Renal cell carcinoma (RCC) is a rare malignancy characterized by a variety of clinical features. It represents approximately 3% of all adult malignancies and ranks 13th in frequency of all carcinomas.[1,2] RCC has been documented to metastasize to every organ in the body although metastasis to the eye and orbit is uncommon. Metastases may present decades after the removal of the primary disease. However, it is uncommon for patients who present with ocular metastasis before primary RCC is identified. We report a rare and unique case of metastatic renal cell carcinoma presenting as a choroidal mass despite no evidence of a primary tumour.

We present a case of a 65-year-old Chinese man who had sought treatment for a right-sided painful blind eye for 2 years which progressively worsened over time. His vision was poor since the age of 15 years and he was unsure of the cause. Initially, he was treated for the painful blind eye secondary to glaucoma and went for enucleation. Intraoperatively, we noticed that his vitreous cavity was filled with hard fibrotic mass. Histopathological examination was reported as right eye metastatic renal cell carcinoma with clear cell variant. Further investigation was done and he underwent exenteration in view of right optic nerve bulkiness which was also related to renal cell carcinoma. Interestingly, no tumour marker was positive and computed tomography (CT) thorax, abdomen and pelvis did not reveal any primary tumour. He did not complain of any adverse urinary symptoms and there were no signs and symptoms to suggest a concurrent renal pathology.

We report a rare and unique case of metastatic renal cell carcinoma presenting as a choroidal mass as the first presenting sign without evidence of a primary tumour. Differential diagnosis of metastases must be considered in patients who present with an ocular mass, despite being asymptomatic of any primary malignancy. This is to ensure that this condition is promptly identified and treatment initiated as soon as possible. By highlighting this case, we seek to bring awareness to this condition and hopefully improve on its current dismal prognosis by early diagnosis.
A 65-year-old, Chinese gentleman, with underlying hypertension, dyslipidemia and ischemic heart disease presented with a right-sided painful blind eye for 2 years which progressively got more intense. He had a history of right eye poor vision since the age of 15 but was unsure of the cause. The pain was associated with redness and tearing of the affected eye. There was a headache, but no nausea or vomiting. There was no aggravating factor and was occasionally relieved by analgesia. On the first visit to the ophthalmologist, he was told to have high intraocular pressure and planned for laser transcleral cyclophotocoagulation and counselled for evisceration. He was referred to us for a second opinion due to intolerable pain. On examination, right visual acuity (VA) had no perception of light for all quadrants. VA Left VA was 6/18, pinhole 6/12 with minimal cataract in otherwise normal. Relative afferent pupillary defect (RAPD) was positive on the right eye. The affected eye was phthisical with the presence of generalized conjunctiva injection and uveal tissue visualised underneath thinned sdera at 11 o'clock. Seidel's test was negative. Intraocular pressure (IOP) was 90 mmHg. Due to cornea opacity, the posterior segment could not be examined. We proceeded with a B-scan ultrasonography examination of the right eye which revealed the loss of globe contour with no obvious mass detected (Figure 1).

A diagnosis of painful blind eye secondary to absolute glaucoma was made, hence evisceration was performed. Intraoperatively, we noticed a multiple strongly adhered hard fibrotic mass on the inner surface of the scleral shell. Histopathological examination showed hyaline stroma infiltrated by atypical cells arranged in the nest and papillary-like pattern, hyperchromatic nuclei, with a surrounding area of osseous metaplasia, haemorrhage and tissues necrosis which was suspicious of metastatic renal cell carcinoma (Figure 2).

A systemic workup was done and the tumour marker showed negative for α-Fetoprotein (AFP), prostate-specific antigen (PSA), carcinogenic embryogenic antigen (CEA), CA 125 and CA 19-9. CT scan of the brain, orbit, thorax, abdomen and pelvis was performed to look out for the origin of the primary tumour. A well-defined heterogeneously enhancing right intraconal lesion was seen, which arose from the distal part of the affected optic nerve, with the lesion abutting the right superior rectus muscle. The rest of the right optic nerve appeared bulky and enhancing (Figure 3). Otherwise, it did not extend intracranially and other sites such as the lung, abdomen and both kidneys showed normal enhancement with no focal lesion seen. Interestingly, there was no CT evidence of a primary renal tumour.

Subsequently, we proceeded with an exenteration of his right eye. A biopsy from the optic nerve was taken. Microscopically, it showed infiltration of malignant cells arranged in papillary architecture with a fibrovascular core which was consistent with papillary adenocarcinoma (Figure 4). Immunohistochemically, the malignant cells were positive for renal cell carcinoma and PAX8, which were suggestive of kidney in origin (Figure 5). He was then referred to the oncology department and started with radiotherapy.
DISCUSSION

Renal cell carcinoma (RCC) previously known as hypernephroma describes adenocarcinoma or clear cell carcinoma of the kidney. It represents approximately 3% of all adult malignancies and ranks 13th in frequency of all carcinomas.1,2 It usually occurs in men between the ages of 30 and 60 years. Metastases commonly occur, with about 40% of patients presenting with metastatic disease.1,2 The occurrence of distant metastasis can appear in approximately one-third of cases after nephrectomy.

However, metastasis can also appear as the first presenting sign of RCC. The most common sites of metastatic spread are the lungs (76%), regional lymph nodes (66%), bone (42%), and liver (41%).1 Among all eye neoplasms, only a minority is due to renal cell carcinoma. In a pathology survey, only 7 out of 196 cases of ocular metastatic carcinoma originated from renal cell carcinomas.3 Ocular structures that are involved include iris (9%),4 ciliary bodies (2%)14 and choroid (88%)5 although eyelid, orbital, extraocular muscles, lacrimal gland, conjunctiva, sclera, retina and optic nerve involvement have also been reported. The choroid is the most preferred site for ocular metastasis due to its plentiful vascular supply. Metastasis to the ciliary body and iris is rare but has been described as a fleshy mass with prominent vascularisation.6 Choroidal metastases generally appear as a unifocal, solitary, yellow or reddish-orange-coloured mass in fundus examination. However, it is difficult to distinguish it from non-pigmented choroidal melanoma and other types of metastases. This reddish coloured tumour can also be seen in cases of choroidal haemangioma and other metastases.6 A study of uveal metastasis in 520 eyes by Shield et al. revealed that the tumour appeared as a solitary mass (71%) with a mean basal width of 9 mm and mean thickness of 3 mm. Other associated findings include subretinal fluid (73%) and retinal pigment epithelial alterations (57%), vitreous opacities, retinal infiltrates and haemorrhages. There is also a finding of vitreous haemorrhage as an initial sign of RCC.7 Haimovici et al. described a case of a 77-year-old man with known renal cell carcinoma who presented with hemorrhagic retinal detachment from choroidal metastasis.8

Reported cases of ocular metastasis from renal cell carcinoma are summarized in Table 1 below. The clinical features of choroidal metastases are variable and till now there is no sufficient data to distinguish them from other types of metastatic carcinoma. Choroidal metastases commonly present with painless loss of vision, loss of peripheral visual field, myodesopsia or pain due to neovascular glaucoma.8 In our case, the patient presented with the right painful blind eye with high intraocular pressure and sought treatment. Given the history of many years of unknown causes for poor vision since childhood and no systemic illness, a diagnosis of secondary glaucoma was made, hence laser transscleral cyclophotocoagulation (TSCPC) was performed once by the first attending ophthalmologist who treated him. He was then referred to our centre for intolerable eye pain despite post-laser treatment of TSCPC and maximum topical antiglaucoma.

Metastasis from renal cell carcinoma frequently causes diagnostic confusion as it may not present with the clinical triad of haematuria, pain, and abdominal swelling. Other signs and symptoms include weight loss, night sweats and malaise. The most common eye symptoms are blurred vision, flashes of lights and floaters. Orbital proptosis, ptosis, lid swelling, diplopia, or cranial nerve palsies are commonly associated with orbital metastasis. Patients may complain of pain due to secondary inflammation and glaucoma. However, these symptoms occur in only less than 10% of cases.8 Almost half of the cases with ocular metastases have eye signs and symptoms that precede the diagnosis1,8 similarly to our case. Interestingly, another feature of RCC is the tendency for long latency periods between the primary diagnosis and metastatic presentation which can be manifested from months to years, with the most extended case reported up to 25 years after the nephrectomy.10 On the contrary, all these signs and symptoms were absent in our case, except for a recent unilateral painful blind eye which accounted for only 10% of RCC cases as reported by Kurl et al.8
A retrospective review conducted by Shields et al[9] revealed that among 520 patients with uveal metastasis, only 2% of them were found to have primary renal cell carcinoma. Shield also revealed that 34% of patients had no previous history of cancer and at the end of the study, the primary site remained unknown in approximately half of these patients (17%) despite extensive investigations.[9] Many of them had a high risk of mortality and eventually died from a disseminated metastatic disease with the primary site still undiscovered as in our case. The majority of RCC cases were detected through systemic evaluation and multi-modality imaging of ultrasonography, CT scan and magnetic resonance imaging. Unfortunately, in our case, a CT scan of the thorax,
abdomen and pelvis revealed no evidence of a primary tumour.

In our patient, we postulated that the lesion was from uveal tissue, judging from visualized uveal tissue seen underneath the thinned sclera. Its origin was unsure as we were unable to view the fundus as the cornea was very opaque. The origin of the lesion could not be ascertained from B-scan ultrasonography due to loss of globe contour with no apparent mass detected. B-scan has substantial clinical variability with findings that usually mimic choroidal melanoma mass, with low internal reflectivity and acoustically hollow lesion.[2,11] In the case of choroidal involvement in RCC, there is a homogenous lesion with the presence of a dome-shaped lesion and collar button configuration seen in the B-scan.[2] Our patient had no known history of renal cell carcinoma, and no suspicion of metastases when performing B-scan. The only finding that alerted us was the presence of hard fibrotic mass during intra-op, which strongly adhered to the inner scleral shell which probably arose from the choroid.

Accurate diagnosis is possible through clinical findings in only 11 (16.4 %) out of 68 cases of ophthalmic metastasis of RCC in the literature, whereas histopathology examination (HPE) is crucial in aiding diagnosis in the rest.[12] This emphasises the role of histopathology and immunohistochemistry in the diagnosis of metastatic renal cell carcinoma as per our case. It was only confirmed after a second biopsy from the optic nerve, which revealed positive nuclear staining for PAX 8 in the immunohistochemistry test (Figure 5).

The management of renal cell carcinoma involves treatments of the primary tumour with one or a combination of surgery, chemotherapy, radiotherapy, or immunotherapy. If nephrectomy for a primary tumour has already been performed, the intraocular and orbital metastasis is generally treated with radiotherapy.[12] Realistically, ophthalmologic treatment, in our case, was exenteration for his intractable pain since he also had optic nerve involvement. Our patient was also referred to the oncology team for radiotherapy.

In short, diagnosing RCC metastasis can be extremely confusing. Patients with intraocular metastasis may remain undiagnosed unless they become symptomatic. A detailed history taking such as previous nephrectomy and specific or non-specific renal signs will be beneficial to aid in the diagnosis. All patients must be carefully examined and investigated, particularly when they present with a suspected ocular metastasis with no cancer history.

CONCLUSIONS

The main highlight of this case is to this date, we are still unable to identify and detect the location of the primary tumour. Renal assessment by the urology team could not rule out the possibility of renal being the primary tumour. There was an absence of urinary symptoms and other signs to suggest a concurrent renal pathology. All relevant tumour markers were negative and CT thorax, abdomen and pelvis showed no evidence of any primary tumour. A study by Ferry et al. revealed that the interval from ocular therapy to the detection of a primary tumour in the kidney can be up to one year.[3] Therefore, even with no apparent source of the primary tumour at the time of assessment, a patient must be closely observed and continuously followed up in the urology department to allow for early detection of tumours shall they arise later. The use of routine surveillance imaging during follow up may allow the detection of early metastasis.

This is a case of a rare disorder which is made more confounding by its uncommon presentation. It appeared as pathology in the eye and had no apparent signs and symptoms to suggest that the primary disease was in the kidney. Unfortunately, the uncommon presentation and the lack of renal symptoms had lulled the patient into complacency. We present a rare and unique case of metastatic renal cell carcinoma presenting as a choroidal mass without evidence of a primary tumour. By highlighting this case, we seek to bring awareness to this condition and hopefully improve on its current dismal prognosis by early diagnosis.

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