Case report

Medical Ultrasonography
2012, Vol. 14, no. 3, 246-250

Papillary renal cell carcinoma in the transplanted kidney – a case report focussing on contrast enhanced ultrasound features

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Abstract

The purpose of the case report is to show that contrast enhanced ultrasound (CEUS) is an important imaging modality for patients with impaired renal function in detecting, characterizing and excluding renal cell carcinoma (RCC) in transplanted kidneys.

To our knowledge this is the first report of CEUS in a tumour of a kidney transplant. CEUS is feasible, reveals comparable results to computed tomography and should be concerned as the method of choice for patients with impaired renal function like renal graft recipients.

Keywords: renal cell carcinoma, kidney transplant, contrast agent, ultrasound

Introduction

Patients with a kidney graft have a higher incidence for malignancies due to the necessary immune suppression to prevent graft rejection. Ultrasound is the method of choice for the evaluation of kidney transplants since its easy accessible position in the iliac fossa. The ability of contrast enhanced ultrasound (CEUS) to evaluate kidney lesions in native kidneys has been described [1,2]. CEUS has been performed in patients with renal grafts but all studies focus on diffuse disease e.g. acute rejection [3-9] and do not concern the focal / neoplastic changes. This is the first case report commenting on the CEUS features of a tumour in a kidney graft.

Received 28.03.2012 Accepted 06.04.2012
Med Ultrason
2012, Vol. 14, No 3, 246-250
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Case report

A 39 years old woman was submitted to our hospital for evaluation of a slightly hypoechoic lesion of 2.5 cm in the transplanted kidney. She was in a good condition, had no complaints and reported no weight loss, fever or sweating. In an ambulant routine sonography the kidney lesion was suspected and the patient underwent a magnetic resonance imaging examination, but no definite diagnosis could be established.

The reason for renal failure had been a rapid progressive glomerulonephritis after missed abortion and had led to constant dialysis. After peritoneal dialysis kidney transplantation was performed in 1992. After rejection, 8 months later, peritoneal dialysis was continued and a second transplantation was performed in 2002 into the right fossa iliaca (opposite side to the first transplantation). The patient's history included elevated blood pressure and a combined mitral vitium.

The ultrasound examination was performed with a Siemens Acuson Sequoia platform (Issaquah, WA, USA) with a curved array multifrequency transducer (2 – 4.5 MHz). Tissue harmonic imaging was applied for B-mode

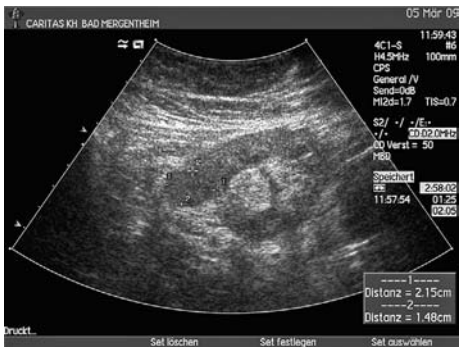


Fig 1. Hypoechoic lesion of about 2 cm at the ventral medial portion of the transplanted kidney.

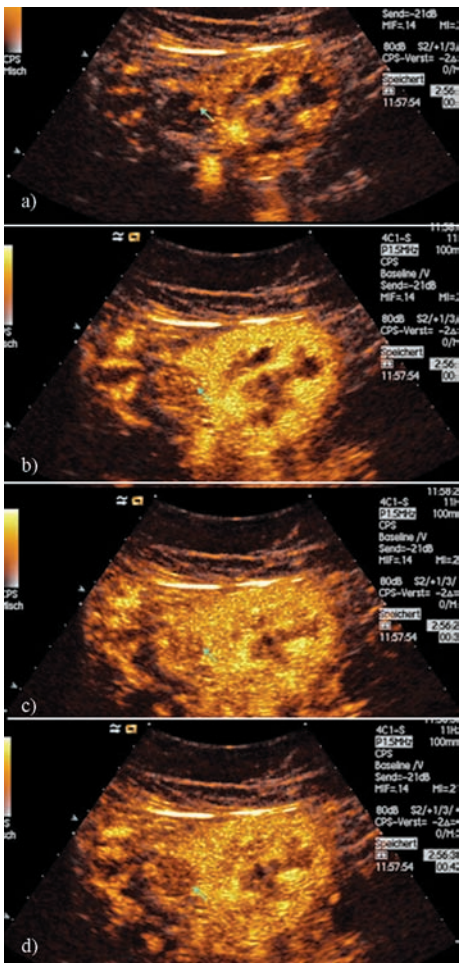


Fig 2. Contrast enhanced ultrasound with 2.4 ml of BR1 of the kidney transplant lesion; the arterial enhancement begins from a single central artery (13 seconds) [a]. The rapid filling appears after 16 seconds, but the lesions stays hypoenhancing in comparison to the surrounding kidney parenchyma (16 seconds) [b]. The lesion is completely enhancing, slightly hypoenhancing (30 seconds) [c]. From the late phase on the contrast enhancement of the lesion decreases in comparison to the surrounding kidney parenchyma, so that the lesion demarcating in fact (42 seconds) [d].

imaging to produce maximum resolution. Conventional Native colour and Power Doppler ultrasound was applied. After that the patient was examined using 2.4 ml of BR1 (SonoVue®, Bracco, Italy) as recently described [10]. Arterial enhancement was defined as ranging from the beginning of the enhancement in the kidney up to 30 seconds, late enhancement from 1 to 3 minutes after injection as described by Quaia and others [11]. Video files were obtained and representative images were stored.

In this case the lesion was hypoechoic compared to the surrounding renal parenchyma, spherical, with moderately blurred margins (fig 1). Colour and Power Doppler ultrasound could not show reproducible vascular signals due to lack sensitivity and the small size of the lesion. In CEUS the tumour showed a delayed arterial enhancement and hypoenhancement throughout the examination (fig 2). The vascularisation began with a single vessel enhancing from the periphery towards the centre of the lesion. Afterwards wash out could be demonstrated resulting in a progressive hypoenhancement during the late phase . Thus a solid kidney neoplasia was suspected and partial resection preserving graft function suggested.

The patient received partial resection of the transplanted kidney. The pathological examination revealed a 2.8 cm papillary renal cell carcinoma. The tumour formula was pT1a, pL0, pV0, pR0, pG1. The postoperative course was uneventful.

Discussion

In patients after organ transplantations there is evidence of a higher risk to develop malignancies. Long-term immunosuppression impairs the immunological response against viral infections. The raise in the development of viral-associated malignancies (e.g. cervical carcinomas, Kaposi's sarcomas lymphomas, hepatocellular carcinomas, anal carcinomas) can be explained [12-14]. Also, DNA damage or interference with DNA repair mechanisms is caused by immunosuppressive therapy. Despite these facts the exact reason is still matter of ongoing research [15]. Immunosuppressant drugs like sirolimus and cyclosporine might lower the risk [14]. Rapamycine could be a substance to lower primary and secondary cancer growth [16].

In kidney recipients with a functioning kidney cancer accounts for 7% of all deaths and the risk is 3 – 5 times higher compared to the general population. Urinary tract tumours, squamous cell cancer of the skin and post transplant lymphoproliferative diseases are frequently described. In a recently published series urinary tract malignancies were the most frequent with 22% [14]. The duration of haemodialysis seems to be an independent

factor in the development of tumours of the urinary tract [17]. Beneath tumours of the prostate and the testicles tumours of the native as well as the transplanted kidney have an incidence of 0.1 – 0.7% of which 10 – 22% are in the transplanted kidney [17-20]. In the largest series published there were 3/1250 (0.16%) [21] and 5/1075 (0.47%) patients with RCC in the transplanted kidney [22]. The time between transplantation is about 3 and 19 years but can be shorter in specific cases.

In patients with renal cell carcinoma in transplanted kidneys in nearly all cases donor origin could be confirmed by genetic studies [21-29]. In a case report Boix and co-workers proved recipient origin via microsatellite analysis [18].

Once the suspicion of a denovo carcinoma is given, the cancer has to be treated accordingly. Because of the immunesuppressant condition of the recipient it is well known that cancer treatment is often not as successful as in normal patients [30]. The treatment is usually surgery, in our case the transplanted kidney could be preserved and the kidney function is still sufficient. Nevertheless, other treatment options have been described such as simply stopping the immunosuppressant therapy leading to organ rejection including cancer regression [31].

CEUS has proven evidence for the characterisation and detection of tumours of the liver, the adrenal glands, the kidneys, the pancreas and the spleen [1,2,32-35]. In addition it has also gained acceptance in diffuse diseases of the liver and the kidneys. It has been commented that with contrast specific software and low mechanical index thus allowing real time sonography the characterisation of kidney tumours is possible with results comparable to computed tomography. There is a trend for papillary renal cell carcinoma to be more frequent hypovascular in contrast enhanced ultrasound in comparison to common clear cell carcinoma but this did not reach statistical significance. In our cohort of 20/106 (18%) patients with a papillary carcinoma the rate was 40%, in 78/106 (71%) patients with clear cell carcinoma it was 20% [1]. This did not reach statistical significance. There is no comparing study concerning detection rates of kidney tumours with CEUS vs. CT. Nevertheless, ultrasound is the method of choice for the evaluation of kidney transplants due to the easy access in the iliac fossa. The use of CEUS in transplanted kidneys is promising since adverse events are rare and the contrast agent shows no risk for impairment of the renal function and is eliminated via the lung 15 minutes after intravenous administration.

Several manuscripts have been published concerning the use of ultrasound contrast agents (UCA) in patients with kidney transplants. All aimed on the evaluation of early complications after transplantation. There was no study concerning the characterisation of renal cell carcinoma. 34 patients were investigated by Lefevre et al [3] using cardiac triggered pulse inversion imaging with Levovist® in patients who had received renal grafts. They reported differences in a heterogenous group of diseases concerning time intensity curve parameters like time to peak as well as wash in and wash out slopes. Farina et al [4] described their experience with a technique not representative for the current state of the art (Levovist® enhanced power Doppler ultrasound) in 56 patients who received renal transplants and 10 healthy controls. 19/56 (34%) suffered from graft rejection. They could differentiate patients with graft rejection by analysis of time intensity curves (time to peak) from patients without rejection and controls. Fischer et al [9] reported on 22 patients who were investigated with a semiquantitative colour coded analysis of the contrast agent arrival after injection of 1.6 ml SonoVue® 6 days after transplantation. They analysed the difference between enhancement of the renal artery and the cortex 8/22 (36%) patients with an acute rejection showed a significantly higher time difference compared to patients with no rejection. 2 patients with perirenal hematoma and no rejection showed similar changes like patients with transplant rejection. Benozzi et al [22] reported on 39 patients with contrast enhanced ultrasound within 30 days after kidney transplantation. 14/39 (36%) had early acute kidney dysfunction. Time intensity curves of CEUS characteristics received on cortical and medullary regions were evaluated as well as native resistance indices. In patients with early graft dysfunction there was a higher resist index, a reduced maximum enhancement, and a reduced regional blood flow. In addition the ratio of cortical to medullary mean transit time and regional blood value was higher. Grzelak et al investigated 63 patients who received renal grafts in the first 5 days after transplantation [36]. 35 patients with good early graft function were compared with 28 patients with delayed graft function of which 10 patients had acute graft rejection and 18 patients with acute tubular necrosis. Using time intensity curve analysis patients with delayed graft function there was a significantly prolonged inflow time. This value was more significant than higher RI in the delayed function group.

In conclusion, we demonstrated the role of contrast enhanced ultrasound findings in the evaluation of a renal mass in a kidney transplant. The sonographic evaluation of a kidney transplant is a routinely performed method and contrast enhanced ultrasound can (a) be safely performed and (b) helps to further characterise renal masses. To our knowledge this is the first study concerning CEUS features of renal tumours in renal transplants.

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