CONTEMPORARY MANAGEMENT OF RENAL ANGIOMYOLIPOMA

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OUTLINE OF TALK

• Overview of renal angiomyolipoma (AML)

• Management of AML

• AML in the setting of tuberous sclerosis

• Future directions
ANGIOMYOLIPOMA: BACKGROUND

• Benign tumor composed of blood vessels, smooth muscle, and fat – triphasic histology (can be monophasic)

• Belong to PEComa (perivascular epithelioid cell) family of tumors – arise from single progenitor cell

• 80% sporadic; 20% in the setting of tuberous sclerosis

• Mean age at diagnosis = 45-55 yrs

• Female > male incidence
  • Express hormone receptors (esp. ERβ, AR)

Boorjian SA et al, Urology 2008
DIAGNOSIS OF AML

• Fat-containing lesion with no calcification on non-enhanced CT
  • < 10 HU

• Fat-poor AML (ddx vs RCC):
  • MRI
  • Biopsy
    • AML characterized by expression of HMB-45
MANAGEMENT OF RENAL AML

• Observation – for most cases (often incidental dx)

• Intervention – if:
  • **Symptoms**
    • Pain
    • Hematuria
    • Hemorrhage (Wunderlich’s syndrome)
  • Concern for malignancy on imaging (rare)

• **Prophylactic (controversial)**
  • Prevention of subsequent symptoms, bleeding
INDICATIONS FOR PROPHYLACTIC INTERVENTION FOR RENAL AML

• Size
  • > 4 cm → increased risk of growth, sxs/bleeding
    • AML enlarges → develop aneurysms with weak, elastin-poor walls → rupture
    • Risk of bleeding: 51% if > 4cm versus 15% if < 4 cm
  • “4 cm cut-off” challenged
    • 8 cm cut-off
    • Presence of aneurysm within AML > 5 mm

• Females of childbearing age
  • AMLs may grow/bleed during pregnancy, with oral contraceptive use (hormone receptors)
MANAGEMENT OPTIONS FOR RENAL AML

• Selective transarterial angioembolization
  • Variety of agents (ethanol, coil, microparticle)

• Surgical resection (esp. if concern for malignancy)
  • Partial nephrectomy (preferred if surgery undertaken)
  • Radical nephrectomy

• Ablation (RFA/Cryo)
  • Feasibility reported, albeit limited data to date

• KEY = RENAL FUNCTION PRESERVATION
ANGIOEMBOLIZATION FOR RENAL AML

• Preferred management for patient presenting with acute bleed

• Option for management in elective setting
  • Affords renal function preservation
  • Post-embolization syndrome (flank pain, fever)

• Re-treatment required in 20-30%
  • Persistent pain, hemorrhage, persistence or increase in lesion size, lesion revascularization
  • Requires continued surveillance after treatment
    • Frequency, imaging modality not well established
    • Cost implications?

Ramon J et al, Eur Urol 2009
Villalta JD et al, J Urol 2011
Murray TE et al, J Urol 2015
• 58 patients treated with partial nephrectomy
• Median tumor size = 3.9 cm
• Median postoperative follow-up = 8 years
• 12% 30-day complication rate
• Median pre/post op creatinine = 1.0/1.1 mg/dL
  • No new-onset CKD
AML ASSOCIATED WITH TUBEROUS SCLEROSIS
TUBEROUS SCLEROSIS

- Autosomal dominant

- Renal AML in up to 80% of patients
  - Can cause CKD/ESRD

- Pulmonary LAM in ~ 30%

- TS-AML
  - Diagnosed at younger age (20-35) than sporadic
  - Often multiple, bilateral tumors
    - Consider renal function preservation!
MOLECULAR BIOLOGY OF TS AML

• TS - mutation in tumor suppressor genes TSC1 (hamartin) or TSC2 (tuberin)

• Hamartin-tuberin complex negatively regulates activity of mTOR

• Mutations in TSC1 or TSC2 genes $\rightarrow$ mTOR activation
  --> cell growth/proliferation
  • Upregulation of mTOR found in TS AML

• Therefore the rationale exists for…

Roach ES et al, J Child Neurol 2004;19:643
• Phase III trial of 118 TS patients with ≥ 3 cm AML
• 1° endpoint: 50% reduction in AML volume
  • Response rate = 42% (everolimus) vs 0% (placebo)
    • Maintained regardless of age, gender, race
    • Median time to response = 2.9 months
• Well tolerated; mostly grade 1-2 AE, no increased rate of discontinuation in everolimus arm
• FDA-approved for this indication
FUTURE DIRECTIONS IN RENAL AML TREATMENT?
SAGE (Sporadic AML Growth Kinetics while on Everolimus)

• Ongoing phase II trial

• Concept = “reset the biological clock” and thereby delaying/reducing need for intervention

• 1° objective = efficacy/tolerability of everolimus in reducing tumor volume of sporadic AML ≥ 3 cm

• 2 objectives = HRQoL, growth kinetics, rate of intervention

• PI = Rob Uzzo
CONCLUSIONS

• Consider AML in ddx of solid renal mass
  • Fat on imaging; may be fat-poor (MRI, bx→HMB45)

• Intervention if symptoms, concern for malignancy
  • Size (> 4 cm? > 8 cm? aneurysm presence?)
  • Age/pregnancy status
  • Relatively poor data for prophylactic intervention→ counsel patients accordingly

• Options = angioembolization, partial nephrectomy
  • Consider patient age + comorbidities (renal function)

• Everolimus for TS-associated AMLs
THANK YOU