Renal Tumors in Transplantation

Kevin Morrison
Clinical-Pathological Correlation
September 15th, 2004

Overview

• Case reports
• Neoplasia in transplantation
• Renal allograft tumors
• Native kidney RCC
• Role of screening
Case #1

- 52 y.o. male
- Cadaveric trsplt Sept 1997
- etiology of renal failure: unknown
- PMHx: superficial TCC

Case #1

- Feb ’03: abdo bloating & wt loss
- U/S – echogenic foci in spleen
- CT – hypodense lesions in allograft
Allograft Ultrasound

CT scan
Case #1: Pathology

- FNA Bx +ve for papillary RCC
- Transplant Nephroureterectomy June 2003
- Pathology: grd I papillary RCC, 51 foci 2-17mm in size
  - All tumor w/in renal capsule
  - No RA or RV invasion

Multifocal Papillary RCC
Multifocal Papillary RCC

Histopathology
Donor info: Case #1

- 14 y.o. male
- Arachnoid cyst hemorrhage
- Liver recipient OK to date
- Contralateral renal recipient: graft functioning

Case #2

- 10 y.o. male
- PUV w/ solitary right kidney
- Cadaveric trsplt 1997
- PMHx: UTI’s, growth delay
Case #2

- 2002 1cm mass in allograft
- 2003 mass incr to 3cm
- Chronic rejection of allograft,
  Creat ~400

CT w/ contrast renal allograft
Non-functioning native kidney

Case #2: Pathology

- 3 x 1.5 x 1cm mass
- proliferation of smooth muscle around blood vessels
- **Dx:** medullary leiomyoma
Histopathology

Donor info: Case #2

- 59 y.o. female
- SAH
- NIDDM, uterine fibroid
- Liver recipient-deceased
- Contralat renal – graft failed
Post-Transplant Neoplasms

- 3-4X incr risk of malignancy
- 15-20% after 10 yrs
- Skin, lymphoproliferative, KS, renal, anogenital & cervical

Post-transplant neoplasms: epidemiology
Cincinnati Transplant Tumor Registry – I.Penn

• 1998 review: 11483 tumors in 10787 patients
• 4305 = cancers skin & lips (29 X incr)
• 1931= post transplant lymphoproliferative disorder (PTLD) (28-49 X incr)
• 465 = Kaposi’s sarcoma (400-500X incr)
• 409 = renal carcinoma (25-75 X incr)
• 353 = cervical carcinoma (14-16X incr)
• 279 = anogenital carcinoma (100 X incr)

Geographic Differences
Transplant Neoplasms: Prognosis

- **PTLD**: mortality 35%
- **KS**: mortality – 57%
- **Skin cancer**: 60% multifocal
- **RCC**: 41% mortality (n= 256 CTTR ’95)

Renal Allograft Tumors
Primary Allograft Tumors

- 43 cases reported
- Potentially lethal
- Clear cell/papillary
- Leiomyoma not reported

Multifocal Papillary: Case #1

- 3 cases reported
- Multifocality →? Genetic defect
- Hereditary papillary RCC
- Met proto-oncogene
Leiomyoma: Case #2

- Autopsy rate 5.2%
- **Origin:** capsular, vessel, pelvis
- F>M
- Rarely clinically significant
- ?role of GH Rx

Allograft Tumors: Treatment

- Observation
- Nephron-sparing surgery
- Radical nephrectomy
Allograft tumors: nephron sparing

- 6 cases of partial nephrectomy
- Maximum 9cm tumor
- F/U 3-48 mo’s w/out recurrr
- Cryoablation –1 case
- RFA – 1 case

Tumor in Cadaveric kidney

??? What to do

Schostak et al 2002
Tumor Transfer

- 15 cases – excision & trsplt
- \(\rightarrow\) No recurrence of tumors
- Incomplete excision \(\rightarrow\) recurr w/ mets & death (2 cases)

Tumor Transfer

- 10,997 Tx 1990-97, Germany
- 30 cases of RCC in allograft – 0.273%
- Mean tumor size 2.2cm, donor avg 50yr
- \(\rightarrow\) Screening for cadaveric donors >45yr
  - Pre-explant U/S
  - Immediate preparation of allograft

Wundelich H et al Urol Int 67(1) 2001
Native kidney RCC in Transplantation

RCC prevalence

- Non-trsplt = 0.04%¹
- Dialysis Px = 1.5-3%²
- Transplant Px = 0.5-3%³

¹Tosaka et al JU 1990, Terasawa et al JU 1994, ²Miller et al AJN’94 ³Heinz-Peer et al Radiology ’95
RCC: Risk Factors

- Smoking
- ? Immunosuppression
- Acquired renal cystic disease

Acquired Renal Cystic Disease

- Bilateral cysts-ESRD
- No genetic cause
- Due to uremia
- Diagnosis
  - Radiologic: 3-5 cysts per kidney
  - Pathologic: cysts involving >25% of kidney
Acquired Renal Cystic Disease

• Incidence incr w/ time on dialysis
• M>F
• 2-7% ARCD → RCC
• Pathophysiology

ARCD and RCC: Pathology

• Cysts w/ mural nodules
• Cysts lined w/ atypical epithelial cells
• Papillary type & clear cell
• Usu lower grade
ARCD and RCC: Imaging

- **U/S**: cheap, no contrast, screening
- **CT**: optimal modality w/ non-ionic contrast
- **MRI**: gadolinium used to detect neovascular.

?? Role of Screening for RCC in Trsplt Px
Screening

- aSx Px prior to trsplt
- early intervention
- Reduce morbidity & mortality

RCC: high incidence in ESRD

- MGH – ipsilateral Nx @ Tx
- n= 260
- 4.2% RCC (n=11)
- 6 clear cell, 5 papillary, 1 chromophobe
- Risk factors: male, GN, ARCD

Denton et al Kid Intnl 2002 61(61)2201-2209
Tx RCC : clinical impact

<table>
<thead>
<tr>
<th></th>
<th>Dialysis Patients</th>
<th>Transplant Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor size</td>
<td>2.8cm</td>
<td>6.75cm</td>
</tr>
<tr>
<td>Metastasis</td>
<td>8%</td>
<td>53%</td>
</tr>
<tr>
<td>Mortality</td>
<td>0</td>
<td>29%</td>
</tr>
</tbody>
</table>

Pope et al 1994 J. Urology, n=20 (Vanderbilt)
Non-screened pop’n

RCC Screening : Pre-transplant

- U/S: n=206
- 22 → CT
- 8 w/ RCC → rad Nx
- RCC = 3.8%
- No false +ve CT
- Avg T size = 2cm
- All organ confined

Gulnikar AC et al Transplantation 1998 (Mississippi)
RCC Screening : Transplant Px

- Doublet et al J.Urol 1997 (Paris)
- N=129 → U/S, 55→CT
- 9 Px → lap radNx → 4/9 RCC
- Prevalence = 3.9%
- all tumors T1 & low grd
- 5 unnecessary surgeries

RCC Screening : Transplant Px

- Heinz-Peer et al Radiology 1995 (Vienna)
  - n=385
  - 6 Nx → 5 RCC’s
- Cogny-Van Trsplt Proc. 1995 (Fr.)
  - n=220
  - 7 Nx → 3 RCC’s
Screening: Drawbacks

- Harm associated w/ test
- Costly to society
- F+ve ➔ anxiety, unnecessary Rx
- F-ve ➔ Px ignore Sx

Malignancy in Renal Trsplt: Clinical Impact

- **Causes of DWGF:**
  1. CVS – 36%
  2. Infection – 17%
  3. Malignancy – 9%
- 5% malignancy = RCC
- Estimate RCC ➔ 0.45% of DWGF

Akinlolu et al Kid Int 2000
AST Clinical Practice Guidelines

Table 33: Urothelial malignancies and renal carcinomas

| Incidence | Renal carcinomas occur in 0.5 to 3.9% of renal transplant recipients. The risk of renal carcinomas among renal transplant recipients is 10 to 100 times higher than that in the general population. 
Consequences | Renal carcinomas represent approximately 3.6% of all tumors observed in transplant recipients. 
Rationale | Renal carcinomas are aggressive in renal transplant recipients. Widespread metastasis to the lymph nodes, liver, and lungs and invasion of the renal veins and inferior vena cava can occur. Approximately 40% of transplant patients with renal cell carcinoma die as a result of their malignancies. Patients with urothelial tumors usually present with metastatic disease and have a median survival time of only 17 mo. 
Recommendations | Urinalysis and radiographic screening for urothelial malignancies and renal carcinomas are not recommended (C). Urine cytologic studies are not recommended for screening for urothelial malignancies, except possibly for patients with histories of analgesic abuse (D). |

Renal tumors in transplantation: Summary

- Allograft tumors – role for nephron sparing
- RCC incidence increased in Trsplt
- Role of Screening controversial