <http://orcid.org/0000-0002-4690-7957>
Molly S. Cardenal <http://orcid.org/0000-0002-7800-2781>
Kimberly M. Winges <http://orcid.org/0000-0001-9271-1640>

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