CASE REPORT

Papillary Renal Cell Carcinoma in a patient with renal transplant

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Abstract

Kidney transplantation is the treatment of choice for patients with end-stage kidney disease (ESKD) on renal dialysis, and is associated with cancers, cardiovascular diseases and infections attributed to the usage of immunosuppressive drugs. A wide variety of cancers across a number of organs occur with substantially increased incidence after renal transplant. Most studies show that cancer risk is the greatest for viral-related malignancies. There is increased risk of native kidney malignancy among transplant recipients compared with the general population. We present a case of a 34-year-old young male patient who presented with papillary renal cell carcinoma (PRCC) in the native kidney 5 years post-renal transplantation.

Keywords: Renal cell carcinoma, Renal transplant.

Introduction

Kidney transplantation is the treatment of choice for patients with end-stage kidney disease (ESKD) on renal dialysis, and is associated with cancers, cardiovascular diseases and infections attributed to the usage of immunosuppressive drugs. Literature shows that the aetiology is multifactorial, but prolonged and intensive use of immunosuppressant drugs in transplant patients leads to alteration of immune function and immune surveillance and is associated with increased risk of cancer.[1-3] Other studies show that there is uncertainty as to whether the increased risk is due to immune suppression or related to pre-existing cancer risk factors or factors related to ESKD or dialysis.

A wide variety of cancers across a number of organs occur with substantially increased incidence after renal transplant. Most studies show that the cancer risk is the greatest for viral-related malignancies. For example, cancers related to human papilloma virus (HPV), human herpes virus 8 (HHV-8), Epstein-Barr virus (EBV), and hepatitis B and C (HBV and HCV) viruses have a high risk in renal transplant recipients, whereas non-viral common epithelial cancers, such as breast and prostate cancers, occur at the same rate as general population.[2,3] The risk of Kaposi's sarcoma related to HHV-8 is more than 200 times in renal transplant recipients compared to the general population. The likely cause of increased incidence of virus-associated cancers is uraemic immune dysfunction supported by the evidence of re-activation of latent EBV infection in uraemic immunodeficiency.[3] Non-Hodgkin's lymphoma (NHL) and non-melanocytic skin cancers are the most common ones in renal transplant recipients; squamous cell carcinoma (SCC) occurs 25 times more frequently in the transplant population than the general population.[1]

Malignancies of the genitourinary tract account for 15% of all the malignant tumours in the Cincinnati Tumour Transplant Register and the carcinoma of the native kidney accounts for up to 5% of all malignancies found in transplant recipients.[4] The 10-year risk of developing a solid malignancy is 20% for kidney transplant recipients.[5] One study reported a 100-fold increased risk of native kidney malignancy among transplant recipients compared with the general population.[6]

Case Report

A 34-year-old young male patient presented at Al-Hada Military Hospital, Taif, Saudi Arabia, with complaint of pain in the right loin for the preceding 3-4 months. He was a known case of chronic renal failure and had renal transplant done 5 years ago. He remained on dialysis three years prior to the transplant. There was no history of hypertension and diabetes mellitus. There was no history of dysuria. The patient was also on immunosuppressive drugs and was taking cyclosporine, prednisolone, atenolol and amlodipine. The graft function was normal. His serum cyclosporine level was 1047.4 ng/ml. He had bilateral mastitis, and was HCV positive. On further investigation, his urine examination was normal and cultures were negative. Serum creatinine was 1.17mg/dl and urea was 46 mg/dl. Renal mass was seen in the right kidney on ultrasonographic examination. Magnetic resonance imaging (MRI) was done and T2-weighted coronal images at posterior and anterior planes showed renal graft in the right lower abdomen and both atrophied native kidneys with isointense solid renal mass at lower pole of the right native kidney measuring 3 x 2.5 cm, in addition to tiny

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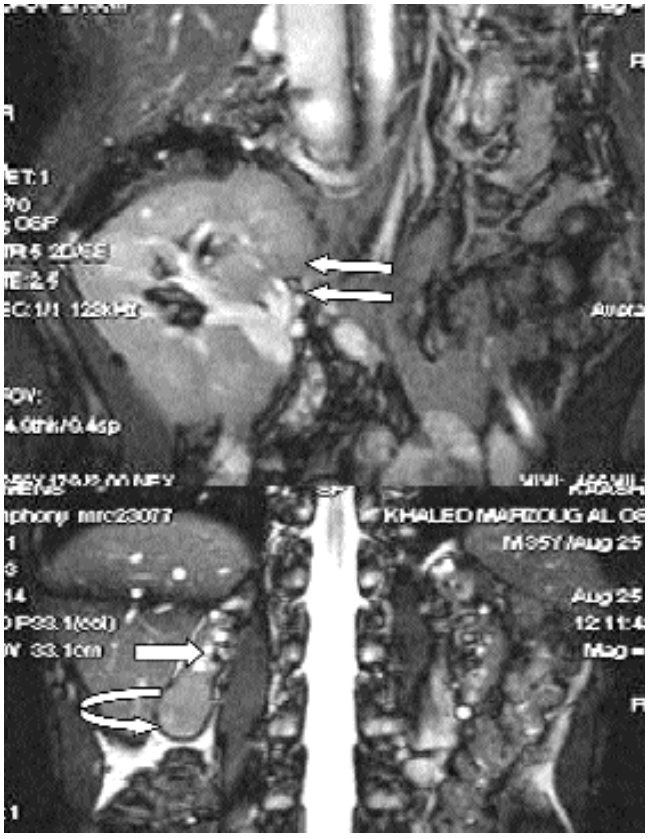

Figure-1: T2 weighted coronal images at posterior and anterior planes of same patient ; illustrate renal graft (double arrows) in right lower abdomen and right atrophied native kidney (single arrow) with isointense solid renal mass (curved arrow) at right native kidney lower pole measuring 2.5 x 3 cm, in addition to tiny cortical renal cysts.

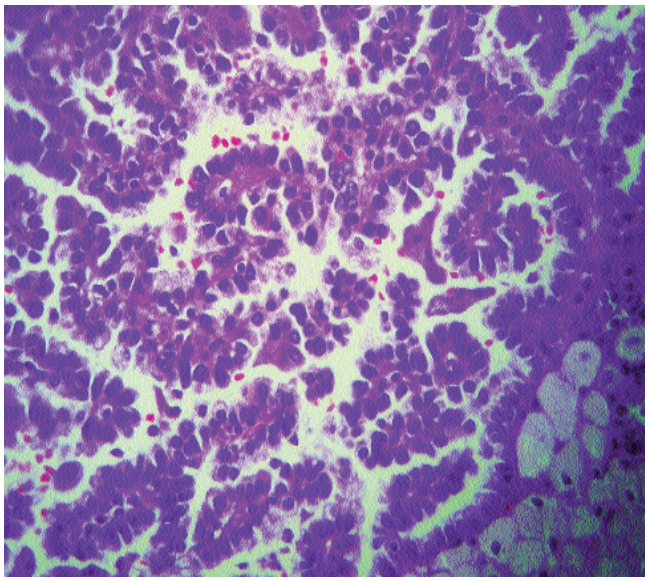

Figure-2: Haematoxylin & eosin (H&E) section showing tumour composed of papillary areas with well formed central fibro vascular cores (200x).

cortical renal cysts (Figure-1). Right nephrectomy was done and the specimen was sent for histopathological examination. On gross examination, the mass involved the lower pole of the kidney. It was yellowish brown measuring 3.0 x 3.0 x 2.0 cm and was encapsulated and well-demarcated from the adjacent renal parenchyma. Microscopically, the tumour was composed of papillary areas with well-formed central fibrovascular cores (Figure-2). There was stromal infiltration by foamy macrophages. Nuclei were grade II according to the Fuhrman grading system. Renal capsule was intact. Small papillary tumour foci were identified in the adjacent normal renal parenchyma. No angio-lymphatic invasion was seen and pelvicalyceal area was tumour-free. It was diagnosed as renal cell carcinoma (RCC), papillary type I. The patient was referred to the Oncology Centre for further management and was lost to follow-up.

Discussion

The incidence of RCC in native kidney of renal transplant recipient patients varies between 0.3% and 4.8%.[7] Male gender, African-American race, recipients aged at least 65 years, a donor aged at least 50 years, microscopic haematuria, patients having a long pre-transplant dialysis interval and acquired cystic kidney disease (ACKD) are significantly associated with the risk of native kidney malignancy in renal transplant recipients.[7] However, another study found no significant relationship between RCC occurrence and patient age, dialysis (when initiated, type and duration), transplantation, drug regimen or incidence of ACKD. A study in 1000 patients transplanted over a 12-year period stated that all of the malignancies occurred in patients with either pre-transplant native renal cysts or with time indeterminate native renal cysts (i.e. patients without pre-transplant native renal ultrasounds who had cysts diagnosed more than 6 months after transplantation).

Cancers in the native kidney in renal transplant recipients are asymptomatic and small in size. Most of the studies showed the mean size ranging from 2.0-4.7cm.[5,6,9] Most tumours are incidental, low-stage and low-grade, having good prognosis.[7] Most of them are bilateral, multifocal and papillary type. The median interval between renal transplantation and the occurrence of RCC was 5.6 years.[7] One study stated the mean of 70.9 months time since transplantation, but it did not find any significant relation between the time of transplantation and development of the cancer.[3] Our patient presented 5 years (approximately 60 months) after the transplantation. We also found the RCC of papillary type, low-grade morphology, Fuhrman's nuclear grade 2 and of low-stage, T1 according to Tumour, Node, Metastasis (TNM) staging system.

A study presented an unusual case of multi-centric RCC, papillary type in renal allograft after 13 years of excellent allograft function probably because of pre-existing genetic mutations in the allograft.[10] Histopathological evaluation showed 29 tumours; 21 were chromophil basophilic papillary carcinoma; 5 were clear cell RCC; and 1 was chromophil eosinophilic papillary carcinoma.

De novo malignancies in native kidney of transplant recipients have good prognosis and the survival rate is better among papillary than clear cell carcinoma.[5,7] However, other studies suggest that malignant lesions typically are more aggressive in transplant recipients compared to the general population and the population of patients on renal dialysis probably due to the immunosuppressed state.[11]

Though transplant recipients have high risk of RCC in the native kidney, there is no recommended protocol for their cancer screening, like routine ultrasonography as a part of follow-up. Since the incidence of malignant tumours is high in post-renal transplant patients, computed tomography (CT) scan and ultrasonography should be performed routinely for early tumour diagnosis.

Conclusion

In the light of findings and in line with literature, routine native renal ultrasonography within one month of transplantation, with surveillance ultrasounds every 2 years in patients with cysts and every 5 years in patients without cysts, are recommended.

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