Does one plus one always equal two?

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See Online for appendix

14 years after deceased-donor kidney transplantation, a 51-year-old man with stable graft function was shown to have an asymptomatic mass in his native kidney during annual ultrasonography in July, 2010. He had end stage renal disease secondary to glomerulonephritis. Post-transplant immunosuppression included ciclosporin, mycophenolic acid, and prednisone, without biological antibody therapy. The doses and blood concentrations of his immunosuppressants were at the mid to lower ends of standard practice. MRI showed a 7 cm right (native) renal tumour and 2·5 cm tumour in his transplant kidney. Radical right native nephrectomy and partial transplant nephrectomy were done uneventfully. Microscopically, both tumours were renal cell carcinoma (RCC) clear-cell type (pT1b in native kidney [figure A] and pT1a in transplant [figure B]) grade 3 Fuhrman nuclear grading (figure inserts). There were no microscopic cancer satellites beyond the capsules of the tumours, intravenous tumour thrombi, or metastasis in any of the 11 perihilar lymph nodes removed.

To assess prognosis and further management we needed to know whether both tumours had formed de novo from the recipient's and donor's kidney or whether one was metastatic. If both were de novo, surgical excision was potentially curative (stage I RCC 5-year survival of about 81%).[1] Alternatively, one being metastatic would indicate a systemic stage IV disease (5-year survival of about 8%).[1] We investigated the genetic identity of both tumours by short tandem repeats (STR) using AmpFISTR kit (Life Technologies, CA, USA). DNA samples from the recipient (buccal) and donor (frozen lymphoid cells), and multiple tissue blocks of both tumours were tested in duplicates. A buccal swab was collected from the recipient to avoid potential contamination by the donor alleles in case of donor lymphoid microchimerism. The identified STR alleles of each tumour were compared with the recipient and the donor alleles. The alleles identified in both tumours were identical to the recipient alleles (see also appendix). We concluded that the RCC in the transplant kidney was a metastasis from the native RCC. 2 months later our patient had a traumatic right humeral fracture. The bone specimen excised showed metastatic RCC. Post-wound healing treatment included weekly temsirolimus infusion and 15 mg oral prednisone daily. Other immunosuppressants were discontinued. When last seen in November, 2011, our patient had a serum creatinine of 129·6 µmol/L, his follow-up MRI showed smaller and fewer metastatic bone lesions, and he had a good quality of life.

The mechanism of metastasis in our patient was most likely haematogenous, because all excised lymph nodes were cancer free and there were many intra-tumoural vascular channels into which tumour cells might get dislodged. Among renal transplant recipients RCC is the most prevalent urological malignancy in both native and transplanted kidneys.[2] Annual ultrasonographic screening after transplant facilitates early detection.[3] RCC occurring in the renal allograft accounts for around 10% of the cases.[4] Metachronous RCCs in graft and native kidneys, with different cell origins have been reported,[5] but simultaneous RCCs in native and transplant kidneys have not been reported previously according to the Israel Penn International Transplant Tumour Registry (consult #1003077), as of Sept 3, 2010. Combining histological and genetic identity studies effectively determined the origin of tumours identified in the context of solid organ transplantation; and emphasised the importance of bench-bedside collaboration.

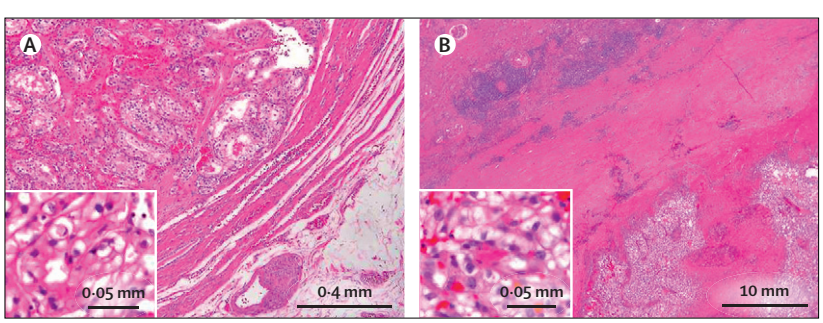

Figure: **Microscopic appearance of the renal cell carcinomas**
(A) Native kidney: tumour cells (left upper) extend up to but not through the renal capsule; insert: tumour cells. (B) Transplant kidney: well-encapsulated tumour cells (right lower) and viable glomeruli and tubules (left upper); insert: tumour cells.

Contributors
MA: genetics testing, writing the report; SJC: patient management, literature search, and writing the report; TEH: pathological analysis, figure, and reviewing the text; BRS: patient management, literature search, and reviewing the text. Written consent to publish was obtained.

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