Genetic cystic, interstitial and tumorous renal disease

Including: Autosomal dominant and recessive polycystic kidney disease; tuberous sclerosis type 1 + 2; Von-Hippel-Lindau's disease; Bardet-Biedl's syndrome

Autosomal dominant polycystic kidney disease (ADPKD)

- Type 1 and 2
- Genetics of ADPKD
    - Both autosomal dominant
    - Genes are called PKD1 (Type 1 – this encodes polycystin 1 on chromosome 16) and PKD2 (Type 2 – encode polycystin 2on chromosome 4) - these proteins are important in renal tubular cell differentiation
- Presentation of ADPKD
    - Flank or loin pain
    - Macro/microscopic haematuria
    - Proteinuria
    - Hypertension
    - Polyuria
    - Headache/neurology from subarachnoid haemorrhage
    - Symptoms associated with cysts in other tissues
    - Causes roughly 5-10% of CKD
- Work-up of ADPKD
    - USS to make the diagnosis
    - If positive family history: 2 cysts in either kidney is diagnostic if <30 years old, between 30-60 4 cysts in total is diagnostic, if>60 8 cysts in total is diagnostic
    - If negative family history: <30 5 cysts in total, 30-60 5 cysts in total and >60 8 cysts in total is diagnostic of ADPKD
    - Patients with a ADPKD and a FH of SAH will need screening MRI brains to monitor for berry aneurysm
    - Genetic testing
- Complications (and treatment) of ADPKD
    - Hypertension: ACE-I
    - CKD: Dialysis or transplant
    - Cyst haemorrhage: analgesia and hydration, nephrectomy is situation is dire
    - Cyst infection: antibiotics (normally longer course due to poor penetrance)
    - Nephrolithiasis As per any no ADPKD patient
    - Extra renal cysts (hepatic, pancreatic, mesenteric, seminal etc) – puncture/de-roof/remove
    - Mitral valve prolapse – aortic regurgitation – as per non-ADPKD patient
    - Diverticular disease/hernias – as per non-ADPKD patient

Autosomal recessive polycystic kidney disease

- Autosomal recessive
- PKHD1 gene on chromosome 6 encoding polyductin and fibrocystin
- Present with very early onset CKD, hepatic fibrosis with portal hypertension

Medullary cystic kidney disease

- Autosomal dominant
- MCKD-1 and 2 genes encoding renal cilia proteins – causes small cysts at corticomedullary junction
- Nocturia, polydipsia and polyuria, can develop hyperuricaemia
- Most get end-stage renal disease by 60

Tuberous sclerosis 1 and 2

- Multi-system hamartomatous disease
- Autosomal dominant – mutations in TSC1 (type 1) and TSC2 (type 2) tumour suppressor genes- protein is hamartin.
- Type 2 is more common
- Renal angiomyolipomas, skin changes (hamartomas, shagreen patches, ungal fibromata) and seizures. Can have cystic kidney disease also
- Renal lesions need surveillance, as does BP (for HTN) and renal function (CKD)- normally done via an annual specialist review with renal USS or CT.

Von-Hippel-Lindau's disease

- Autosomal dominant
- Multisystem masses both benign and malignant – retinal angiomatosis, phaeochromocytoma, renal tumours (RCC), Lindau tumours, pancreatic tumours
- VHL gene (short arm of Chr 3) inactivation (tumour suppressor) leading to abundance of vascular growth factors
- Need VHL genetic testing to confirm
- MDT approach

Bardet-Biedl's syndrome

- Autosomal recessive
- Retinitis pigmentosa, polydactyl, mental retardation, hypogenitalism and obesity
- Renal: renal dysplasia and abnormal calyces