Disclosures

	Company/Organization
I am a member of an **Advisory Board** or equivalent with a commercial or non-commercial organization	Amgen, Janssen, Astellas
I have received payment from a commercial organization	GU Tumour Group at Bcca
I hold a patent for a product referred to in a CME/CPD program or that is marketed by a commercial organization.	CDRD
I am currently participating in or have participated in a clinical trial within the past two years.	Amgen, Janssen, Astellas

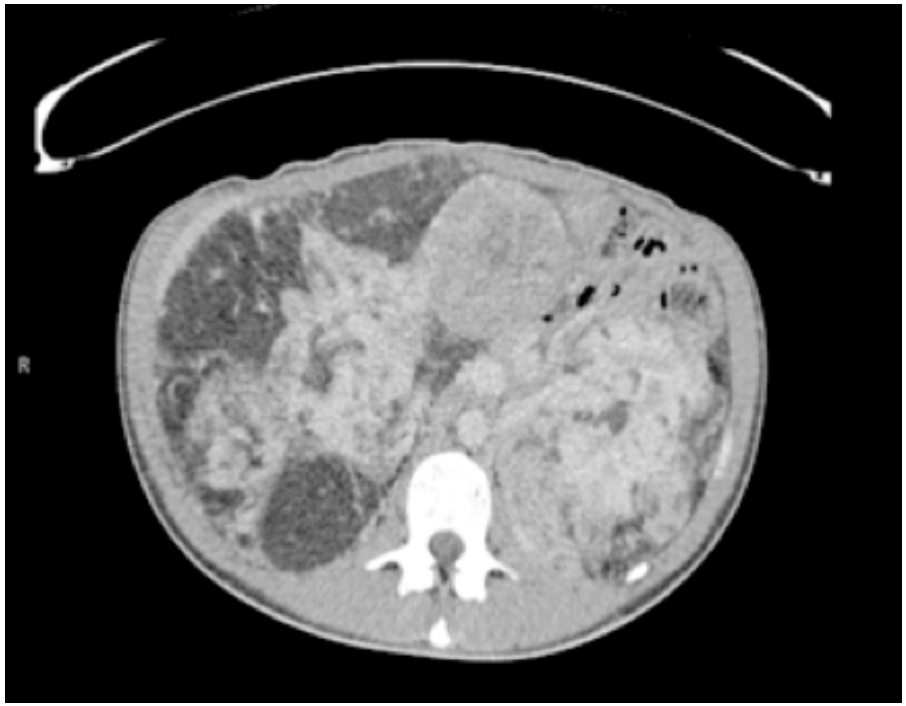
Case: Mr. JW

- 35 year old male
- Multiple features of TS complex:
  - Facial angiofibromas
  - Treated SEGAs
  - Seizure disorder
  - Retinal Hamartomas
  - *Bilateral renal AMLs*

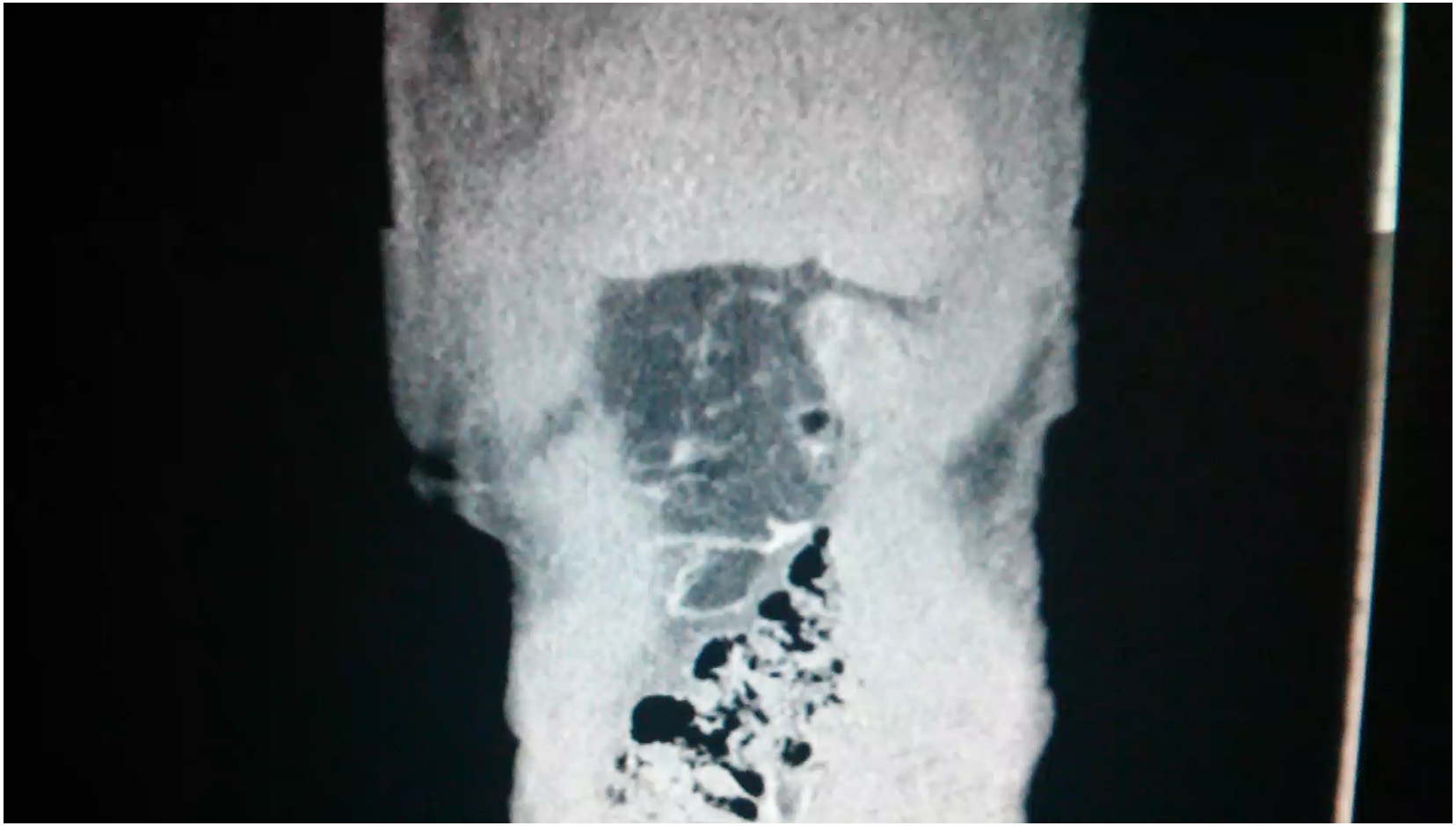
Case: Mr. JW

- 4 episodes of gross hematuria managed with embolization of right renal AML at four different intervals since age 17
- ?Follow-up lost
- 18 years later developed right flank pain, weight loss, anorexia, fevers, fatigue
- Investigated with CT abdo/pelvis with contrast

Case: Mr. JW



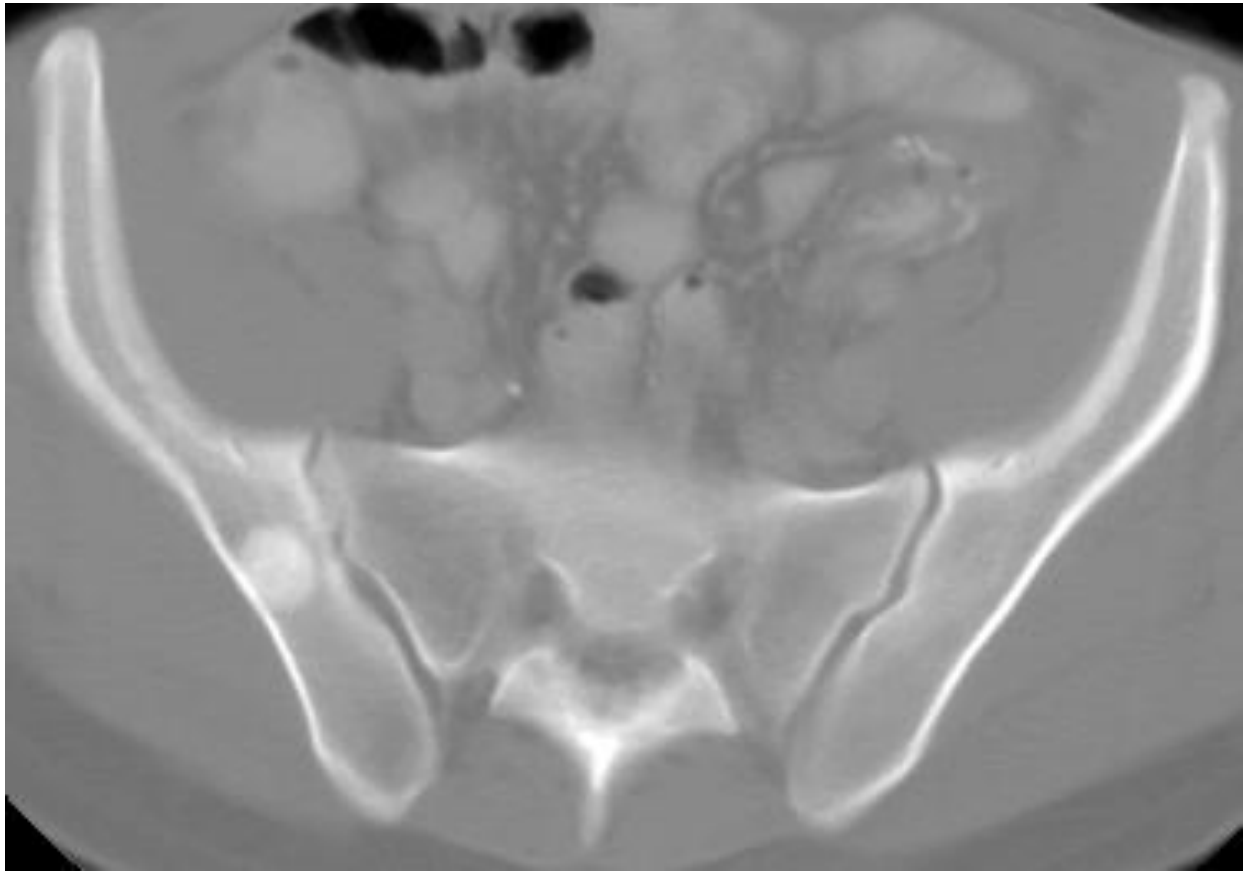
Case: Mr. JW



Case: Mr. JW

- CT demonstrated 27 cm AML replacing the right kidney and a 12 cm left renal AML
- Within medial aspect of the right renal mass, a 7 cm enhancing, well-circumscribed, soft tissue lesion concerning for RCC
- Possible sclerotic bony lesions in RIGHT Pelvis

CT Scan- Sclerotic Bone Lesion METS??



Radiology

CT of Sclerotic Bone Lesions:

Imaging Features Differentiating Tuberous Sclerosis Complex with Lymphangioleiomyomatosis from Sporadic Lymphangioleiomymatosis[1]

Radiology: Volume 254: Number 3—March 2010 ▪ *radiology.rsna.org*

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Figure 1

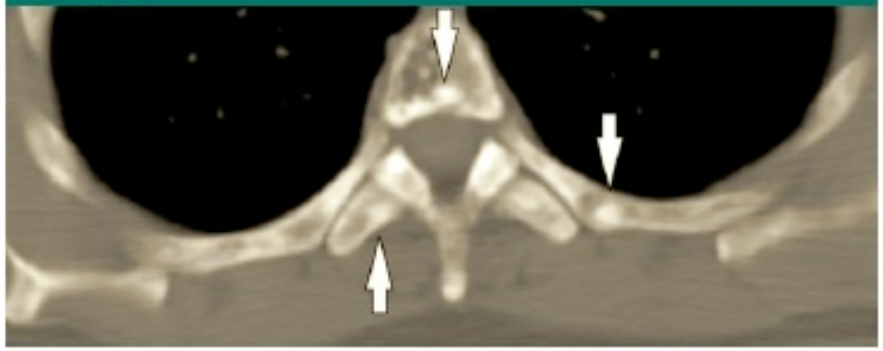


Figure 2

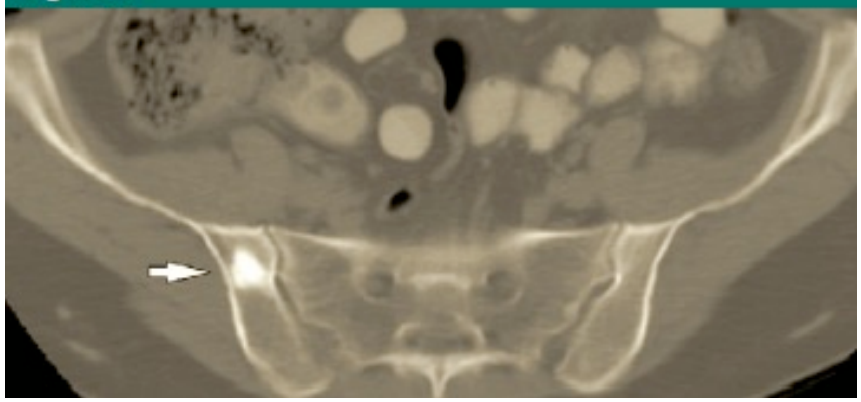
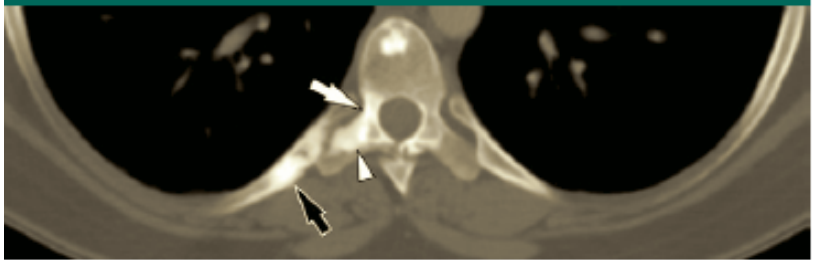


Figure 3



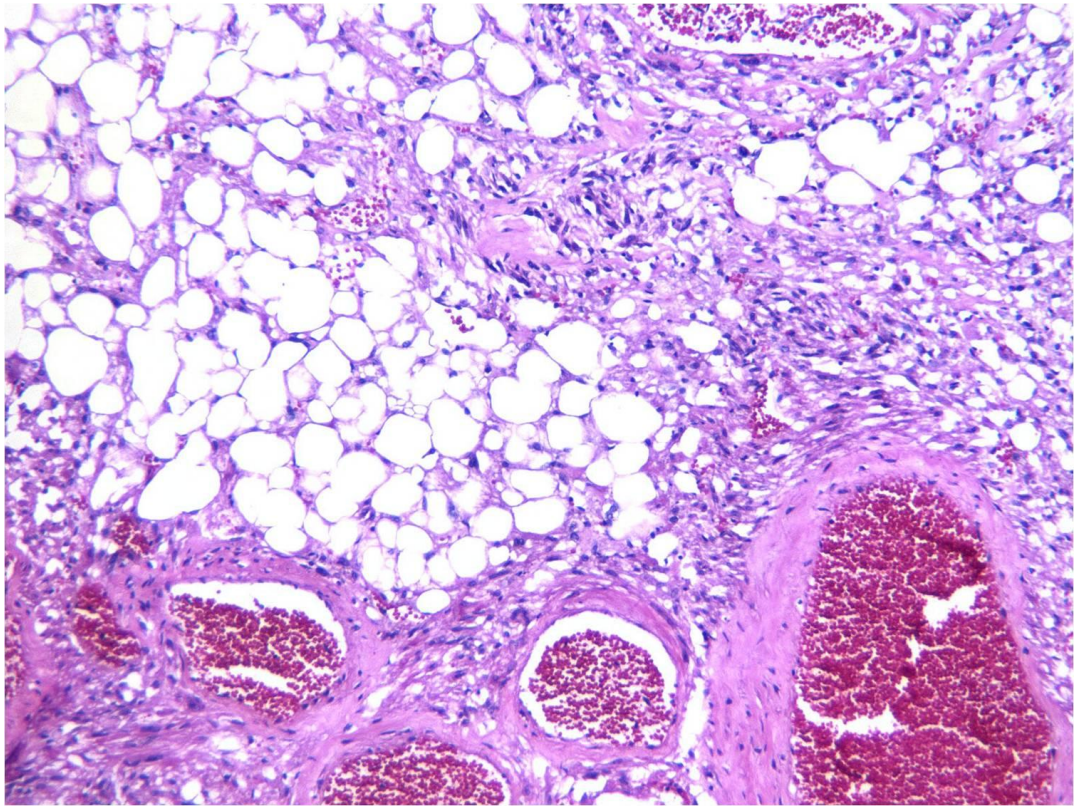
Worry? Sclerotic Bone Lesion?

- Sclerotic bone lesions are the third most common imaging finding in TSC
- Represent areas of concentric osteosclerosis in the medullary cavity
- Almost always located in the spine and commonly in the pelvis, but can also be seen in the ribs, sternum and the axial skeleton

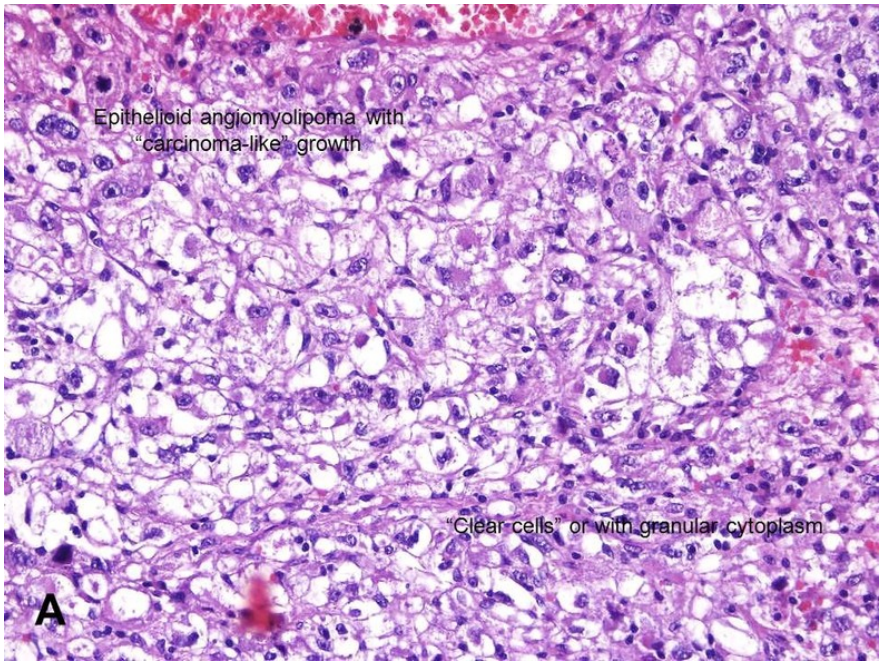
Case: Mr. JW

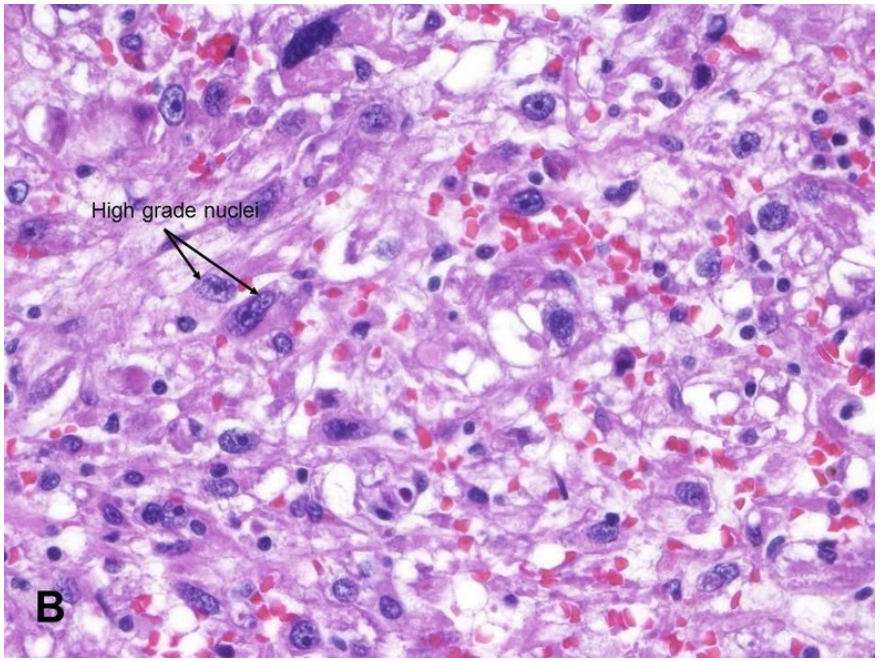
- Managed with open right radical nephrectomy
- Pathology revealed AML with areas of transformation to epithelioid AML (AMLE)

Angiomyolipoma



Epithelioid AML





Epithelioid AML

- Consists of cells with abundant eosinophilic cytoplasm, and pleomorphic and hyperchromatic nuclei
  - stain positive for HMB-45, melan-A, smooth muscle cells markers such as HHf-35, SMA and caldesmon, but negative for epithelial markers (cytokeratin)
- Because of deficient fat content, EAML is difficult to diagnose with preoperative radiological studies
- Additionally EAML has a malignant tendency, so differentiating it from AML is important

eAML

Study	No. of tumors	Size: mean (cm) (range)	% Epithelioid cells: mean (range)	Nuclear atypia	Mitosis: incidence range atypical	Necrosis, % tumors	Follow-up		Adverse outcome
							Available	Mean (months) (Range)	
Aydin *et al*[11]	15	8.6 (1–30)	51 (10–100)	93%; Diffuse: 40%, Focal: 53%	47%; 0–10/10 HPF: 6.7%	27	15/15	61.2 (1–239)	0
Brimo *et al*[12]	40 (at least 26 consultation cases)	7.2 (1–17.7)	68 (5–100)	58.4%; severe: 65%	72.5%; 1–6/10 HPF: 17%	37.5	34/40	34 (1–156)	26% recur/mets, 4 DOD, 4 AWD
Nese *et al*[13]	41 (No. of consultation cases-not reported)	11.9 (2–37)	Pure	Pattern A: 50%, B: 37.5%; A/B: 12.5%	79%; 0–13/50 HPF	73	33/41	44.5 (4–240)	17% recur, 49% mets, 33% DOD

Abbreviations: AML, angiomyolipoma; AWD, alive with disease; DOD, dead of disease; mets, metastasis; recur, recurrence.

He et al, Mod Path. 2013 Oct;26(10):1355-64

eAML and TSC

Am J Surg Pathol • Volume 33, Number 2, February 2009

Renal Angiomyolipoma

Clinicopathologic Study of 194 Cases With Emphasis on the Epithelioid Histology and Tuberous Sclerosis Association

Hakan Aydin, MD, Cristina Magi-Galluzzi, MD, PhD,* Brian R. Lane, MD, PhD,† Linda Sercia, BS,* Jose I. Lopez, MD,‡ Brian I. Rini, MD,§ and Ming Zhou, MD, PhD**

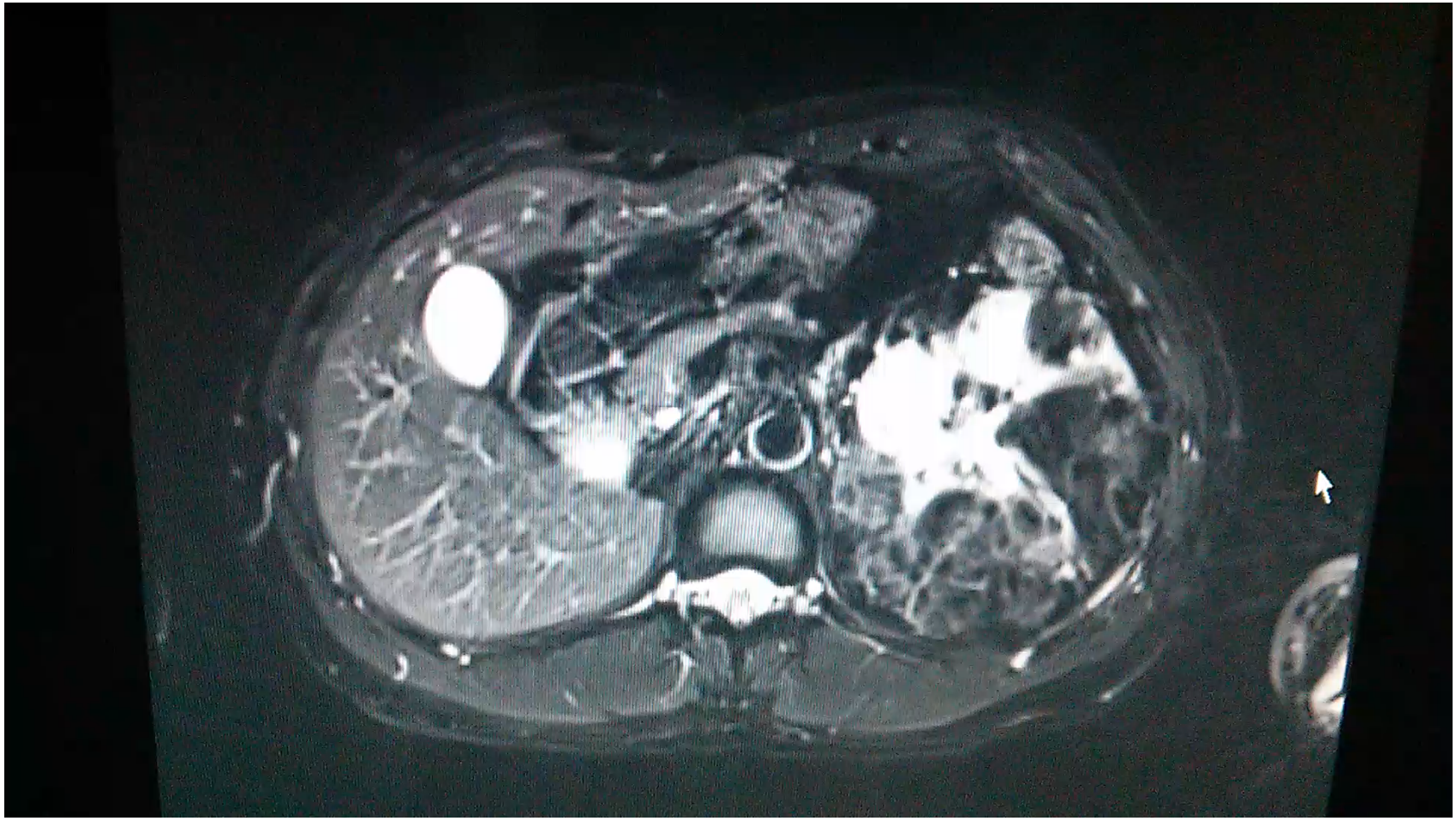
- eAML found in 15 cases (7.7%) of patients with AML (n=194)
- Average amount of epithelial component 51% (range: 10% to 100%)
- 16 (8.2%) AMLs occurred in patients with definitive TSC
- Epithelioid component, and epithelial cysts, were associated more in TSC and non-TSC AMLs (25% vs 6.2%), and 6 (3.4%)
- However, all 15 cases of EAMLs in the study had benign clinical outcomes despite adverse pathologic features

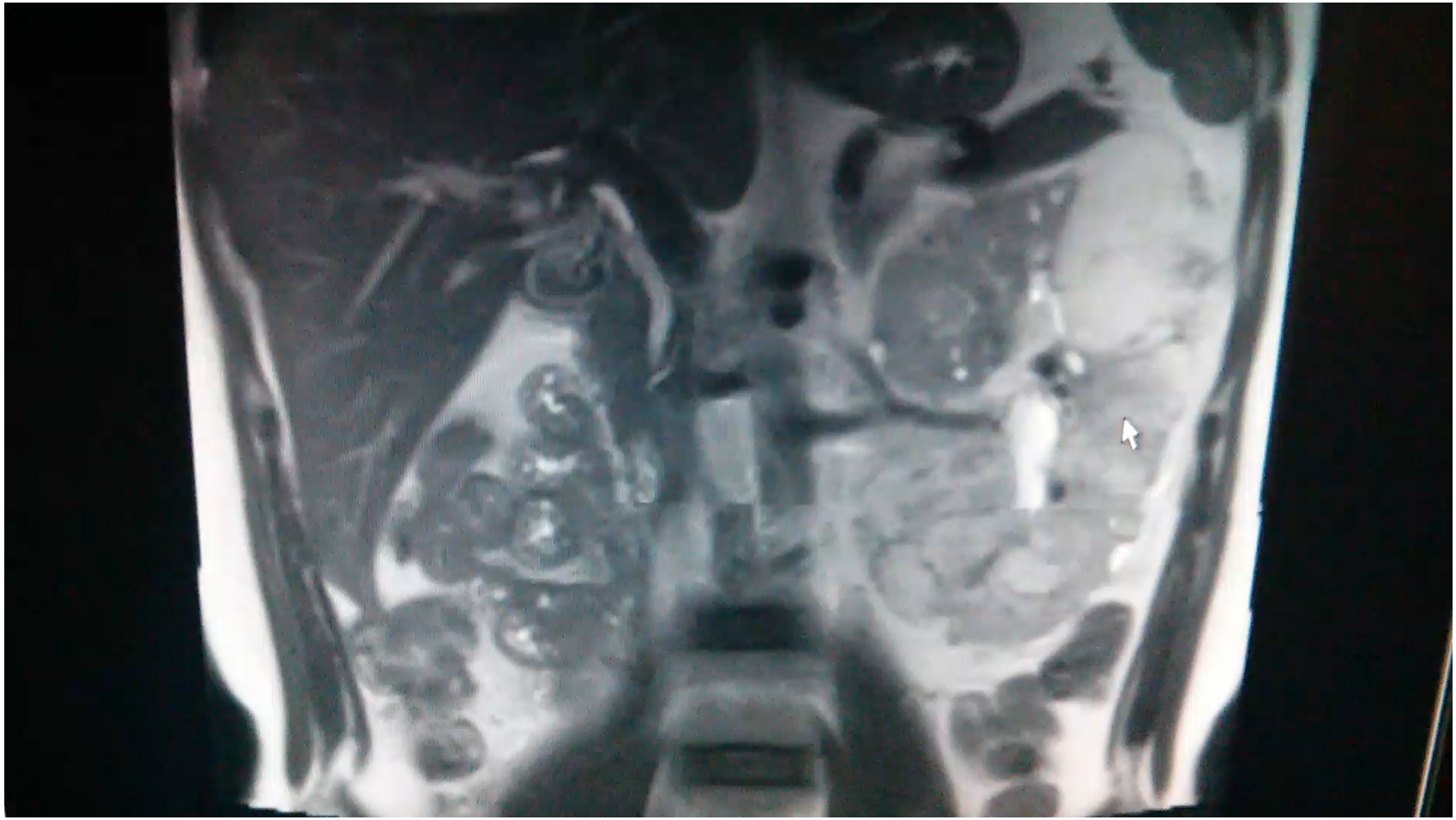
Post-operative management

- 2 issues:
  - Epithelioid AML – how to follow?
  - 15 cm AML in the LEFT kidney
  - GFR: 62
- Discussed:
  - Issues of risk of spontaneous hemorrhage
  - Lack of benefit of “localized” embolization
  - Renal function

Management

- Started on everolimus 10mg po daily
- Well tolerated, no hypertension or fatigue
- Patient noticed reduced angiofibromas and improved facial skin
- LFTS up (2x normal), now normalized
- 6 months post op MRI:





Follow-up

- Reduction of 30% in size of AML

Questions:

-How long does he stay on this?

-Still about 10 cm, and he has not had a bleed since starting treatment

Case 2

- 37 year old female
- Multiple features of Tuberous Sclerosis (TS) complex:

-renal angiomyolipomas (AMLs)

-mental retardation

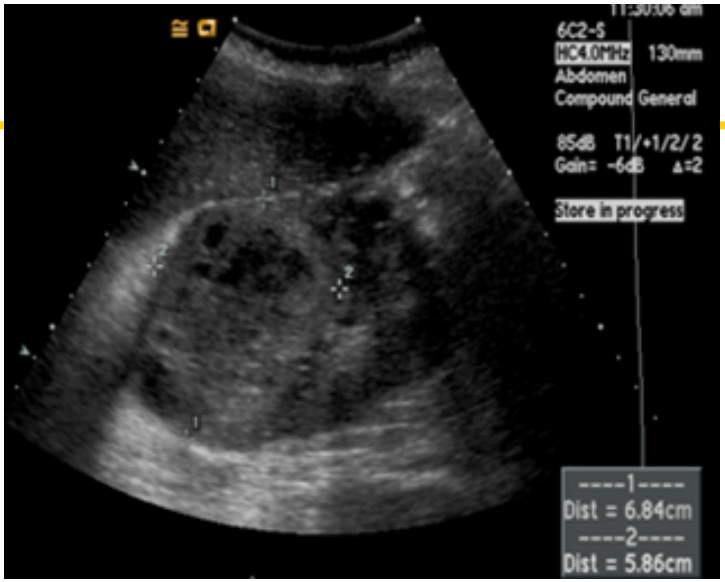
-seizures

-adenoma sebaceum

Case 2

- Microcytic anemia and microscopic hematuria noted by Family MD
- Investigations included abdominal ultrasound
- Hypervascular, 7 cm lesion in the upper pole of the right kidney on ultrasound
- Urology referral

Case 2 Ultrasound / CT



Case 2

- CT abd and pelvis: 9 cm centrally necrotic, vascular mass suggestive of renal cell carcinoma
- CT Chest – Normal
- CT Head - cortical tubers, no metastases

Case 2

- 8 months previously, worsening seizures, deteriorating at home
- Admitted to hospital
- Started on everolimus 10mg daily
- Well tolerated

Case 2

- Repeat CT 4 months later showed reduction of renal AML by 50%
- Seizures stopped
- Hematuria and anemia improved
- Remains on everolimus 4 years later

Summary

- TSC is a complex disease
- Even the AML / Renal component is complex
- Surgery for AML should be last choice
- Consider everilomus for management of AML TSC to reduce bleeding risk and maximize renal function