

Asynchronous Multifocal Renal Cell Carcinoma In The Contralateral Kidney 10 Years After Primary Diagnosis

J Hull, K Anson, H Pandha

Citation

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Abstract

We present a case of multifocal asynchronous renal cell carcinoma which developed almost a decade after the primary was resected. Although detected in an asymptomatic patient within a current surveillance programme, the anatomical location of the tumours precluded any form of nephron-sparing intervention. We discuss the biological and clinical aspects of asynchronous recurrence of renal cell carcinoma in the contralateral kidney.

INTRODUCTION

Renal Cell Carcinoma (RCC) accounts for 90 % of all renal tumours and approximately 1-2 % of all malignancies. In 75% of all cases the presentation is of unilateral NOMO disease. However, between 1.8 – 3.8 % of patients present with synchronous or asynchronous bilateral disease₁. Bilateral disease exists both in hereditary (e.g. von Hippel-Lindau disease₁) and sporadic forms₂. Renal bed recurrence or distant metastases may occur as late as 24 years after the diagnosis of the primary is made₃, and may be treated by surgery and/or immunotherapy. Asynchronous recurrence confined to the remaining kidney is treated surgically to maximise preservation of native renal tissue by tumour enucleation₄ or partial nephrectomy₅. If this is not technically possible, the patient is considered for nephrectomy and dialysis. We present a case of patient with asynchronous multifocal RCC occurring 10-years after initial nephrectomy and discuss the management dilemmas this posed.

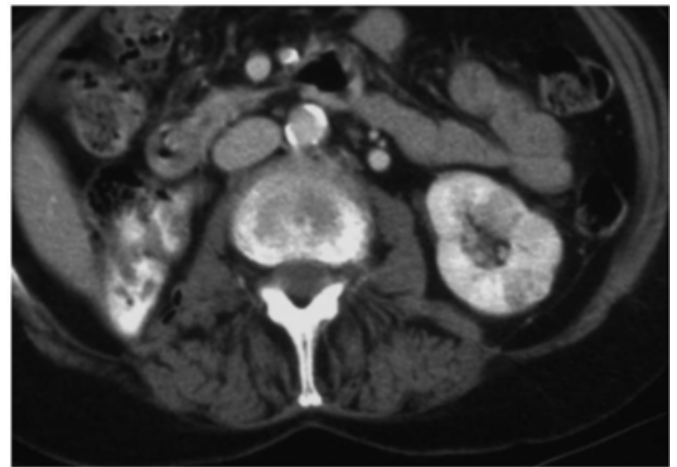
CASE REPORT

A 73-year-old female presented with a short history of malaise associated with a tumour arising from the right kidney. She underwent open nephrectomy for a G2pT1b multifocal clear cell carcinoma. There were no other adverse histological features or family history of malignancy. No adjuvant therapy was given. She was evaluated twice yearly by clinical examination and abdominal ultrasound and remained completely asymptomatic. However in the tenth year of follow-up, abdominal ultrasound revealed multiple lucencies in the remaining kidney consistent with multifocal

carcinoma. Figure 1.

Figure 1

Figure 1: Computer axial tomography scan showing multifocal carcinomas within the remaining kidney. There is no evidence of disease elsewhere within the abdomen.



Staging investigations indicated no evidence of local invasion or distant metastases. Needle biopsy of one lesion confirmed clear cell carcinoma and identical histology to the contralateral multifocal tumour removed 10 years previously. Due to their anatomical location, partial resection or selective destruction of individual tumours was not feasible. The patient declined nephrectomy and the inevitable need for dialysis support. Over the last 12 months, she has progressed radiologically within the kidney despite interferon-alpha and, subsequently, thalidomide.

DISCUSSION

NOMO RCC has been reported to recur at any site in 20-50% of patients. In approximately half of these cases disease will recur within two years^{6,7,8,9}. Patients at highest risk of recurrence within this time are those with high pT stage, high tumour grade and the development of symptoms¹⁰. In contrast to our patient, previous studies have found that up to 75% of patients become symptomatic at the time recurrence is detected⁶. Multifocal intrarenal RCC in our patient is a different clinical entity to concomitant bilateral RCC, which may be associated with von Hippel-Lindau¹ disease or a positive family history of RCC². Our patient had no family history of any malignancy (and declined any form of genetic analysis). Multifocality occurs in 7-25% of RCCs but little is known about its biological behaviour and malignant potential of satellite tumours^{11,12,13}. Multifocality in RCC cannot be predicted reliably, although has been associated with papillary histology but, surprisingly, low tumour grade and low stage. In a necropsy series of 260 RCCs, 36 cases had multifocal nodules within the same kidney, which ranged 3mm to 23mm in size. Remarkably, in 31 of these 36 cases, multiple RCC tumours were also found in the contralateral kidney, but there was no association with metastasis outside the kidney¹⁴. Within the same kidney, multifocal RCC have similar patterns of chromosomal alterations by cytogenetic and comparative genomic hybridisation analysis, as well as comparable telomerase activity especially in clear cell RCC. A recent study evaluated different tumours in the same kidney, and demonstrated identical loss of heterozygosity and shift patterns suggesting a common clonal origin. The findings suggested that satellite tumours are the result of intrarenal metastases from the primary tumour¹⁵. There is no comparable data with respect to recurrent multifocal disease in the contralateral kidney as in our patient.

Previous reports of recurrent asynchronous RCC have shown that disease is usually located in the renal poles¹⁶ allowing nephron sparing surgical techniques such as enucleation, cryoablation or partial nephrectomy to be considered. These procedures have been associated with good long-term outcome^{5, 17,18,19}. Novick et al reported a 67 % 3 year survival rate after operative therapy compared to only 17 % in those patients treated non-operatively²⁰. He also observed a 90 % 3-year-survival rate in follow up of enucleated tumours in a solitary kidney.

The fact that multifocal asynchronous disease may occur

without symptoms and after a significant time delay highlights important issues with regards optimal surveillance. Our patient underwent our local surveillance protocol and her recurrent tumour discovered as a result. It remains unclear as to the most appropriate follow up for this patient group. Current European guidelines suggest case specific surveillance decisions for multifocal organ confined disease²¹. Multifocal disease, as in our patient, may preclude nephron sparing intervention. The patient and clinician may be left no alternative but to consider radical nephrectomy and dialysis, with obvious and profound consequences with regards to quality of life and health service costs²². In one study, this approach has been associated with a 44 % 5-year survival²³. After due consideration our patient declined this option. She has subsequently failed to respond to interferon and thalidomide and is now considering further experimental therapies. Her disease is still confined to the remaining kidney.

CONCLUSION

In summary, we present a case of multifocal asynchronous RCC that developed almost a decade after a primary RCC was resected. Although detected in an asymptomatic patient within a current surveillance programme, the anatomical location of the tumours precluded any form of nephron-sparing intervention. The management options of close surveillance, immunotherapy or nephrectomy plus dialysis need to be discussed in great detail with the patient and carers.

CORRESPONDENCE TO

Hardev S Pandha FRCP FRACP PhD Senior Lecturer in Medical Oncology Department of Oncology St George's Hospital Medical School Cranmer Terrace London SW 17 ORE Tel 020-87251255 ext 5815 Fax 020-87250158 hpandha@sghms.ac.uk

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Author Information

James Hull, MRCP

Senior House Officer, Department of Oncology, St George's Hospital Medical School

Ken Anson, MS FRCS (Urol)

Consultant Urologist, Department of Urology, St George's Hospital Medical School

Hardev S. Pandha, FRCP FRACP PhD

Senior Lecturer in Medical Oncology, Department of Oncology, St George's Hospital Medical School