Angioembolization for Renal Neoplasms

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UBC Urology Grand Rounds

Case Presentation: AML

- 62 yr F with growing AML (4 to 5.5 cm) on serial imaging

Questions:
What are the indications for treatment?
How do you decide between Angio and Partial Nx?
Case Presentation: RCC

- 62 yr M presents with flank pain and 8cm RCC with tumor hemorrhage. Hemodynamically stable, requires 2 u pRBCs on admission.

Questions:
Would you consider angio as initial treatment?
What are the benefits of angio prior to nephrectomy?

Outline

- Introduction
- Angioembolization for AML
- Review of AML treatment at VGH
- Angioembolization for RCC
- Conclusions
History of Angioembolization

- First described 1973:
  - Postbiopsy AVF (Bookstein, Goldstein)
  - Palliation of large RCC (Almard 1973)
- Early application for bleeding tumors, AML
- '80s-'90s: Growing interest in angio preop to nephrectomy

Embolic Materials

<table>
<thead>
<tr>
<th>Material</th>
<th>Feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Permanent</td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>Protein denaturation, Activation of coagln cascade</td>
</tr>
<tr>
<td>Coils</td>
<td>Dacron wool tails</td>
</tr>
<tr>
<td>Nonspherical (PVA) Particles</td>
<td>Heterogenous</td>
</tr>
<tr>
<td>Spherical microparticles</td>
<td>Homogenous, predictable</td>
</tr>
<tr>
<td>B. Absorbable</td>
<td>Allow vessel recanalization</td>
</tr>
<tr>
<td>Gelfoam</td>
<td></td>
</tr>
<tr>
<td>Autologous Clot</td>
<td></td>
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</tbody>
</table>
Embolic Materials

- No study clearly proves superiority of one particle/agent
- Similar:
  - Success rate (Jacobson, 2003)
  - Complication rate (Jacobson, 2003)
  - Post-infarction syndrome incidence (Swartz, 2006)

- New materials always emerging
  - Acrylic embospheres
  - HepaSpheres

Complications of Renal Angioembolization

<table>
<thead>
<tr>
<th>TABLE 3. Acute toxicity of renal embolization in 118 patients</th>
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</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td>Lumbar pain</td>
</tr>
<tr>
<td>Nausea</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Hematuria</td>
</tr>
<tr>
<td>Fever</td>
</tr>
<tr>
<td>Vomiting</td>
</tr>
<tr>
<td>Ileus</td>
</tr>
<tr>
<td>Serum creatinine ≥2 mg/dl</td>
</tr>
<tr>
<td>Pneumonia</td>
</tr>
<tr>
<td>Temporary renal insufficiency</td>
</tr>
</tbody>
</table>

Zielinski, 2003
Postembolization Syndrome

Features (all self-limiting): (Wotkowicz, 2008)
- Fevers, malaise
- Pain
- Transient hypertension
- Transient hematuria

Incidence: 15 - 80% (Jacobson 2003, Kallman)
- depends on size of infarct
  - Narcotic Use proportional to parenchymal loss (Jacobeson, 2003)

Introduction

Postembolization Syndrome

- Treatment
  - Overnight observation
  - Tylenol
  - Narcotics
  - ? Prednisone (Bissler et al., 1999)
    - 2mg/kg/day prednisone
    - Tapered over 2 week period
    - 7/9: no pain or fever
    - 2/9: fever treated successfully w/ Tylenol
Potential Utility of RAE for Renal Neoplasms

- AML
- RCC:
  - Preoperative to Definitive Nephrectomy
    - Large vein thrombus
    - Hostile hilum
    - Very Large tumors
  - Preop to Lap Partial Nephrectomy
  - Palliative
- TCC
- Metastasis

Quality of Evidence

- Level 1 evidence lacking
  - Majority of studies Retrospective or Observational
- AML:
  - No RCTs comparing angio to partial nephrectomy
- Preop RCC:
  - 1 retrospective comparative study (Angio + Sx vs. Sx alone)
  - No Prospective RCTs
Angioembolization for AML

AML: Diagnosis

- CT SCAN: modality of choice
  - Fat considered diagnostic for AML (<-10 HU Precontrast)
  - Absence of Calcification

- MRI
  - T1 unenhanced: HIGH, LOW
  - T2: LOW, HIGH

- US
Indications for Treatment of AML

- Symptomatic:
  - Pain
- Suspicion of malignancy
- Prophylaxis (Controversial)
  - Tumor Size (>4cm)
  - Females childbearing age
  - Followup/access to ER care inadequate

Observation is chosen in >50% of AMLs in most series (most of these <4-5cm)

Size Threshold for treatment

<table>
<thead>
<tr>
<th>References</th>
<th>% Symptomatic at Presentation</th>
<th>% Surgical or Radiological Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Less Than 4 Cm.</td>
<td>4 Cm. or Greater</td>
</tr>
<tr>
<td>Dickinson et al10</td>
<td>10</td>
<td>68</td>
</tr>
<tr>
<td>Kesler et al13</td>
<td>40</td>
<td>54</td>
</tr>
<tr>
<td>Chen et al14</td>
<td>60</td>
<td>91</td>
</tr>
<tr>
<td>Khi and George15</td>
<td>0</td>
<td>93</td>
</tr>
<tr>
<td>Kennedy et al16</td>
<td>67</td>
<td>94</td>
</tr>
<tr>
<td>Van Saal et al17</td>
<td>14</td>
<td>83</td>
</tr>
<tr>
<td>Steinert et al18</td>
<td>24</td>
<td>62</td>
</tr>
<tr>
<td>Osterling et al literature review (1986)</td>
<td>23</td>
<td>82</td>
</tr>
</tbody>
</table>

* Size determined at 4 cm or less at 4 cm.
Modes of Treatment for AML

- Angioembolization
- Partial Nephrectomy
- Total Nephrectomy
- Conservative
- Hormonal
- Sirolimus

Management of AML at other centers

<table>
<thead>
<tr>
<th></th>
<th>Nelson (n=336) (%)</th>
<th>Tsai (n=62) (%)</th>
<th>Seyam (n=60) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>40</td>
<td>48</td>
<td>52</td>
</tr>
<tr>
<td>Angio</td>
<td>6</td>
<td>3</td>
<td>10 (all last 6 yrs)</td>
</tr>
<tr>
<td>Partial Nx</td>
<td>19</td>
<td>23</td>
<td>18</td>
</tr>
<tr>
<td>Total Nx</td>
<td>35</td>
<td>26</td>
<td>20</td>
</tr>
</tbody>
</table>
How do we choose between Angio and Surgery?

- Controversial, must be based on:
  - Efficacy
  - Morbidity
  - Preservation of Renal Function
  - Tumor Characteristics (bleeding, malignancy, size, etc.)
  - Operative Time
  - Patient and Surgeon Preference

Efficacy of Angioembolization

- Review of 14 series on angio (Nelson, 2002)
  - Rates of reangio = 14% (Persistent symptoms, recurrent bleeding)
  - Durable response to median f/u 23 mos

- Efficacy may depend on operator, the embolic agent used:
  - Ethyl Alcohol (Lee 1998):
    - 4/21 (19%) required repeat embol
  - Particles & coils (Williams 2006)
    - No cases of subsequent hemorrhage @40 months
Followup Post AE

Partial Nx for AML: Efficacy

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Median F/U (mos)</th>
<th>Local Recurrence</th>
<th>Recurrent symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boorijan 2006</td>
<td>58</td>
<td>96</td>
<td>3.4%</td>
<td>0</td>
</tr>
<tr>
<td>Fazeli &amp; Novick 1998</td>
<td>27</td>
<td>39</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Heidenreich</td>
<td>28</td>
<td>58</td>
<td>0</td>
<td>/</td>
</tr>
<tr>
<td>Yip</td>
<td>16</td>
<td>26</td>
<td>0</td>
<td>/</td>
</tr>
</tbody>
</table>

- Surgery offers a reliable cure
- Angio may require repeat angio (14%) or surgery
Angio vs Partial: Morbidity

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Length of Hospital Stay</td>
<td>1 day</td>
<td>2-6 days</td>
</tr>
<tr>
<td>Blood Loss</td>
<td>N/A</td>
<td>350cc</td>
</tr>
<tr>
<td>Postop Complications</td>
<td>Up to 85% postembolization syndrome</td>
<td>12% overall 5% urine leak 8% ileus</td>
</tr>
</tbody>
</table>

Angio vs Partial: Renal Function

<table>
<thead>
<tr>
<th></th>
<th>Median F/U</th>
<th>Change in RF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angio (Williams 2006)</td>
<td>11 23</td>
<td>GFR 95.75 --&gt; 101.97</td>
</tr>
<tr>
<td>Partial Nx (Boorijan 2006)</td>
<td>58 96</td>
<td>Cr 1 --&gt; &gt;1.1</td>
</tr>
</tbody>
</table>
Tumour Characteristics: Size and Location

- **Size**
  - Larger tumors better candidate for Angio? (Kennelly)

- **Location**
  - Near Hilum: may not be amenable to partial OR angio

Tumor Characteristics: Tuberous Sclerosis

**Features of TSC**

- AML more likely to grow:
  - De Luca: 47/51 sporadic AML show NO GROWTH over 5 yr
  - Seyam: TSC grew 4.7cm, Sporadic grew 0.6 cm over 3 yrs

- AML more likely to hemorrhage (44% vs. 14%)

- Higher suspicion for RCC

**Considerations:**

- Nephron-sparing approach is the rule (more aggressive tumors)
- Management strategy continues to evolve
Acute Hemorrhage

Angio considered first line:
- Better renal preservation. (Surgery risks nephrectomy for hemostatic control)
- More rapid pt stabilization

- Chang 2007:
  - 7 patients bleeding AML; all required transfusion preembolization
  - No need for postop OR in ANY case

VGH Experience with AML over the past 10 years (99-09)

Methods:
Inclusion Criteria:
I) Review of Sunset Pathology site using keywords:
   - AML, angiomyolipoma, nephrectomy, TSC, tuberous sclerosis
II) Review of Sunset Radiology site using keywords:
   - AML, angiomyolipoma, angioembolization, embolization, TSC, tuberous sclerosis

Exclusion Criteria:
- All autopsy specimens
- All cases undergoing Surgery for other indications (i.e., trauma, malignant mass, transplantation, etc.)
VGH Experience with AML over the past 10 years (99-09)

<table>
<thead>
<tr>
<th></th>
<th>Angioembolization</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Pts</td>
<td>17</td>
<td>42</td>
</tr>
<tr>
<td>Number of procedures</td>
<td>22</td>
<td>42</td>
</tr>
<tr>
<td>Mean Age</td>
<td>47</td>
<td>53</td>
</tr>
<tr>
<td>% Female</td>
<td>65</td>
<td>79</td>
</tr>
<tr>
<td>% Multifocal AMLs</td>
<td>35</td>
<td>7</td>
</tr>
<tr>
<td>% with Acute Hemorrhage</td>
<td>50</td>
<td>14</td>
</tr>
<tr>
<td>% Requiring repeat procedure</td>
<td>5</td>
<td>0</td>
</tr>
</tbody>
</table>

VGH Experience with AML over the past 10 years (99-09)

<table>
<thead>
<tr>
<th>Surgery for AML</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Radical Nephrectomy</td>
<td>60% (25/42)</td>
</tr>
<tr>
<td>Partial Nephrectomy</td>
<td>40% (17/42)</td>
</tr>
<tr>
<td>Mean AML size</td>
<td>5.85 cm</td>
</tr>
<tr>
<td>Median AML size</td>
<td>4 cm</td>
</tr>
<tr>
<td>Malignant AML (epitheliod)</td>
<td>10% (4/42)</td>
</tr>
<tr>
<td>Cystic AML</td>
<td>7% (3/42)</td>
</tr>
</tbody>
</table>
VGH Experience with AML over the past 10 years (99-09)

<table>
<thead>
<tr>
<th>Embolization Agent</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Particles</td>
<td>40%</td>
</tr>
<tr>
<td>Coils</td>
<td>25%</td>
</tr>
<tr>
<td>Alcohol</td>
<td>15%</td>
</tr>
<tr>
<td>Mix</td>
<td>20%</td>
</tr>
</tbody>
</table>

Conclusions about ANGIO for AML

- Trend to using more angioembolization (Sayem, 2006)
- Both RAE and Surgery are effective treatments for AML
- Future Directions:
  - RCT comparing angio and partial Nx
  - Studies with long term f/u to assess rates of recurrence and retreatment
Angioembolization for RCC

Rationale for Angioembolization for RCC

- Preoperative to Definitive Nephrectomy
  - Large vein thrombus
  - Hostile hilum
  - Very Large tumors
    - decreased blood loss
    - ease of dissection

- Preoperative to Partial MIS Nephrectomy
- Palliative
Limited Evidence Available

- No Prospective Randomized studies
- No consensus on indications, morbidity and outcome benefit
- Many of large studies conducted 1980’s (prior to improved techniques)
- Mixed Expert Opinions

Most reported outcomes:
- Intraoperative blood loss
- Duration of surgery
- Palliation of symptoms

Does Preop RAE decrease Operative Blood Loss?

- Rationale: Renal artery occlusion results in collapse of parasitic renal veins

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Average Tumour Size</th>
<th>Average Transfusion Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preop Angio</td>
<td>24</td>
<td>595 cc</td>
<td>250 cc</td>
</tr>
<tr>
<td>Surgery alone</td>
<td>69</td>
<td>257 cc</td>
<td>800 cc</td>
</tr>
</tbody>
</table>

BAKAL, 1993

- However, several studies demonstrate no difference in blood loss (Kalman, 2003)
RAE for RCC with IVC thrombus

- **Rationale**
  - Must remove entire thrombus for good chance of cure
  - 35-40% of cases show distinct vascularity of tumor thrombus

- **Evidence**
  - In hypervascular thrombi, preop RAE often causes shrinkage of the thrombus (Craven et al, 1991)
  - No change in overall survival in multivariate analysis (Sweeney, 2003).

- **Risk of pulmonary embolis:**
  - Known risk of pulmonary embolis during Nx for RCC with IVC thrombus.
    - Without Angio: Risk of 3.4% (6/149 cases) in Level 1-IV thrombus (Schuck, 2009)
    - Theoretically, preop thrombus embolization may further increase risk (Swartz, 2006)

Can RAE improve cancer control?

- **METHODS (Zielinski, 2000)**
  - Retrospective Review of pts undergoing
  - 118 pts receiving preop RAE matched to control group of 116 pts without preop RAE (Matched based on age/sex/stage/size/grade)
  - 95% pT2 or pT3
Outcomes

Overall survival:

- Preop Angio Sx alone
  - 5 yr (p<0.01) 62% 47%
  - 10 yr (p<0.01) 35% 23%

Survival of pT3 tumors
Summary: Possible Benefits of Preoperative RAE

- Increased ease of dissection
- Decreased Intraoperative Blood loss
- Facilitates tumor thrombus resection
- Improved Cancer control
- Immunological “autovaccination”

What is the optimum delay time to Nephrectomy?

- Likely 24-48 hours:
  - Maximize edema (Swartz, 2006)
  - Minimize period of post-infarction syndrome
  - Before collateral vessels form (Wallace, 1981)

- Concomitant RAE & Nx has been described (Lin, 2003)
  - Single anaesthetic
  - Lower cost
  - Less Postinfarction syndrome (0/8 in their study)
RAE prior to MIS Nephrectomy

Methods (Galluci, 2007)
- 50 pts with small, solitary, predominantly exophytic renal tumors
- Mean tumor size 3.5cm, 30/50 in a polar location
- Average of 6 hours after embolization → partial MIS Nx
- NO VASCULAR CLAMPING

Outcomes
- Mean OR time 90 minutes (mean embol time an additional 43 mins),
- Average EBL 200c
- Average hospital stay 6 days
- Complications
  - 1 infected hematoma
  - 1 conversion to lap radical (hilar tumor)
Palliative RAE for RCC: Symptom Control

Control Bleeding and Local Pain:
- Marx, 1982
  - 13/13 severe recurrent hematuria resolved (3 had late recurrences)
- Maxwell, 1987
  - 7/7 gross hematuria resolved (previously transfusion dependent)
  - 8/9 flank pain resolved
  - Median survival of 6 mos

Treatment of Paraneoplastic syndromes
- 1 case malignant hyperCa → normocalcemia (Jacobs)

Why is angioembol for RCC rarely performed today?
- RCC detected earlier resulting in less bulky disease
- Lack of prospective and controlled studies
- Advances in surgery & anaesthesia often make surgery viable option in palliative cases
Thank you