Benign renal tumours

Extremely common – esp. in females < 45 yrs
May arise from cortical tissue (adenoma/oncocytoma) or differing mesenchymal elements
Types:

- Benign renal cyst
- Renal cortical adenoma
- Metanephric adenoma
- Oncocytoma
- Angiomyolipoma
- Cystic nephroma
- Mixed epithelial stromal tumour of kidney (MESTK)
- Leiomyoma
- Others
  - Fibroma
  - Lipoma
  - Lymphangioma
  - Haemangioma
  - Juxtaglomerular tumour (reninoma)

Benign renal cyst

Commonest renal lesion – accounts for 70%
Male:female 2:1
Seen in 50% individuals over 50 yrs
Growth rate 2.8mm/yr (Terada 2002) – faster in young pts
Large symptomatic cysts may require Rx: percutaneous aspiration/sclerosis successful in 90% (Hanna 1996) using 95% alcohol. More recently laparoscopic decompression reportedly safe (Roberts 2001)

Renal cortical adenoma

Controversial diagnosis
Small tumours arising from renal cortex well documented. Post-mortem studies indicate incidence of 7-23% [incidence on USS screening much lower @ <1%; Tosaka 1990]. Typically well-circumscribed lesions with uniform cells and unremarkable nuclear features, usually arranged in tubulopapillary or papillary arrays. Bell reported low rate of metastasis (~5%) of such lesions when <3cm when compared with a rate of 66% for lesions >3cm (Bell 1938, 1950). Led to pervasive 3cm rule. However now generally believed that all solid epithelium-derived tumours potentially malignant. Reasons:

- Increase with age
- Male:female ratio 3:1
- Associated with smoking
- More common in VHL disease and acquired renal cystic disease
- Commonly exhibit trisomy 7/17 (as in papillary RCC)
- No histopathological distinction from RCC

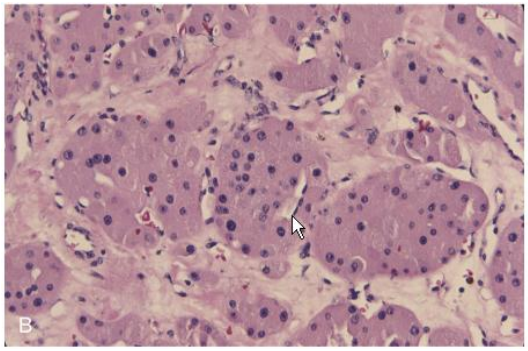
Metanephric adenoma

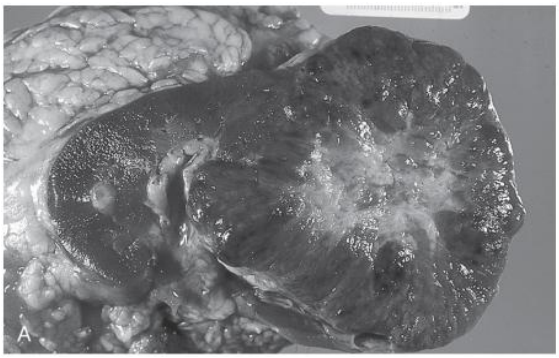
Rare renal tumour associated associated with benign clinical course
Usually incidental mass lesion requiring nephrectomy

Occasional presentation with flank pain, haematuria, mass, polycythaemia and hypercalcaemia
Microscopically characteristic – small cells intense basophilic staining resembling nephroblastoma (Wilm's tumour) – also positive for Wilm's tumour protein-1 with similar IHC characteristics and often regress with scar/calcification.
Largest series Davis 1995: 44% symptomatic. Mean size 5.5cm. One case of metastasis described, although may be aggressive variants.
Follow-up post-nephrectomy uncharacterised due to rarity. Recommend follow-up as for low-risk RCC.

Oncocytoma
Originally described by Klein and Valensi 1976
3-7% of all renal masses
Almost universal benign growth
Mahogany brown tumour; well circumscribed but lacking true capsule
Central stellate 'scar', usually lacking fibrosis or hypervascularity
Uniform round, polygonal cells with dense eosinophilic staining and little cytological atypia. Derived from distal convoluted tubule.
Packed with mitochondria at ultrastructural level
A/w loss of chromosome 1 and Y; LOH on chromosome 14q and 11q13; typical chromosomal abnormalities associated with RCC (chr. 3,7,17) very rarely seen in oncocytoma
CT findings of central necrosis and stellate scar poor predictive value in differentiating oncocytoma from necrotic RCC (Licht 1995)
Difficult to differentiate from granular clear-cell RCC or eosinophilic chromophobe RCC on biopsy
Co-exists with RCC in 7-32% of cases [Campbells]. Therefore surgical treatment advocated – partial if strongly suspected (BHD and features) and favourable location.
Oncocytoma a/w multicentricity, bilaterality and metachronous recurrence in 4-13%. Intermittent USS surveillance therefore advocated by some.
Associated with Birt-Hogg Dube syndrome and familial oncocytosis
BHD
- Short arm of chromosome 17 – codes for folliculin
- Hair follicle tumours
- Spontaneous pneumothorax
- Renal oncocytoma

Familial oncocytosis
- Genetic defect unknown
- Renal oncocytomas
  - Multicentric
  - Bilateral
  - Early age of onset





Angiomyolipoma

Uncommon

0.3% incidence in post-mortem series; 0.1% in USS screening

Term first coined in 1951 by Morgan

80% sporadic; 20% a/w tuberous sclerosis [Autosomal dominant condition characterised by mental retardation (twits), epilepsy (fits), adenoma sebaceum (facial angiofibromas - zits), and ash-leaf patches]

Thought to be derived from perivascular epithelioid cells

Probably hormone (?oestrogen) dependent

- More common in females
- Extremely rare before puberty
- Accelerated growth in pregnancy (increased risk of rupture)
- Rapid growth associated with OCP usage

Presentation

- Asymptomatic >50%
- Loin pain
- Haematuria
- Anaemia
- Massive retroperitoneal haemorrhage (Wunderlich's syndrome) 10%

<u>Characteristics of AML by subtype</u>

	Sporadic AML	AML in TS
Frequency	80%	20%
Male:female	1:4	1:2
Peak age	50 yrs	30yrs
Distribution	Unilateral single	Bilateral multicentric
Growth rate	<5% per year	20% per year
Symptoms	Usually asymptomatic	Often symptomatic

<u>Radiological findings</u>

USS Typical but non-diagnostic finding is a well-circumscribed highly echogenic lesion with acoustic shadowing (small calcified RCC rarely shadows on USS – Seigel 1996)

CT Most reliable diagnostic modality
Presence of fat (-20 HU) within the lesion on CT virtually excludes RCC* and considered diagnostic (Bosniak 1998)
* all 5 reported cases of RCC containing fat also contained areas of

calcification, which has *never* been reported in AML (Lemaitre 1997)
Up to 14% of AMLs do not have identifiable fat and should be treated as RCC until proved otherwise

MRI Fat-suppressed images may be helpful in difficult cases or when CT contraindicated for other reasons

Angio 50% AMLs a/w aneurysmal dilatation

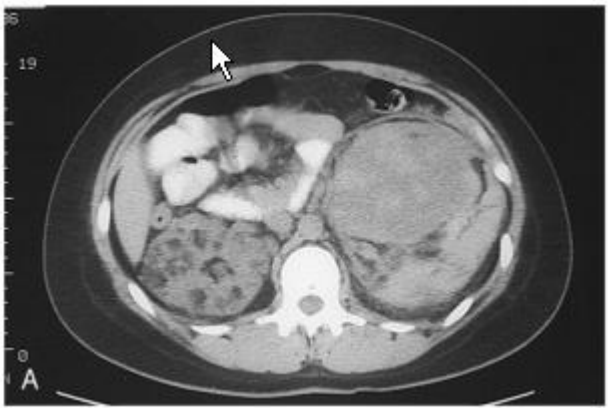
<u>Clinical behaviour</u>

Universally benign

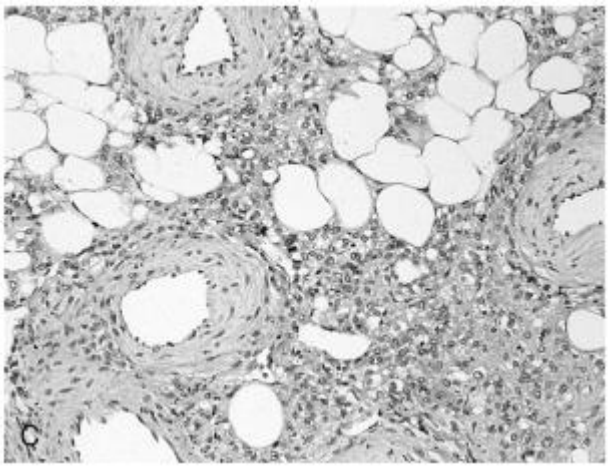
Non-renal AMLs found in LN, retroperitoneum and even into renal vein reported but thought to be due to multicentricity rather than metastasis

Occasionally cellular atypia identified and differentiating from sarcoma may be difficult (fat = liposarcoma; smooth muscle = leiomyosarcoma; vascular – fibrosarcoma). In such instances positive staining for **HMB-45** (monoclonal antibody vs. melanoma-associated antigen) highly specific for AML rather than sarcoma

Recently an epithelioid variant of AML has been described which displays pathologic features associated with aggression in a number of other cancers (necrosis, nuclear atypia and mitosis) and is reportedly associated with metastasis (Bissler 2004). However, a recent large multicentre retrospective series including the Cleveland Clinic reported on 15 cases of epithelioid AML with long term follow-up (mean 5.1 years). Despite unfavourable pathology, none had local recurrence or distant metastases (Aydin 2008).



Bilateral AML in TS


Fat, smooth mm., thick-walled BV

Despite benign behaviour AMLs may be life-threatening due to rupture
Risk of rupture related to size: multiple studies have shown that AMLs >4cm a/w symptoms and an increased risk of rupture (most studies broadly agree with findings of Oesterling1986

<4cm 20% symptomatic
>4cm 80% symptomatic (9% acute rupture)

Growth rates (combined figures from Steiner 1993, Kenelly 1994, DeLuca 1999) <5cm only ~8% show interval growth on extended follow-up. Other than TS, no reported specific factors to identify which tumours will grow

Management

Surveillance recommended for asymptomatic lesions < 4cm. Interval imaging at 6 months or 12 months to determine growth rate. No studies defining when discharge safe for stable tumours.
Intervention considered for:

- Large tumours > 4cm
- Symptomatic tumours
- Women contemplating pregnancy in whom emergency intervention would be difficult or undesirable

NB. For patients with TS, bilateral or multicentric tumours, or renal insufficiency should be considered for NSS

Transarterial selective embolisation

Currently considered modality of choice
Originally reserved for patients with TS: recent large series confirm safety and efficacy in all AMLs
Largest single study to date Ramon 2008 (Israel): 48 AMLs embolised with polyvinyl alcohol and particles. Mean tumor size 10.3cm. Successful SAE in 91% with surgery avoidance in 96%. Minor complications in11%. Post-embolisation syndrome in 12.5%. 5 yr follow-up = no deaths, no RP haemorrhage, no deterioration in creatinine, 98% renal preservation. Older combined series report reduced efficacy, with re-treatment rates of approximately 15% (Harabayashi 2004)
Overall complication rate from combined series 10%:

- Groin complications (bleed, haematoma, infection)
- Post-op haemorrhage
- Post-embolisation syndrome (fever, loin pain)
- Abscess formation
- Cyst formation
- Failed embolisation

Alternative treatments

- Partial nephrectomy
- Simple nephrectomy
- Radical nephrectomy (if diagnosis in doubt)

Tuberous sclerosis

- Described by Bonneville in 1880
- Incidence 1:6000 – 1:14500
- TSC1 gene on chromosome 9q

TSC2 gene on chromosome 16p (adjacent to PKD1 gene)

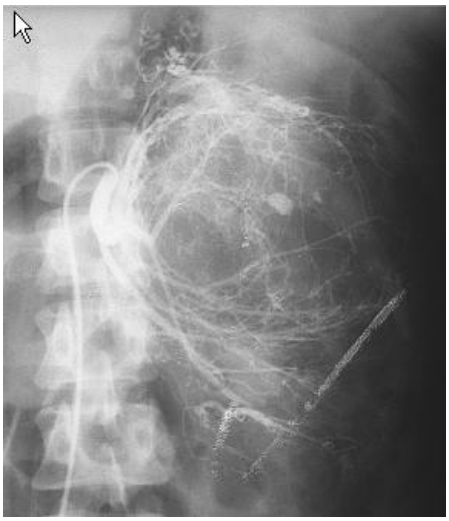
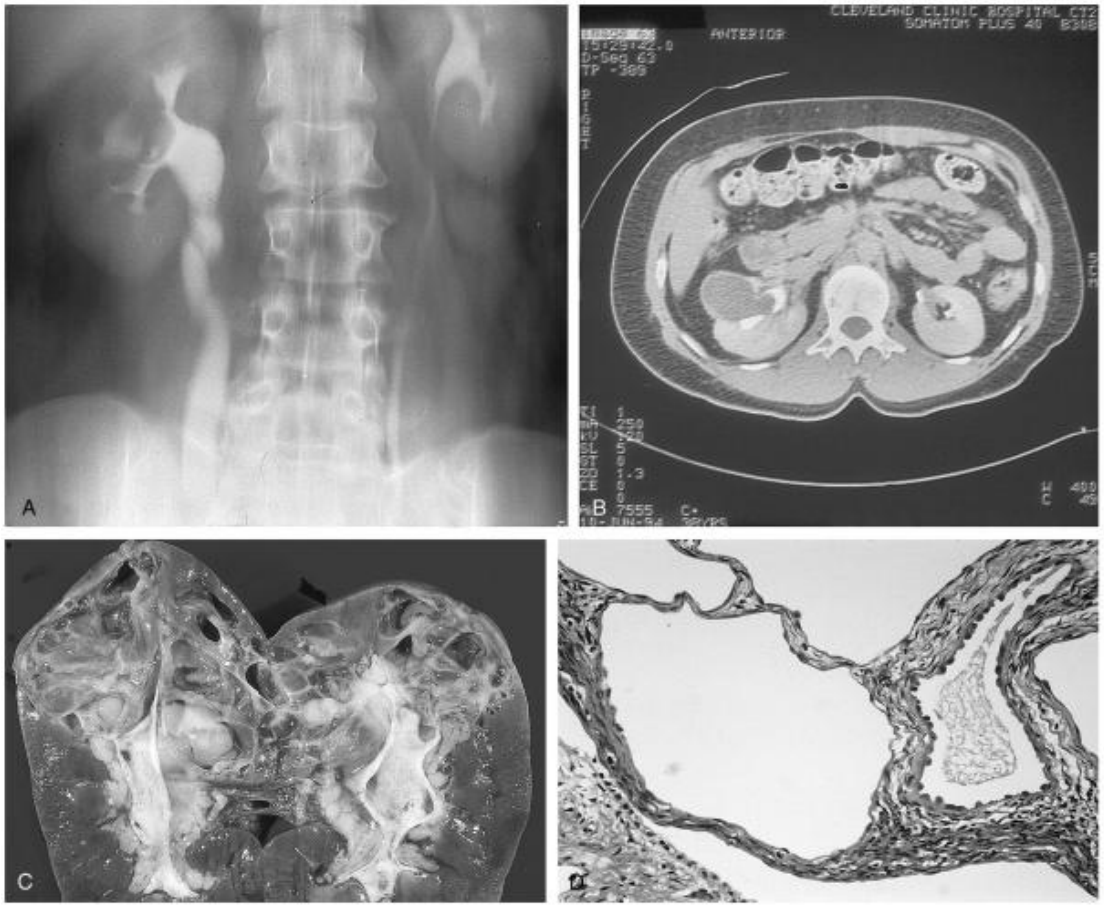


Figure: increased vascularity/aneurysmal dilatation

Cystic nephroma
AKA multiloculated cystic nephroma – now reclassified as RESTs (renal epithelial-stromal tumours)
Benign tumour
Bimodal age distribution: 2-3 yrs; 30-50 yrs
Commoner in male children and adult females
Macro: well circumscribed, encapsulated, multiloculated with intervening septa
Micro: cuboidal cells lining cysts with hobnail appearance
Asymptomatic in kids; haematuria, pain, hypertension in adults
Virtually all have appearances of Bosniak III/IV cysts on imaging – therefore usually post-surgery finding. May be suspected by finding of curvilinear calcification and herniation into renal pelvis
If suspected on imaging - partial OK in adults; radical nephrectomy in kids as differentiation from cystic Wilm's tumour difficult



A, Intravenous urogram demonstrates indentation of the midportion of the right renal pelvis, suggesting a mass effect. **B,** CT scan reveals a multiloculated cystic mass herniating into the collecting system. **C,** Nephrectomy specimen harboring a multiloculated mass that protrudes into the collecting system. **D,** Cystic nephroma illustrating diagnostic findings: multiple cysts lined by hobnail-shaped epithelial cells and intervening stroma notable for increased cellularity.

Mixed epithelial stromal tumour of the kidney
Recently described (Adsay 2000)
Usually in perimenopausal women taking oestrogen therapy
Positive staining for oestroegen and progesterone receptors
Solid and cystic components – appearance similar to cystic nephroma macroscopically. Bosniak III/IV on CT.
Benign clinical course after radical nephrectomy in all 12 patients described by Adsay

Leiomyoma
Arise from capsule, peri-pelvic tissues, or rarely renal vein
Incidence of ~5% in post-mortem series
Vast majority asymptomatic. Occasionally grow to a large size causing pain, haematuria or gastric complaints [largest resected lesion 57cm, in diameter!]
Mx – surveillance if asymptomatic and obvious; partial if symptomatic and suspected. Radical otherwise

Other renal tumours
Fibroma - small medullary 1-7mm in diameter. Rarely symptomatic. 10 clinical cases in literature usually presenting with filling defect
Lipoma – Arise from renal capsule. Occasionally confused with AML.
Lymphangioma – cavernous tumour, females in 30s
Solitary fibrous tumour – DD fibrosarcoma – WLE advised
Juxtaglomerular tumour (aka reninoma)
- Females 20-40 yrs
- Derived from endothelial cells – therefore positive staining for factor 8
- Small (<3cm) solid tumours easily seen on CT/USS
- Present with high BP, low K+, polydipsia, polyuria, headache
- Surgical excision curative