DOI: 10.5603/OJ.2023.0006

Simultaneous choroidal melanoma and renal cell carcinoma in middle-aged patient

Qusai F. Abu Salim[1], Mona Mohammad[1], Jakub Khzouz[2], Rami Ghanem[3], Yacoub A. Yousef[1]

[1]Department of Surgery (Ophthalmology), King Hussein Cancer Centre, Amman, Jordan
[2]Department of Pathology and Laboratory Medicine, King Hussein Cancer Centre, Amman, Jordan
[3]Department of Surgery (Uro-oncology), King Hussein Cancer Centre, Amman, Jordan

ABSTRACT

BACKGROUND: Although rare, choroid melanoma is the most common intraocular malignancy amongst adults. Similarly, renal cell carcinoma (RCC) is another rare malignancy that counts for 2–3 percent of all adult malignancies. Second primary cancers are not uncommon, even though they occur less frequently than primary cancers.

CASE PRESENTATION: We present a rare choroidal melanoma case in a 55-year-old adult who presented with a one-month history of the painless gradual decrease of vision. His investigations revealed a clinical diagnosis of large choroid melanoma, and upon metastatic workup, he was incidentally found to have synchronous RCC. Both malignancies were treated surgically (and the pathology confirmed the clinical diagnosis of choroidal melanoma and RCC). The patient was free of metastatic or recurrent disease at 12 months follow-up.

KEY WORDS: uveal melanoma; renal cell carcinoma; synchronous

Ophthalmol J 2023; Vol. 8, 25–28

INTRODUCTION

Uveal melanoma (UM), the most common primary intraocular malignant tumor in adults, accounts for only five percent of all melanomas. The disease is more common in Caucasians [1].

In Jordan, the incidence of uveal melanoma is 1.39 cases per million population per year), which is less than in the Western Caucasian population, with a mean age of 45 years [2].

The tumor may involve any part of the uveal tract: choroid (85%), ciliary body (4–7%), or the iris (2–4%) [3]. Besides, small and medium-sized tumors are usually treated by Iodine-125 radioactive plaque therapy [4]. In contrast, large tumors are usually treated by enucleation [5], despite the fact that radiotherapy can achieve 90% local control of UM, up to 50 percent of patients develop hematogenous metastases in the decades following their initial diagnosis. These metastases affect the liver in over 90% of patients. Metastatic UM is always fatal, with an average survival time of fewer than six months [6]. Conversely, renal cell carcinoma (RCC) accounts for approximately 2% to 3% of all adult malignancies [7]. It is also worth noting that one-third of patients who undergo nephrectomy experience distant metastasis [8].

Importantly, both the detection of second primary cancer and the detection of early-stage primary

CORRESPONDING AUTHOR:
Yacoub A. Yousef, MD, Consultant Ocular Oncologist, King Hussein Cancer Centre, Queen Rania Street, P.O. Box 1269 Al-Jubeiha, Amman 11941 Jordan, tel: 962-6-5300-460, ext. 1304, fax: 962-6-534-2567; e-mail: yyousef@khcc.jo

cancer can improve survival. Second primary cancers are not uncommon, even though they occur less frequently than primary cancers [9–11]. A retrospective case review of 139 patients with uveal melanoma who were subsequently evaluated by whole-body [18-fluorine-labeled] 2-deoxy-2-fluoro-D-glucose (^{18}FDG) positron emission tomography/computed tomography (PET/CT) imaging showed six patients (4.3%) had second primary cancers as (50%) were synchronous (found at initial staging), and the remaining 3 patients (50%) were metachronous (found at follow-up staging) [12].

We present a case of a middle-aged man who was seen in the King Hussein Cancer Center (KHCC) outpatient clinic in Amman/Jordan with these two malignancies and no other medical history. This case demonstrates the possibility of two different primary tumors coexisting in the same patient, which has significant implications for the individual management of these conditions.

CASE PRESENTATION

A 55-year-old gentleman who has no medical co-morbidities with an unremarkable family history of malignancies presented to the clinic with a one-month history of a painless drop of vision in the right eye. On eye examination, visual acuity for the right eye was 6/24, and the left eye was 6/9.

A slit-lamp exam showed a mild right eye cataract; a dilated fundus exam showed a right eye ciliary body melanotic mass on the temporal side with overlying exudative retinal detachment.

The left eye exam was unremarkable. Ocular B-scan ultrasound (U/S) and ultrasound biomicroscope (UBM) scans (Fig. 1) showed a right mushroom-shaped choroidal lesion associated with overlying retinal detachment and low-to-moderate- internal reflectivity, with the following dimensions (thickness 13.5 mm, base dimension 17.0 mm x 16.0 mm). These clinical and sonographic features were consistent with the right eye's large-sized ciliary body melanoma.

During systemic workup for disease staging, full body CT scan showed a 4.2 cm enhancing cortical mass lesion in the anterior aspect of the upper part of the right kidney that indents the renal sinus with no extension to the renal vein or inferior vena cava (IVC), with no evidence of distant metastasis or no enlarged lymph nodes. Additional investigations were done by taking a biopsy from the renal mass under the U/S guidance. Pathology showed papillary renal cell carcinoma World Health Organization/International Society of Urological Pathology (WHO/ISUP) grade 2. The cells were positive for cytokeratin 7 (CK7) and epithelial membrane antigen (EMA) with granular cytoplasmic positivity for alpha-methylacyl-CoA racemase (AMACR) and negative for transcription factor E3 (TFE-3) immunostaining. All are suggestive of RCC. The second primary renal cell carcinoma diagnosis was made following consultation with an uro-oncologist surgeon. The management plan was modified to treat the non-metastatic right ciliary choroidal melanoma separately from the second primary renal cell carcinoma. Accordingly, the multidisciplinary treatment plan for the large-sized ciliary body melanoma was right eye enucleation and orbital implant insertion, given the large tumor size beyond the radiotherapy capacity. The right RCC was planned for the right laparoscopic partial nephrectomy.

Therefore, the patient underwent a right laparoscopic partial nephrectomy with intraoperative ultrasound without complications. The pathology report confirmed the diagnosis of papillary RCC, type 2 ISUP grade 3, pT1aNX (Fig. 2).

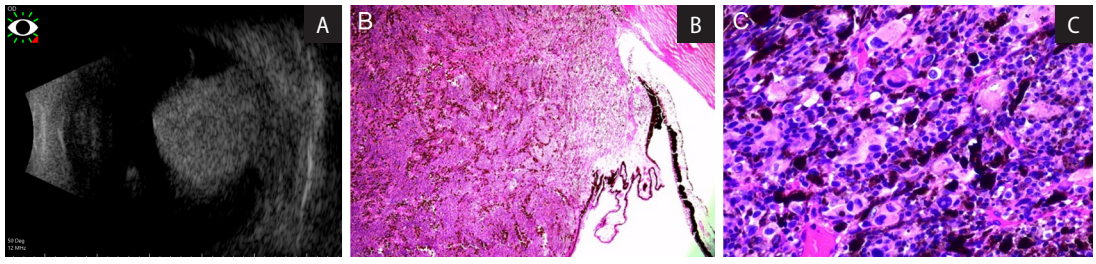

Figure 1A. B-scan ultrasound shows a mushroom-shaped choroidal lesion associated with overlying retinal detachment and low-to-moderate- internal reflectivity suggestive of choroidal melanoma; **B.** 4x hematoxylin and eosin (H&E) slide (ciliary body malignant melanoma): Pigmented predominantly spindle cell tumor arranged in fascicles arising from the ciliary body; **C.** 40x (ciliary body malignant melanoma): the tumor is of mixed cell type with foci showing Large and small Epithelioid cells with abundant eosinophilic cytoplasm, prominent nuclei, and inclusions. This tumor exhibits prominent tumor-infiltrating lymphocytes and macrophages. Abundant melanin pigmentation is seen

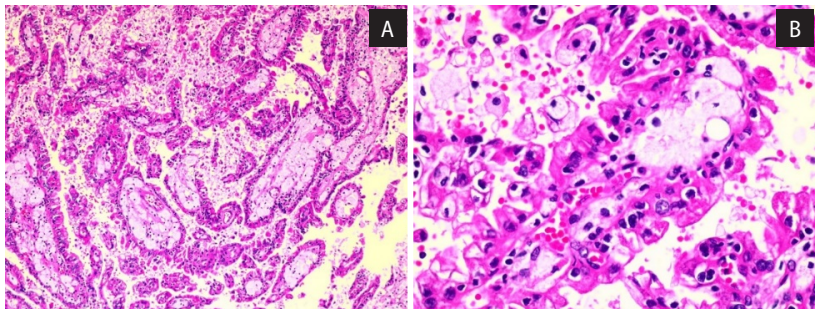

Figure 2.A. 10x haemotoxylin and eosin (H&E) (kidney tumor): this low-power view shows a papillary tumor lined by malignant eosinophilic cells arranged around Lympho-vascular cores with prominent foamy histiocytes; **B.** 40x H&E: high power view of one of the cores shows a single layer of eosinophilic cells with irregular hyperchromatic nuclei arranged around the core containing foamy histiocytes

Four weeks later, after full recovery from the previous operation, the patient underwent a right eye enucleation and orbital implant insertion. The pathology showed ciliary body melanoma, mixed cell type, pT4b with no extra-scleral extension with features including domed shaped, placed inferotemporal anteriorly (ciliary body) with a greatest basal diameter of 28 mm and 10mm distance from the optic disc (Fig. 1). At 12 months follow-up, the patient was doing well with the excellent prosthetic eye, with no disease recurrence for either the eye or the kidney, and the whole-body CT scan showed no distant metastasis.

DISCUSSION

Despite being infrequent, the prevalence of multiple primary malignancies is increasingly widely identified because of advanced diagnostic equipment and the extended survival of cancer patients. The reasons for different multiple neoplasms are unclear, but several risk factors, including family history, genetic mutation, environmental factors, smoking, and radiation exposure, have been suggested to be involved. Multiple primary tumors are considered the presence of more than one synchronous or metachronous cancer in the same patient. The diagnostic criteria for multiple primary cancer remain the same criteria advocated by Warren and Gates in 1932 [13]. Namely:

- each cancer must be definitively malignant by histopathology;
- they must be histologically different;
- the possibility of metastasis among the cancers must be excluded.

In this case report, we described a synchronous occurrence of different pathological conditions (uveal melanoma and RCC), which were managed accordingly.

In the literature, two studies showed cases of clinical second primary neoplasms long with uveal melanoma had been reported between 2000 and 2020. Ten out of 333 patients (3.3%) had synchronous second cancers, and six out of 139 patients (4.3%) had second primary cancer (50%) were synchronous, and (50%) were metachronous [12]. In the present case, the 55-year-old middle-eastern patient with an olive-brown skin colour has a negative medical and family history. He has no history of chemotherapy or radiation exposure. The UM and RCC were asymptomatic and were diagnosed incidentally. And all lesions were resected successfully.

Uveal melanomas have an incidence of 6 per 1 000 000 per year in white adults and are more common in white than in non-white races, with a mean age of 60.14. The main treatment for UM depends on the size and location of the tumor. Large tumors or tumors close to the optic nerve usually require enucleation. Smaller tumors can be treated by local excision, local radiation, or proton beam irradiation [15]. Differential diagnoses of the patient involved hemorrhage in the subretinal or suprachoroidal space, choroidal hemangioma, solitary choroidal granuloma, and choroidal metastasis. The clinical and echographic features were typical for primary uveal melanoma, which was confirmed with histopathology after enucleation.

Renal cell carcinoma is the most common malignant tumor of the adult kidney and the most lethal of all malignancies. It is more common in males in the 6^{th} and 7^{th} decade and usually involves the upper pole. It has a satisfactory prognosis after surgical resection. Radical nephrectomy is the primary treatment for localized RCC [16]. There was no sign of renal problems in the patient's medical history. Normal blood test results, urine analysis, and kidney function tests ruled out renal impairment. As

the case presented here is not in the advanced stage of UM and RCC, there were no complications or signs of organ impairment except right-eye vision. Important to remember that UM and RCC in their early phases can be missed, left untreated, and escalate to irreversible symptoms, particularly in developing countries. It is essential to establish whether these tumors are hereditary by interviewing patients with multiple primary neoplasms. This information might be helpful for doctors to assess cancer risk and optimize treatment. This case report has a limitation: we did not test for the specific mutation of the patient and his relatives as this test is unavailable. However, the systemic workup for this patient who presented with uveal melanoma could reveal another primary tumor, and this approach saved his life.

REFERENCES

1. Finger PT. Intraocular Melanoma. In: Devita VT, Lawrence TS, Rosenberg SA. ed. Cancer (Principles & Practice of Oncology) Ophthalmology 10th ed. Wolters Kluwer 2011: 1770–1779.
2. Yousef YA, Mohammad M, Al-Nawaiseh I, et al. Retinoblastoma and uveal melanoma in Jordan: incidence, demographics, and survival (2011-2020). Ophthalmic Genet. 2022 [Epub ahead of print]: 1–8, doi: 10.1080/13816810.2022.2090008, indexed in Pubmed: 35848346.
3. Shields CL, Shields JA, Gross NE, et al. Survey of 520 eyes with uveal metastases. Ophthalmology. 1997; 104(8): 1265–1276, doi: 10.1016/s0161-6420(97)30148-1, indexed in Pubmed: 9261313.
4. Jaradat I, Zewar A, AlNawaiseh I, et al. Characteristics, management, and outcome of patients with uveal melanoma treated by Iodine-125 radioactive plaque therapy in a single tertiary cancer center in Jordan. Saudi J Ophthalmol. 2018; 32(2): 130–133, doi: 10.1016/j.sjopt.2017.12.002, indexed in Pubmed: 29942182.
5. Zewar A, Nawaiseh I, Jaradat I, et al. Management and Outcome of Uveal Melanoma in a Single Tertiary Cancer Center in Jordan. Turk Patoloji Derg. 2016; 32(3): 186–192, doi: 10.5146/tjpath.2015.01357, indexed in Pubmed: 27562393.
6. Kujala E, Mäkitie T, Kivelä T. Very long-term prognosis of patients with malignant uveal melanoma. Invest Ophthalmol Vis Sci. 2003; 44(11): 4651–4659, doi: 10.1167/iovs.03-0538, indexed in Pubmed: 14578381.
7. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2007. CA Cancer J Clin. 2007; 57(1): 43–66, doi: 10.3322/canjclin.57.1.43, indexed in Pubmed: 17237035.
8. Motzer RJ, Bander NH, Nanus DM, et al. Infrequent ras oncogene point mutations in renal cell carcinoma. J Urol. 1990; 143(1): 175–178, doi: 10.1016/s0022-5347(17)39905-6, indexed in Pubmed: 2403598.
9. Choi JY, Lee KS, Kwon OJ, et al. Improved detection of second primary cancer using integrated [18F] fluorodeoxyglucose positron emission tomography and computed tomography for initial tumor staging. J Clin Oncol. 2005; 23(30): 7654–7659, doi: 10.1200/JCO.2005.01.4340, indexed in Pubmed: 16234527.
10. Diener-West M, Reynolds SM, Agugliaro DJ, et al. Collaborative Ocular Melanoma Study Group. Second primary cancers after enrollment in the COMS trials for treatment of choroidal melanoma: COMS Report No. 25. Arch Ophthalmol. 2005; 123(5): 601–604, doi: 10.1001/archopht.123.5.601, indexed in Pubmed: 15883277.
11. Rheingold SR, Neugut AI, Meadows AT. Second cancers: Incidence, risk factors, and management. In: Kufe DW, Pollock RE, Weichselbaum RR. et al. ed. Cancer medicine, 6th ed. BC Decker, Hamilton, Ontario 2003: 2623–2631.
12. Chin K, Finger P, Kurli M, et al. Second cancers discovered by 18FDG PET/CT imaging for choroidal melanoma. Optometry J Am Optom Assoc. 2007; 78(8): 396–401, doi: 10.1016/j.optm.2007.03.013.
13. Warren S, Gates O. Multiple primary malignant tumors. Surgery of literature and statistical study. Am J Cancer. 1932; 16: 1358–1414.
14. McLaughlin CC, Wu XC, Jemal A, et al. Incidence of noncutaneous melanomas in the U.S. Cancer. 2005; 103(5): 1000–1007, doi: 10.1002/cncr.20866, indexed in Pubmed: 15651058.
15. Wang Z, Nabhan M, Schild SE, et al. Charged particle radiation therapy for uveal melanoma: a systematic review and meta-analysis. Int J Radiat Oncol Biol Phys. 2013; 86(1): 18–26, doi: 10.1016/j.ijrobp.2012.08.026, indexed in Pubmed: 23040219.
16. Khalil Ibrahim A. Trends of adult primary malignant renal tumors over 6 years. Pak J Med Sci. 2013; 29(6): 1385–1388, doi: 10.12669/pjms.296.3736, indexed in Pubmed: 24550959.