Incidental Finding Of Renal Cell Carcinoma In Patients With Previous Choroidal Melanoma: Possible Genetic Linkage Through Defects In Chromosome 3

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INTRODUCTION

Choroidal metastases from renal cell carcinoma primary are well documented (1). To our knowledge, there are only 2 previous reports of a choroidal melanoma associated with RCC (2,3). In both cases the RCC preceded the development of the choroidal melanoma. One patient had diffuse metastatic disease the other previously resected RCC. In both of our cases the renal cell carcinoma was discovered incidentally at routine surveillance scanning following treatment of choroidal melanoma.

Uveal melanoma is a rare tumour affecting 6-7 cases per million in North America (4). Similarly renal cell cancer incidence is reported as 6-12 cases per 100000 population (http://www.cancerresearchuk.org). Finding two patients with both independent, rare tumours, within the same institution raises the question of genetic predisposition to malignancy. We explore and discuss the possible mechanisms behind this association.

CASE REPORT AND MANAGEMENT

CASE REPORT 1

An 83 year old female presented to her general practitioner in 1999 with reduced visual acuity in her right eye. Ophthalmology referral was sought and a choroidal (also known as uveal) melanoma was diagnosed associated with a detached retina of the eye. Choroidal melanoma is a clinical diagnosis, treated on suspicion and observation (5). Accordingly she was treated by temporary insertion of ruthenium plaque brachytherapy rather than enucleation. No formal tissue diagnosis was established. Complete response was observed with no local recurrence at follow up.

At routine follow up CT scanning 17 months following initial diagnosis a 5cm upper pole lesion was identified incidentally in the left kidney. In view of the suspicion of metastatic melanoma CT guided biopsy was performed which confirmed a low-grade neoplasm of renal origin.

In view of the patient's general frailty and age, along with the low grade, the patient was treated conservatively and died of unrelated illness with no evidence of metastases or increase in tumour size 33 months after diagnosis of her renal lesion.

CASE REPORT 2

A 72 year old female presented in 2002 with reduced visual acuity in her right eye associated with floaters. At ophthalmology review a peripheral lesion in the right temporal region was identified and thought to represent a choroidal melanoma. To confirm this diagnosis serial ultrasound scanning was performed which demonstrated the lesion to increase in size over the following month.

The patient proceeded to treatment by temporary ruthenium plaque insertion, with a complete local response. Routine
surveillance ultrasound scanning of the liver identified textural changes of the liver parenchyma and CT scanning was carried out. This identified a 2cm possible cyst or mass at the lower pole of the right kidney as an incidental finding, the liver was normal. MRI confirmed the lesion was solid rather than cystic 4 months after initial presentation.

In view of the possibility of metastatic melanoma CT guided biopsy was performed, the initial biopsy inconclusive with repeat biopsy confirming renal cell carcinoma.

The patient recently underwent partial nephrectomy which confirmed the presence of clear cell carcinoma with chromophil elements. She remains alive and well 34 months after surgery with no evidence of metastatic disease from either primary.

**DISCUSSION**

The von Hippel-Lindau (VHL) tumour suppressor gene has been mapped, using genetic linkage studies, to the short arm of chromosome 3 at 3p25-26 (6). Defects in this gene result in von Hippel-Lindau disease, an autosomal dominant condition characterised by highly vascular tumours of multiple organs, including the CNS, kidney, adrenal and pancreas. There is a 70% probability of these patients developing renal cell carcinoma (RCC) by the seventh decade (7).

Fifty to sixty-five percent of non-familial sporadic clear cell RCCs demonstrate mutations of the VHL gene (8). 85% of these tumours demonstrate loss of heterozygosity at the VHL locus.

Primary choroidal melanoma associated with subsequent diagnosis of renal cell carcinoma has not been previously reported. We propose a causal link between both conditions due to common susceptibility of chromosome 3 to mutation.

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**REFERENCES**

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