Carcinoma in a Transplanted Kidney Detected with MAG3 Scintigraphy

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We report on two cases of infiltrative renal tumor developing in two kidney transplant recipients from a single cadaveric donor source. Interestingly, while this is only the second case of a de novo renal allograft tumor, both were morphologically infiltrative. The fact that both tumors were infiltrative may be secondary to immunosuppression therapy. While computed tomography (CT) evaluation of suspected renal pathology provides excellent anatomical detail, renal transplant recipients are initially evaluated using ultrasound and renal scintigraphy to avoid contrast reagents which could further impair renal function, as well as to reduce the image procedure cost and the patient radiation dose. Unfortunately, infiltrative tumors may be isoechoic on ultrasound, providing a confusing or conflicting report when compared to scintigraphic findings. This case report is significant radiographically because the original neoplasm was initially detected using technetium-99m-labeled mercaptoacetyltriglycine (^{99m}Tc-MAG3) scintigraphy and was not appreciated by sonographic studies, even retrospectively. This case demonstrates the usefulness of ^{99m}Tc-MAG3 scintigraphy to follow-up evaluations of renal transplants by providing detailed anatomical information as well as functional analysis of the kidney.

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Although renal transplant recipients have an increased frequency of malignant neoplasms in their native organs, development of a renal allograft tumor is an unusual and rare complication (*1*). There has been only one documented case of a de novo neoplasm, an infiltrative lymphoma, originating within the transplant kidney itself (*2*).

A failing renal allograft can present a complex and confusing diagnostic dilemma. Normally the transplant evaluation determines any degree of rejection, acute tubular necrosis, peritransplant fluid collections, obstruction, vascular insults, cyclosporin toxicity, or the degree of renal function, rather than image a renal tumor. Correlation of clinical history and laboratory findings with sonography and scintigraphic imaging provides information which is used to determine surgical versus medical management.

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CASE REPORTS

Patient 1

A 26-yr-old male received a cadaveric renal allograft because of end-stage renal disease. Initial evaluation using ultrasound with Doppler and ^{131}I hippuran scintigraphy were normal. Follow-up evaluation using sonography alone at 1 and 6 mo post-transplantation demonstrated no interval change.

At 12 mo post-transplantation, the patient presented with signs and symptoms of renal rejection. Sonographic examination demonstrated an enlarged kidney with normal echotexture (Fig. 1). Doppler evaluation revealed decreased diastolic flow with resistive indices compatible with rejection. Technetium-99m-MAG3 dynamic blood flow and delayed static images revealed impaired renal function and a photopenic area within the hilum extending into the lower pole (Fig. 2). The most likely differential diagnoses included an infectious process or infiltrating tumor. The central and infiltrative pattern of the defect made renal infarction less likely. Since the sonogram revealed no evidence of altered echogenicity, the photopenic area on ^{99m}Tc-MAG3 images was felt to represent a more focal area of chronic rejection. A renal biopsy showed chronic rejection and the patient's immunosuppression medications were adjusted.

One month later, the patient presented with fever, abdominal pain located over the allograft, rising creatinine and intermittent hematuria. The kidney sonogram examination remained unchanged. Compared to the previous ^{99m}Tc-MAG3 scintigraphy, the lower pole photopenic area appeared enlarged. A renal biopsy revealed a poorly differentiated carcinoma; either a transitional cell carcinoma (TCC) or a bronchogenic metastases. Because some TCC tumors may be successfully treated with renal parenchymal sparing subtotal nephrectomy, further tumor characterizations with a retrograde cystogram and contrast-enhanced magnetic resonance imaging (MRI) were investigated. However, due to the extent of the tumor involvement, a total transplant kidney nephrectomy was performed. Pathological examination confirmed tumor thrombus in the renal vein, with infiltrating carcinoma invading the majority of the kidney, but most conspicuous at the hilum and lower pole (Fig. 3). Tissue pathology was reported as poorly differentiated carcinoma compatible with an urothelial origin or a bronchogenic origin. Radiographic evaluation for metastatic disease revealed foci in the lung, liver, bone and brain. The patient initially improved on hemodialysis but died 1 mo later.

Patient 2

CT evaluation was performed on an asymptomatic 23-yr-old male who received the contralateral cadaveric kidney and revealed a renal mass. Unfortunately, neither ^{99m}Tc-MAG3 nor

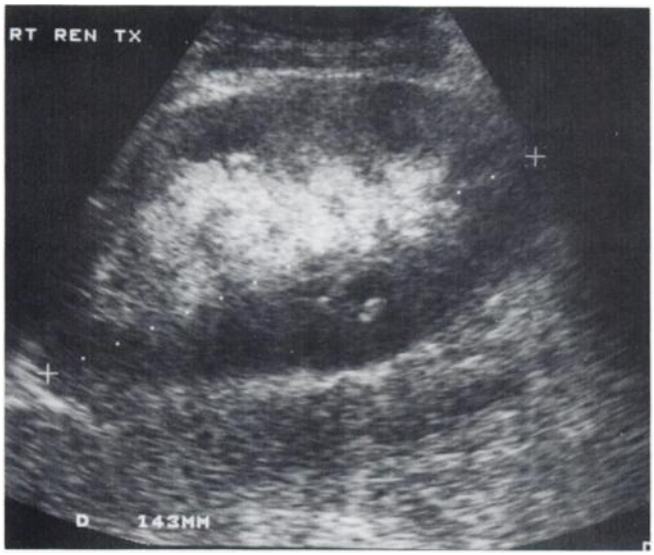

FIGURE 1. Ultrasound examination showing an enlarged transplant kidney but no evidence of mass or hydronephrosis.

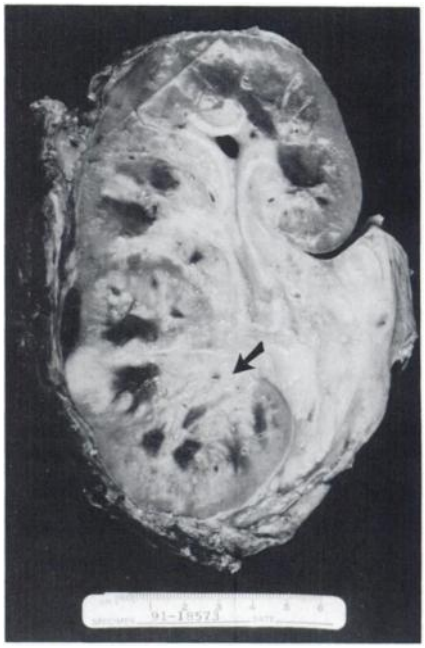

FIGURE 3. Photograph of the surgical specimen showing an infiltrating mass (arrow) in the hilum and lower pole of the kidney. The tumor has a pale discoloration compared to the normal renal parenchyma.

ultrasound imaging was performed prior to the cadaveric nephrectomy. Pathology confirmed involvement of the renal parenchyma with a carcinoma histologically identical to that of the contralateral cadaveric kidney.

DISCUSSION

With both transplant kidney recipients developing a histologically identical carcinoma, the original tumor focus should be the mutual donor. When renal parenchymal infiltration is extensive, differentiation between invasive renal cell carcinoma (RCC), TCC, squamous cell carcinoma of the renal pelvis, lymphoma or metastatic disease may prove a difficult imaging challenge (*3,4,6*). Because infiltrative metastatic disease usually has a cortical location (*5,6*), a multiplicity of lesions (*4,6*) and is sonographically hypoechoic (*4,6*), the tumor radiographic characteristics were more suggestive of a urothelial origin. In our case, attempted differentiation of tumor etiology did not alter the surgical approach or the procedure performed, as the extent of the tumor involvement required a radical transplant nephrectomy. However, preoperative attempts at differentiation of tumor origin are not merely an academic exercise, since histological expectations and tumor extension can alter treatment planning (*3–6*).

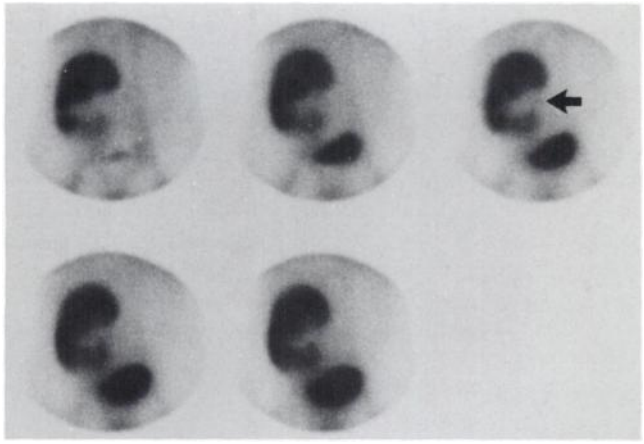

FIGURE 2. Transplant renal scintigraphy: anterior images obtained every 5 min following intravenous injection of 7.5 mCi of ^{99m}Tc-MAG3 showing a photopenic area (arrow) corresponding to the mass seen on the surgical specimen.

Infiltrative renal tumors are exceptionally rare and are more difficult to detect (*3–9*) whereas a well-defined expansive mass is easily identified radiographically. This is explained histologically because the abnormal cells proliferate the kidney using the nephrons, collecting ducts and blood vessels as scaffolding (*4*). While chronic immunosuppressive therapy alone allows the tumor to have unusually rapid extension and invasive capabilities (*10*), upper urothelial and renal pelvis tumors can present in uncharacteristic patterns even in nonimmunosuppressed patients (*3,11,12*). As TCC can be sonographically isoechoic (*3–5*), and many infiltrative renal tumors are isodense on noncontrasted CT (*4,6*), infiltrative renal tumors are best evaluated with contrasted CT (*6,13*). However in renal transplant recipients, CT and MRI are reserved for those cases in which conventional examinations are insufficient or inconclusive (*14*). Thus, failing renal allografts are initially evaluated using sonography and renal scintigraphy.

Unfortunately, infiltrative tumors may be isoechoic on ultrasound (*3–5*), providing a confusing or conflicting report when compared to scintigraphic findings. In our case, the image resolution of the agent ^{99m}Tc-MAG3 clearly demonstrated a photopenic area with an infiltrative pattern which matched the pathological findings. This would be expected since prior to ultrasound, CT and MRI availability, ^{99m}Tc dimercaptosuccinic acid (DMSA) was used to investigate renal structural anomalies. Although DMSA is preferred, ^{99m}Tc-MAG3 is an acceptable alternative and re-emphasizes

that renal scintigraphic imaging can provide excellent anatomical imaging of space-occupying lesions (*15*).

Several imaging modalities are being investigated for the evaluation of post-transplant complications. Currently there is interest in the future potential of enhancing agents to revolutionize the diagnostic effectiveness of ultrasound. Experiments with rabbits and perfluoroctylbromide demonstrated enhancement in acute tubular necrosis (*16*) and renal infarction (*17*). Dai has recently published findings in human trials of increased attenuation in solid renal carcinoma (*18*). While these reports are promising, it is too early to draw conclusions concerning the utility of the enhancing agents for detection of renal infiltrating tumors. In addition, new information regarding a fever response to the enhancing agent administration may negate the benefits for renal allograft surveillance.

Although MRI is an excellent modality for anatomical detail, noncontrasted MRI has had limited value in routine renal allograft evaluation. Early reports of signal intensity changes in the cortico-medullary demarcation have proven to be nonspecific in differentiation between acute tubular necrosis, acute rejection and chronic rejection (*19,20*). A recent article suggests that contrasted dynamic MRI is useful in the evaluation of allograft function (*21*). Admittedly, if our patient had been followed with contrasted dynamic MRI, the tumor may have been detected earlier. However, routine follow-up with contrasted MRI incurs the risk of allergic response. Since gadoteridol, gadodiamide and gadopentetate dimegtumine are cleared by glomerular filtration, precautions are advised in patients with impaired renal function (data on file, Squibb Diagnostics, Princeton, NJ; Sanofi Winthrop Pharmaceuticals, New York, NY; and Berlex Laboratories, Wayne, NJ). Also, the cost of renal allograft care would escalate tremendously.

CONCLUSIONS

Technetium-99m-MAG3 scintigraphy is an inexpensive, versatile modality for renal transplant evaluations. One of the most important concepts in kidney assessment is the recognition of the intimate relationship between structure and function. Our case demonstrates the usefulness of ^{99m}Tc-MAG3 scintigraphy in follow-up evaluations of renal transplant patients, because it provides excellent functional analysis and detailed anatomical information. Technetium-99m-MAG3 imaging does not require operator expertise of sonography or additional intravenous reagents to illustrate the findings. There are no adverse effects of ^{99m}Tc-MAG3. In addition, ^{99m}Tc and scintigraphic imaging equipment is readily available in small community medical centers. Therefore, in patients with renal insufficiency, allograft recipients, or contraindications to contrast, renal scintigraphy is a viable imaging option.

Normally imaging of renal allografts with sonography and scintigraphy provides collaborative information. When there is a distinct finding on only one study, further investigation with another modality is warranted. Although there is current interest in renal allograft evaluation using dynamic MRI or sonography with enhancing agents, their cost-effectiveness, accessibility and risks versus benefits are considerations for their future imaging role in renal allograft evaluations.

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