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Case Report

Sarcomatoid Renal Cell Carcinoma in a Renal Allograft

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Abstract

We present a case of poorly differentiated sarcomatoid renal cell cancer in renal transplant allograft with loco-regional and widespread metastasis. Once thought of as a separate entity, sarcomatoid differentiation is now believed to represent high grade tumor differentiation of renal cell cancers and it carries a grave prognosis. Of all the cases reported, very few have been reported in renal transplant allografts. Our case highlights the very aggressive nature of such cancers and we hope to familiarize clinicians regarding its presentations and likely outcomes through a review of literature.

Keywords: Allograft; Malignancy; Immunosuppression; Sarcomatoid; Renal Cell Cancer; Renal Transplant

Abbreviations

AKI	:	Acute Kidney Injury
ADPKD	:	Autosomal Dominant Polycystic Kidney Disease
CKD	:	Chronic Kidney Disease
DDKT	:	Deceased Donor Kidney Transplant
RCC	:	Renal Cell Carcinoma
sRCC	:	Sarcomatoid Renal Cell Carcinoma

Introduction

Renal Cell Carcinoma (RCC) is the most common primary kidney cancer arising in the renal cortex and accounts for 80-85% of the cases, followed by transitional cell carcinoma of the renal pelvis. RCC of the allograft kidney in a renal transplant recipient is very rare and is almost always donor derived. The most common histologic variant of RCC is the clear cell type. Sarcomatoid differentiation is not a distinct histologic variant and can present in any of the subtypes of RCC and when present carries a poor prognosis. Early identification and management of Sarcomatoid Renal Cell Carcinoma (sRCC) may reduce patient morbidity and mortality. We present a rare case of sRCC in a transplant allograft presenting with widespread metastasis. We also highlight the diagnostic and therapeutic challenges encountered and our patient's unfortunate outcome.

Case Presentation

A 70-year-old female with history of Hypertension, Asthma and Chronic Kidney Disease (CKD) stage 5 secondary to Autosomal Dominant Polycystic Kidney Disease (ADPKD) who had a pre-emptive Deceased Donor Kidney Transplant (DDKT). Her post-transplant course was relatively uncomplicated except for persistence of hematuria. She had no major post op complications. Her immunosuppressive regimen consisted of stable doses of mycophenolate mofetil, tacrolimus and prednisone. Patient's baseline creatinine ranged between 0.9-1.1 mg/dl. CT scan of the abdomen-pelvis done four months after transplant to evaluate for hematuria revealed innumerable cystic lesions of varying size and density that replaced majority of the native renal parenchyma bilaterally along with a stable hyperdense cyst of 3.2 x 3.2 x 3.8 cm in the lower pole of the right native kidney which was thought to be the hemorrhagic cyst and was also seen on the previous CT scans

prior to DDKT. In the renal allograft, no mass or complex cyst was found. Patient did not have any symptoms and her routine clinic visits were uneventful. Her serial renal allograft USG done 16 and 25 months post-transplant (to follow up for hematuria) did not show any abnormality except persistent grade 2 hydronephrosis. A follow up CT scan of the abdomen-pelvis done 29 months post-transplant revealed a unexpected finding of a 3.4 x 2.9 x 2.3 cm mass in the lower pole of the allograft kidney bulging into the renal collecting system, concerning for malignancy. She promptly underwent a CT guided biopsy of the allograft mass and the pathology was consistent with bland myofibroblastic proliferation with no evidence of epithelial or lymphoid malignancy. Due to high clinical suspicion of a malignancy and to rule out sampling error, the mass was re-biopsied and the pathology showed dense lymphoplasmacytic infiltrate without any myofibroblastic proliferation and no evidence of epithelial or lymphoid malignancy. Urine cytology was also negative as well. Due to inconclusive biopsies it was decided to follow patient clinically with serial imaging.

She was followed up in clinic Q6 months with no major medical complaints till she got admitted 42 months post-transplant with severe pain in her abdomen and unintentional weight loss of 20 pounds in last 2 months. Laboratory data was significant for Acute Kidney Injury (AKI) with creatinine of 4.2mg/dl (baseline 0.9-1.1 mg/dl), metabolic acidosis and hyperkalemia. CT scan of the abdomen-pelvis revealed significant increase in the size of the renal allograft mass up to 5 cm and associated worsening hydronephrosis in the transplant kidney (Figure 1).

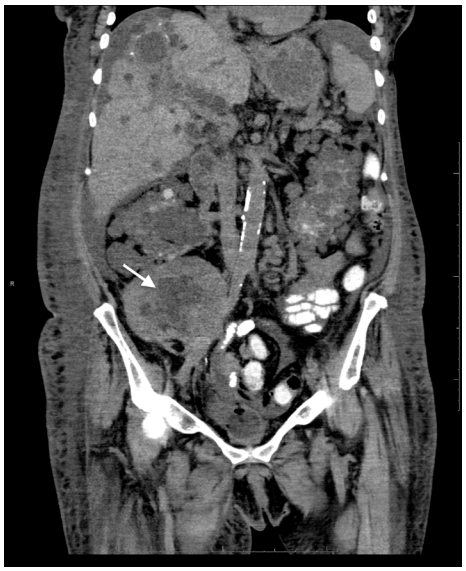

Figure 1: Non-contrast CT scan abdomen/ Pelvis showing (arrow) heterogeneous enlargement of right lower quadrant renal allograft with hypodense lesion suggestive renal cell carcinoma along with mild hydronephrosis.

It also showed moderate to severe right native kidney hydronephrosis suggestive of ascending tumor into the right native ureter and moderate abdominal pelvic ascites. She underwent her 3rd image guided percutaneous biopsy of the renal allograft mass and paracentesis. The biopsy was consistent with pleomorphic cells in a background of extensive necrosis concerning for poorly differentiated sarcomatoid carcinoma (Figure 2).

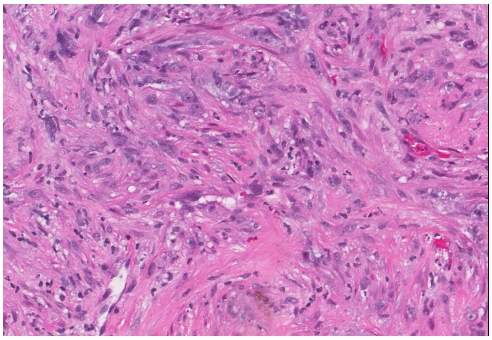

Figure 2: H & E stain of renal tissue showing distorted renal architecture which is replaced by smooth muscle differentiation with extreme nuclear pleomorphism.

Cytology of the abdominal fluid was negative for malignancy. A Tc99m-MAG3 scan suggested a fistulous connection between the kidney and the bowel. Patient underwent an emergent renal allograft nephrectomy and exploratory laparotomy. Her abdomen revealed numerous matted lesions covering the peritoneal wall and interspersed throughout the bowel and mesentery. The transplanted kidney was grossly enlarged with irregular nodularity and was firmly adhered to the distal ileum and proximal cecum with a fistulous connection. En-block resection of the transplant kidney (Figure 3), distal ileum and proximal cecum was performed. Pathology of the resected mass was consistent with poorly differentiated sarcomatoid carcinoma with metastatic involvement of the abdominal wall and segments of small and large intestine with no vascular involvement.

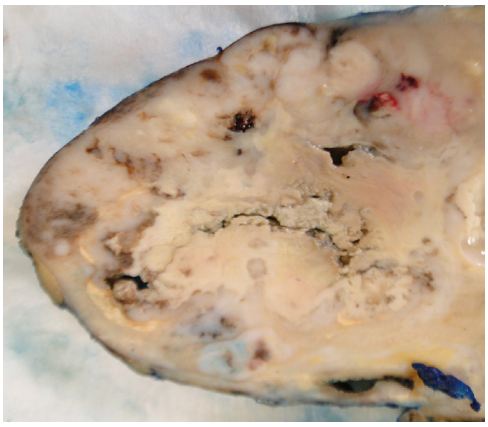

Figure 3: Gross specimen of renal allograft showing a firm gray-white tumor with areas of necrosis.

Follow up CT scan of the chest, abdomen and pelvis showed multiple pulmonary nodules in bilateral lungs and metastatic involvement of the peritoneum, bladder wall, with significant enlargement of para-aortic and retroperitoneal lymph nodes. She was initiated on hemodialysis and was deemed not a candidate for chemotherapy or target therapy after oncology evaluation. Her hospital stay was complicated by a pulmonary embolism, severe bleeding while on anticoagulation, placement of an IVC filter, gram negative bacteremia/ septic shock. Her clinical course deteriorated rapidly, and she died 4 months after her presentation and diagnosis.

Other Relevant Information Pertinent to the Case

- Sister kidney - has no signs of any malignancy and renal function is stable at 5 years post-transplant.
- Cadaver Donor - The donor was a healthy 46-year-old male who died after a gunshot wound to the head. Ultrasound of the bilateral donor kidneys revealed cysts and the pre-transplant biopsies of the cysts during organ recovery were suggestive of benign ganglioma.

Discussion

Renal Cell Carcinoma (RCC) is the seventh (in men) and ninth (in females) most common cancer of the western world [1] and is also relatively common de-novo malignancy seen in renal transplant patients. With the ever-increasing numbers of kidney transplant in US and now with more aggressive cancer screening protocols, we may see a further rise in the incidence of RCC in our transplant population. Based on OPTN data, about 20,000 patients received a kidney transplant in 2017. This rate of kidney transplant was a robust 20% increase from kidney transplants that were performed 5 years back in 2012. While kidney transplants patients have an overall increase in the longevity of life and improved quality of life over dialysis patients, they also at increased risk of malignancies in the post-transplant period. This is in part related to the immunosuppressive medications that are essential for their allograft survival. The incidence of RCC in kidney transplant population has been reported to be 5-6 times higher than general population [2-4]. Out of the various types of RCC, clear cell RCC is the most common (75% incidence in general population) followed by papillary RCC (10-15% incidence) with chromophobe being the least common (5% incidence) [5]. There are other rare RCC histological subtypes (cystic-solid, collecting duct etc.) that have been reported but all together they have an incidence of ~5% or less. Sarcomatoid Renal Cell Carcinoma (sRCC) is not a separate histological category as its histological features can be seen with all other types of RCC. sRCC have spindle like cells, high cellularity and cellular atypia, a feature similar to sarcoma. On immunohistochemical examination there is evidence of epithelial and mesenchymal differentiation [6,7]. They are typically aggressive cancers and since they are detected at later stages, they carry an extremely poor prognosis. The mortality is even higher with high-risk tumor characteristics such as necrosis (that our patient had) and microvascular invasion [6,8].

Based on a review of 101 sRCC cases, men were more commonly affected (1.6:1), the mean age at diagnosis was 60 years and the median tumor size reported was 9.2 cm [8]. Our patient, a female was in comparable elderly age group but presented with a smaller size allograft mass (3.4 cm on initial presentation). This series reported an overall incidence of 8% of sRCC. The incidence was highest in collecting duct RCC (29%) probably erroneous due to low incidence of collecting duct RCC as reported by authors. Otherwise, the incidence of sRCC in clear cell RCC, chromophobe RCC and papillary RCC was 8%, 9% and 3% [8]. The histologic type of RCC associated with sarcomatoid changes did not however change the prognosis. In the above series, median survival was reported to be around 19 months [8]. Other series have reported a median survival of 6-12 months [9-11]. Our patient unfortunately, had a much more aggressive course and she died 4 months after presentation. Donor derived malignancies in renal transplant patients is a recognized phenomenon. More and more cases of donor derived malignancies are being reported, which could be due to increase in donor age [12]. The incidence of donor derived malignancy is reported to be low – about 2/10,000 cases [13] but it does carry significant mortality. Kauffman et all [14] reported a mortality of around 50% in donor derived cancers in renal transplant recipients. Renal cell cancer in an allograft is also a rare occurrence and always raises a suspicion for a donor derived malignancy. In a retrospective review of around 10,000 renal transplant patients, only 16 (0.14%) developed allograft tumors and all were RCC [15]. A slightly higher incidence of 0.32% is reported by Cincinnati transplant tumor registry of about 7500 kidney recipients [16].

As per a review series [16], RCC was the most common donor derived malignancy found (in about 20% of all donor derived malignancies). Of all RCC in a renal transplant patient around 10% arise in renal allograft [17]. The authors reported a fairly good prognosis for donor derived RCC with a 5-year survival of about 70%. In this review, only 15% patient presented with metastatic RCC and these patients died within 15 months of diagnosis [16]. The pathology of RCC was however not described. Llamas, et al. [18] reported two very interesting cases of sarcomatoid RCC diagnosed within 7 months after transplant in 2 separate recipients who received their kidneys from the same donor. One of the recipients died due to tumor dissemination and this prompted workup on the second recipient leading to diagnosis of sRCC and subsequently allograft nephrectomy and regional lymph node excision. A well-timed diagnosis remains the most important prognostic factor. Nephrectomy does remains an essential part of

the management. One can argue against nephron sparing surgery due to the aggressive nature of this disease as it becomes very challenging to achieve negative margins during surgery. These tumors do demonstrate regrowth with local, regional and distant metastasis. As we reported in our patient due to extensive loco-regional disease an en-bloc resection of allograft with distal ileum and caecum were performed. A number of systemic therapy options including doxorubicin, ifosfamide, interferon alpha, gemcitabine and medroxyprogesterone have been tried but with very limited success [6]. In our patient, due to extensive disease and multiple comorbidities was not deemed a candidate for any systemic therapy.

A timely diagnosis and management of sRCC could alter the prognosis. Our case underscores the importance of always suspecting a malignancy in a transplanted kidney when a nephrologist is presented with a complex mass in an allograft. Despite two negative initial biopsies and even with having a close outpatient follow up, our patient ended with an unfortunate outcome. Given the rarity of the disease and its very aggressive nature, it was not until the last clinical presentation of the patient and the third biopsy that sRCC in the transplanted allograft was identified. In retrospect, one may question, if an even more aggressive approach with a complete or partial allograft nephrectomy could have been taken after first two inconclusive biopsies. There are no definite guidelines regarding workup of such allograft masses after an inconclusive pathology. Our patient was a diagnostic challenge given the negative initial biopsies and the rapid progression of the malignancy to a metastatic disease leading to a terminal outcome. All nephrologists need to be acquainted with sRCC as diagnosing and treating sRCC could be challenging

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Disclosure

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