Renal and ureteral involvement in Erdheim-Chester disease

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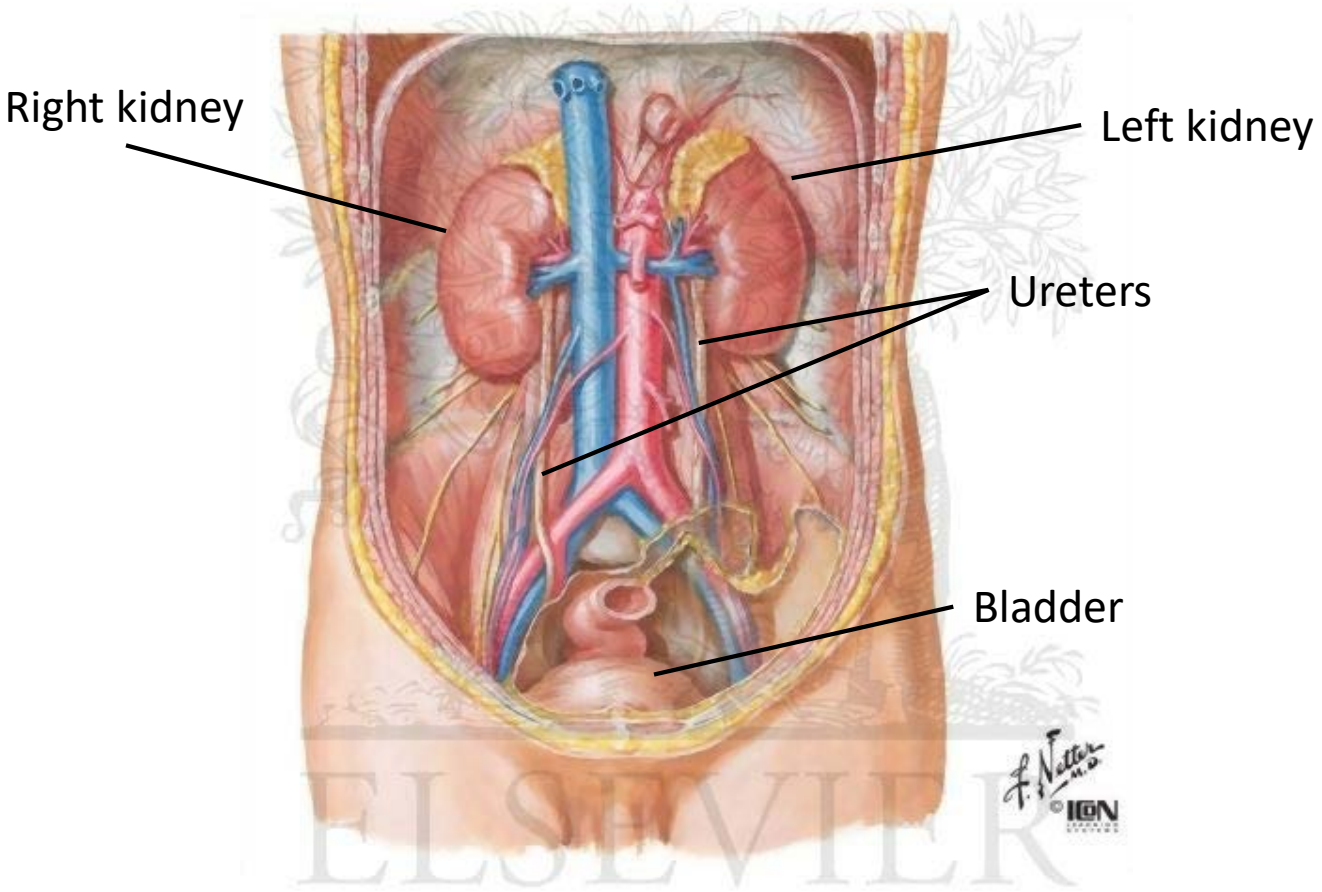
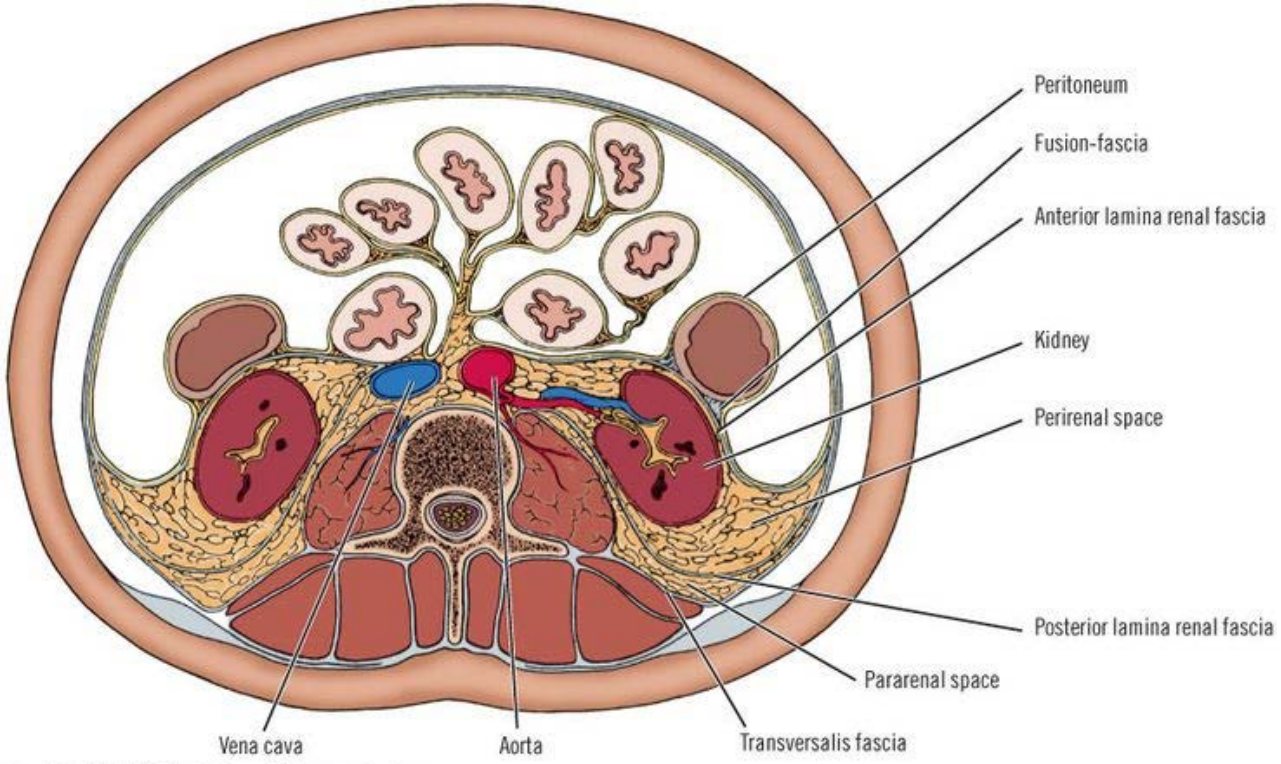
The kidneys and the urinary excretory system



The kidneys and the retroperitoneum



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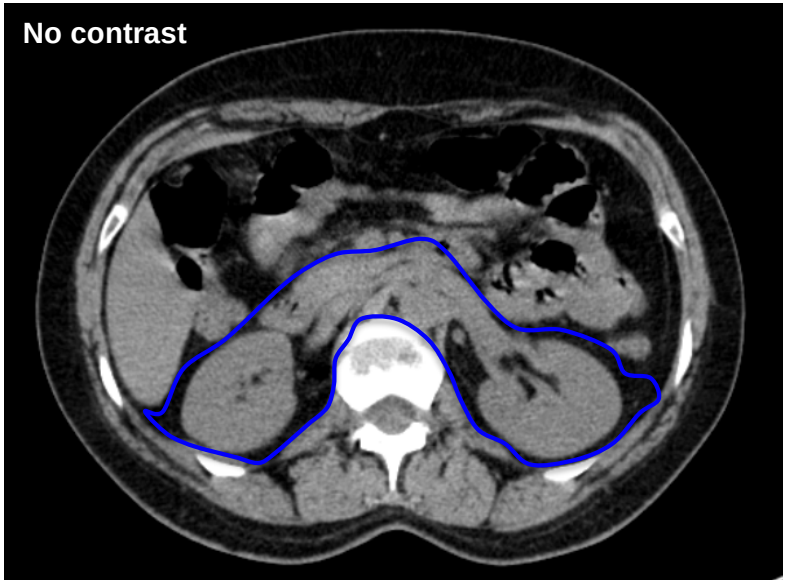
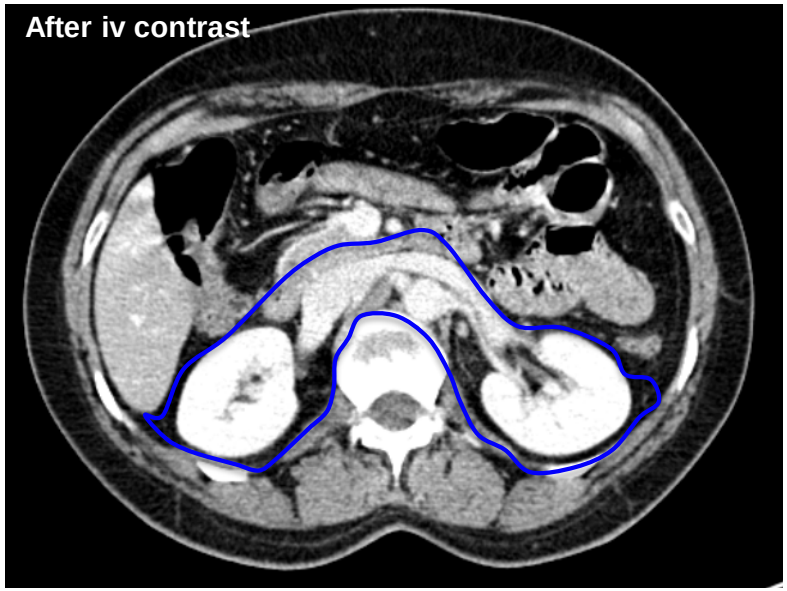
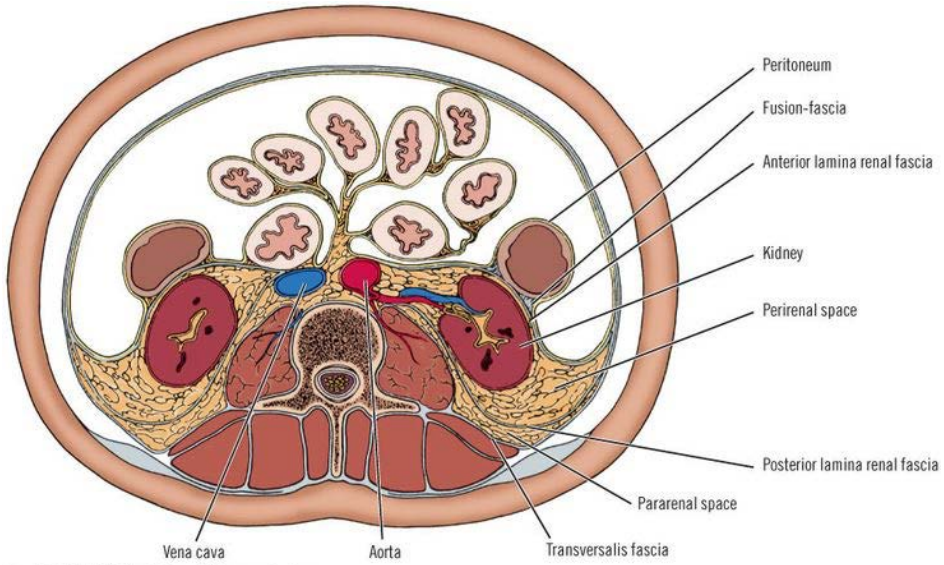
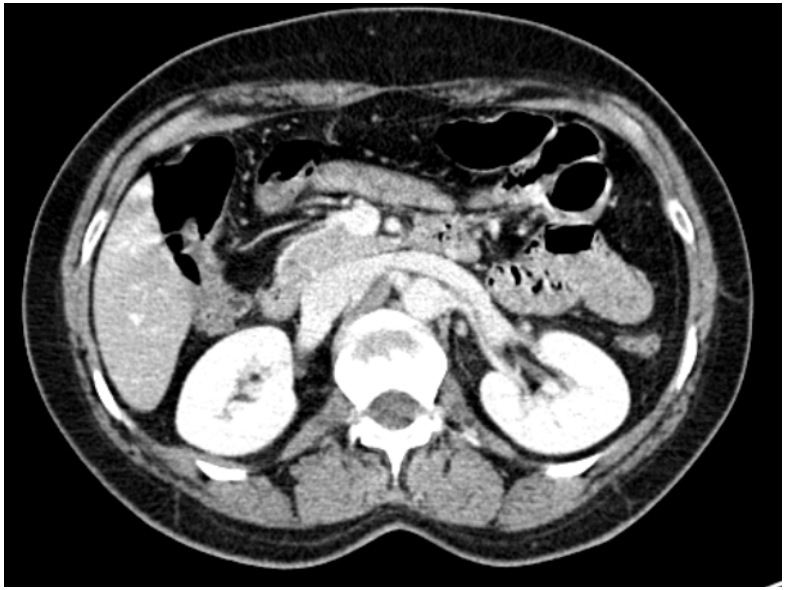


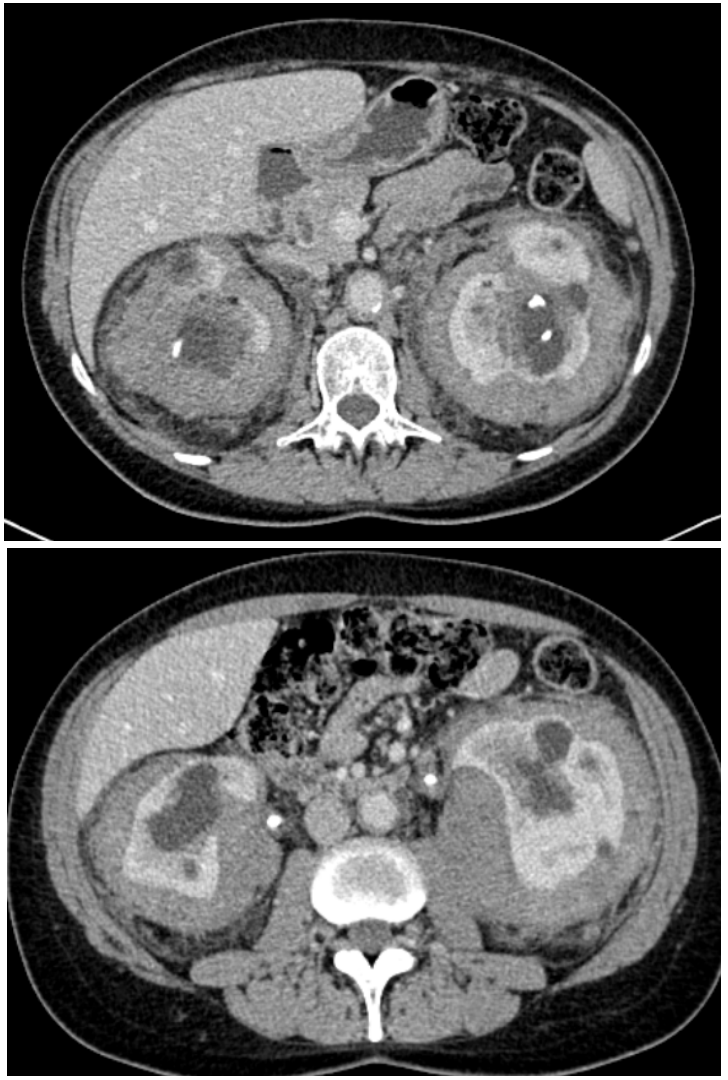




Perirenal infiltration in ECD (*hairy* kidneys)



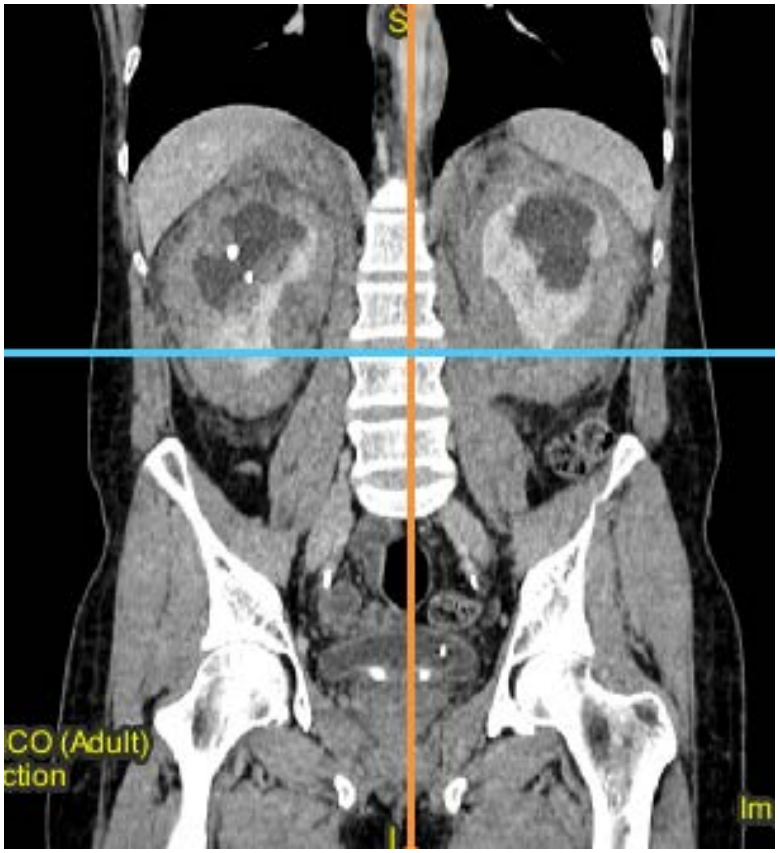
Abdominal CT scan in a healthy 38 yo lady



Abdominal CT scan in a 50-yo ECD man

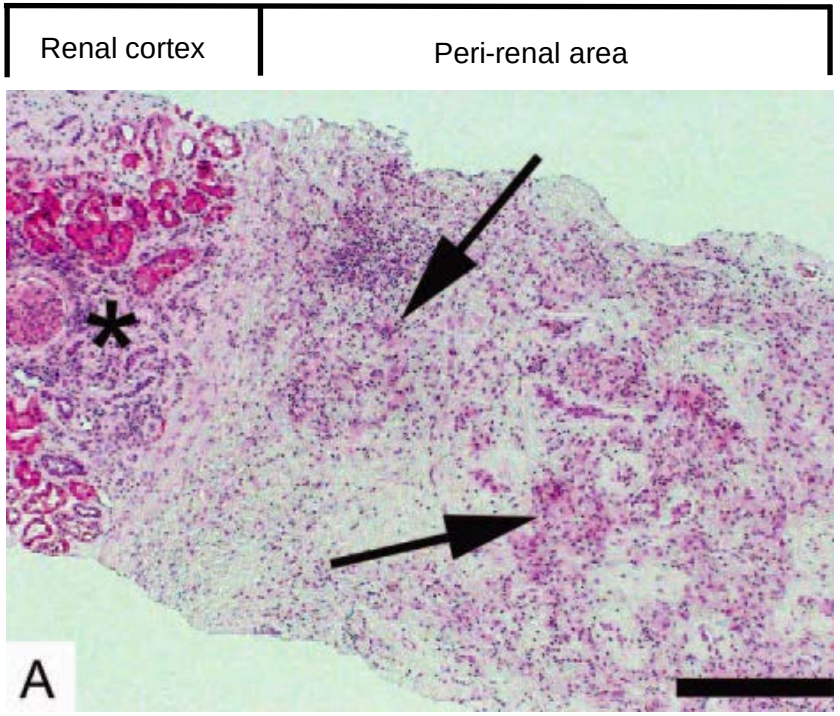
Perirenal infiltration in ECD (*hairy* kidneys)

Abdominal CT scan in a healthy 38 yo lady



Abdominal CT scan in a 50-yo ECD man

Perirenal infiltration in ECD (*hairy* kidneys)



- Approximately 50-70% of the cases (in our series, 17/28 pts, 62%)
- The infiltration is often limited to the peri-renal space
- It usually extends to the renal hilum (renal artery and vein), the renal pelvis and the proximal ureter
- Peri-renal disease may limit the ability of the kidney to dilate when the ureters are compressed
- Good site for diagnostic biopsy

Imaging studies for retroperitoneal/perirenal ECD

Imaging technique	**PROs**	**CONs**
Sonography (ultrasound)	Allows visualization of hydronephrosis; non-invasive, no radiation	Poor visualization of peri-renal or peri-ureteral tissue; limited usefulness for peri-renal tissue follow-up; operator-dependent
Computed tomography (CT)	Optimal visualization of all renal and ureteral complications of ECD; non-operator dependent	Radiation dose; potential nephrotoxicity; contraindicated if allergy to iodinated contrast medium
Magnetic resonance imaging (MRI)	Optimal visualization of all renal and ureteral complications of ECD; non-operator dependent; no radiation	Contraindicated in patients with severe renal failure, allergy to metals, bearing pacemakers or metal prosthesis
Positron emission tomography (PET)-CT	Allows evaluation of metabolic disease activity (active vs inactive); no significant contraindications	Radiation; does not reliably assess dimension of the lesion; high cost
(retrograde) urography	Optimal visualization of the site of ureteral stenosis; guides stent or nephrostomy placement	Radiation; does not assess dimension of the infiltrative lesions; quite invasive

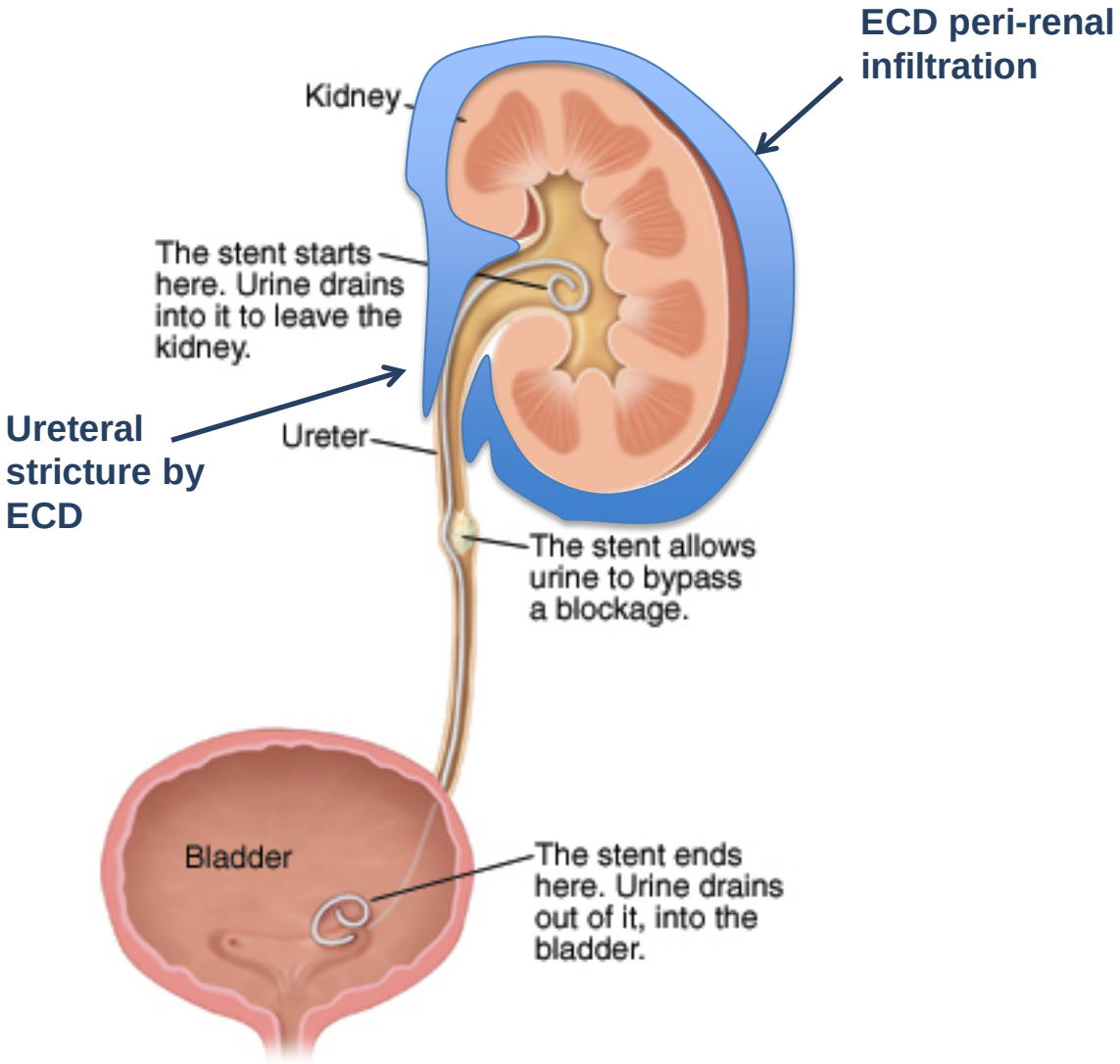
Ureteral obstruction in ECD

- Approximately 20-50% of the cases
- May be unilateral (often bilateral)
- Usually insidious onset, often asymptomatic or with dull back pain
- ECD infiltration usually causes stenosis of the proximal(upper) third of the ureter (unlike idiopathic retroperitoneal fibrosis)

How to relieve ureteral obstruction

Double- J ureteral stents

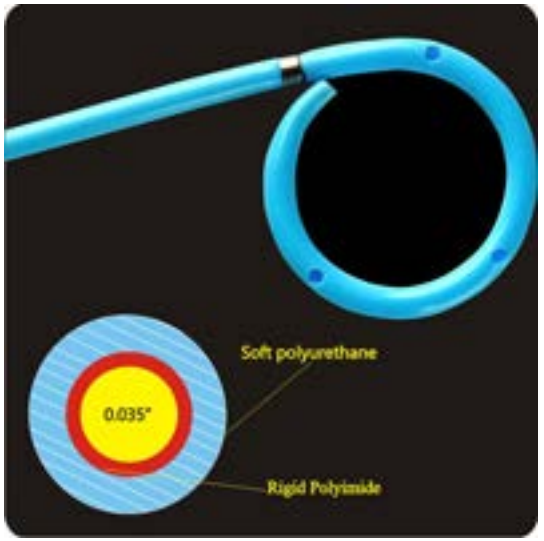
- Placed via cystoscopy
- Duration: 6-12 mths
- Complications: irritation, lower urinary tract symptoms, infections, bleeding
- Allow “internal” renal drainage avoiding external nephrostomy tubes



How to relieve ureteral obstruction

Double-J “tumor” stents

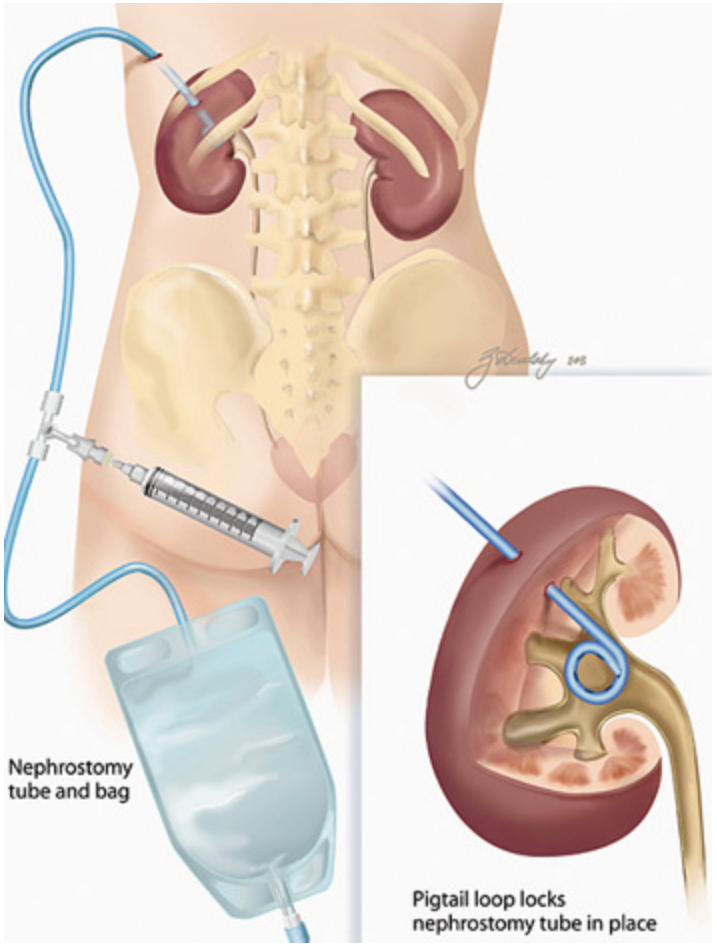
- Placed via cystoscopy
- Duration: 6-12 mths
- Reinforced internal layer for resistance to compression
- Different reinforced segments depending on the site of ureteral obstruction



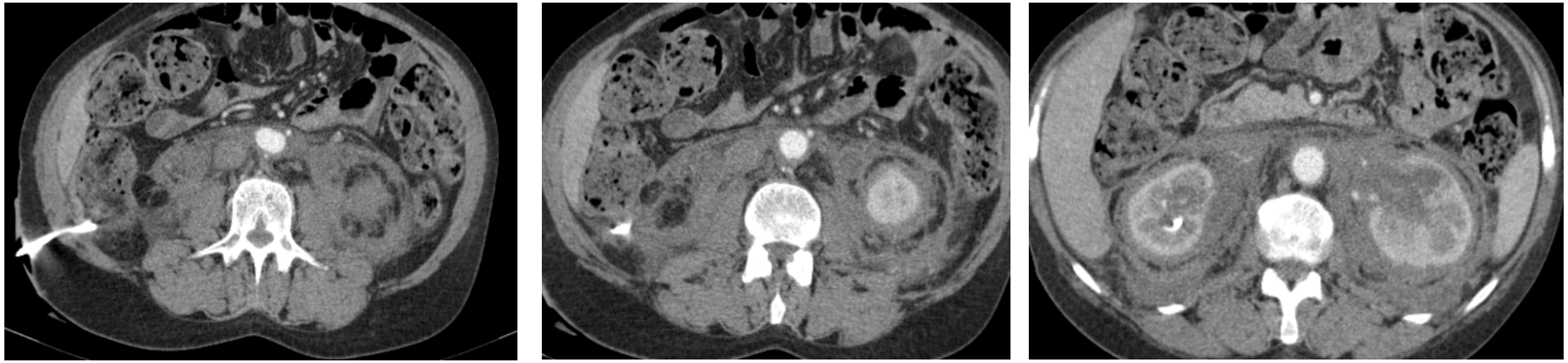
How to relieve ureteral obstruction

Nephrostomy

- Placed percutaneously
- Complications: infections, bleeding, poor quality of life
- Allows efficacious drainage of the obstructed kidney(s)



How to relieve ureteral obstruction

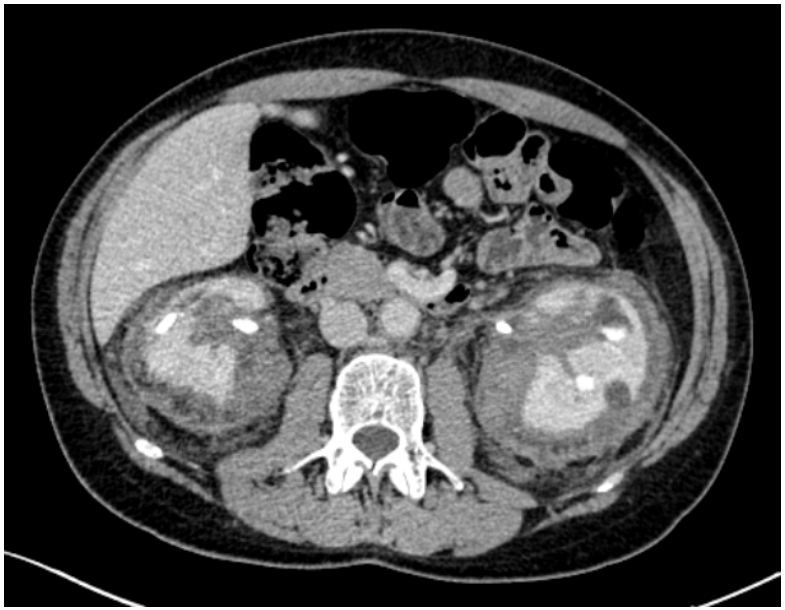


Abdominal CT scans show a nephrostomy tube in the right kidney of a 47-yo ECD patient

How to relieve ureteral obstruction

Ureteral obstruction must be treated with stents or nephrostomies AND medical therapy.
Although effective, this approach may not completely resolve obstruction and surgical ureterolysis can be performed (andecdotal reports, none in our series of 28 cases)

With stents, before therapy



With stents, month 6 of Everolimus therapy

Functional consequences of ureteral obstruction in ECD

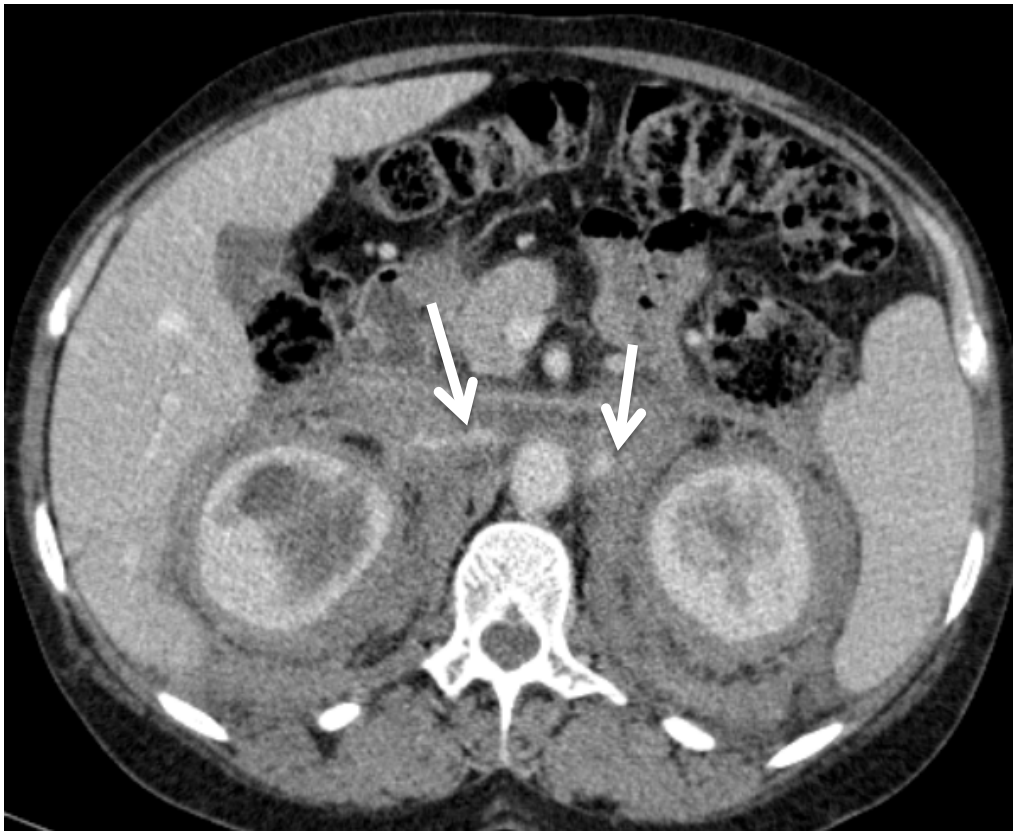
- Acute renal failure (uncommon)
- Chronic renal failure (chronic kidney disease, CKD) of varying degrees → possible progression to *end-stage renal disease*
- Renal atrophy
- Infection (pyelonephritis)

End stage renal disease

- Hemodialysis preferred over peritoneal dialysis
- Renal transplantation: no contraindications

47-yo man with ECD and (moderate) chronic renal failure; CT scan shows hydronephrosis and renal hypotrophy/atrophy (right > left)

Renal artery (and vein) stenosis in ECD

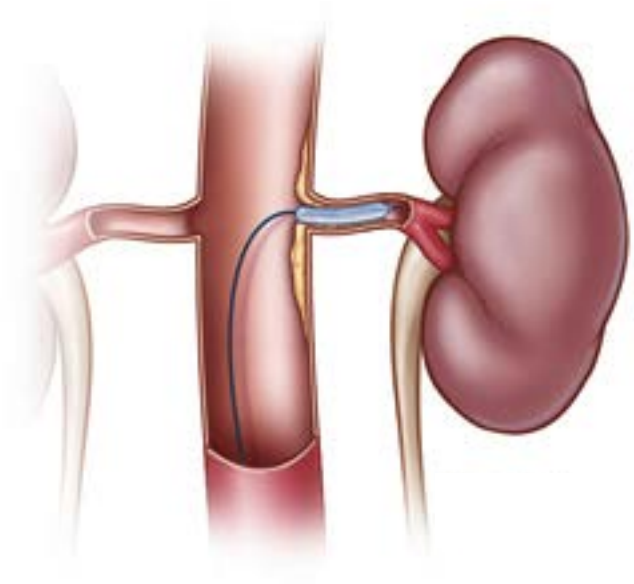


- Compression of the renal arteries causes *reno-vascular hypertension* , a particularly severe form of arterial hypertension
- It may also cause renal atrophy
- When bilateral, it can progressively lead to chronic renal failure
- Diagnosed by angio-CT, angio-MRI and traditional angiography

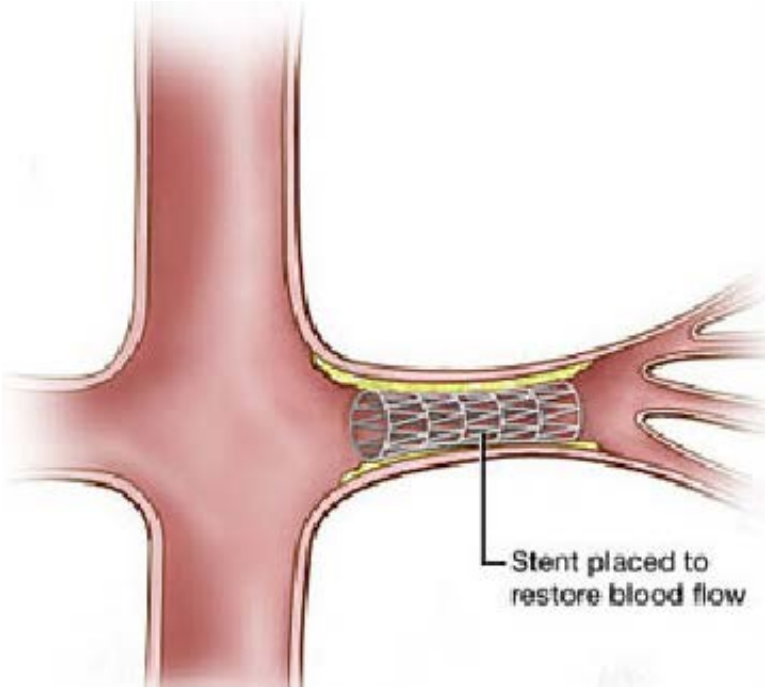
When to suspect renal artery stenosis in ECD

- Worsening hypertension
- Hypertension requiring multiple anti-hypertensive drugs
- Renal asymmetry on imaging studies
- Serological abnormalities
    - Worsening renal function (creatinine increase)
    - Hypokalemia (low K, below 3.5 mEq/L)
    - Increase in renin activity and aldosterone levels
    - Metabolic alkalosis (increase in pH and bicarbonate levels)

How to treat artery stenosis in ECD



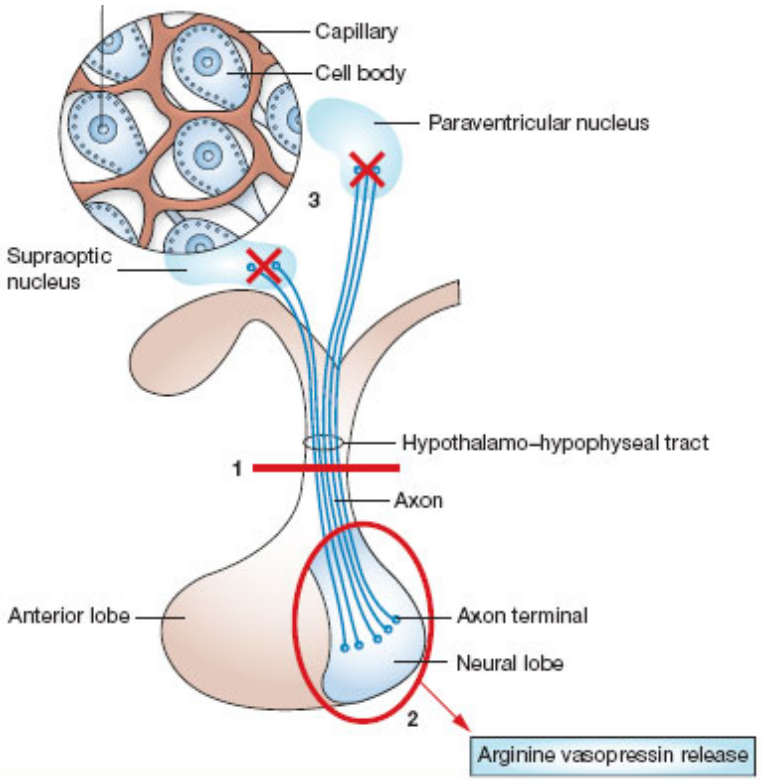
Renal artery ANGIOPLASTY



Renal artery STENTING

Other manifestations: diabetes insipidus (DI)

- DI occurs in approximately 20-25% of ECD pts
- Usually years before the onset of systemic symptoms
- Due to infiltration of the pituitary gland (hypophysis) or the tract between the hypothalamus and hypophysis
- Low/absent production of the Anti-Diuretic Hormone (ADH)
- The kidney does not reabsorb water (polyuria→ polydipsia)
- LUTS (lower urinary tract symptoms). Frequency, urgency etc.



How to treat diabetes insipidus (DI)

- Fluid replacement in the acute phases
- Administration of ADH analogs such as desmopressin (Minirin®), either as tablets or nasal spray
- DI rarely resolves completely despite effective therapy for ECD
- IMPORTANT to differentiate LUTS due to DI from those deriving from other conditions/complications
    - Infections
    - Lower urinary tract irritation by stents
    - Neurological complications
    - Non ECD-related diseases (prostate hypertrophy, etc)

Conclusions

- ECD causes renal/perirenal and ureteral involvement in 50-70% of patients and is often overlooked
- Obstructive uropathy (hydronephrosis) is the most common complication and often requires urinary decompression (stents, nephrostomy) + medical therapy (IFNa, vemurafenib, other drugs)
- Although rarely, chronic renal failure can develop
- Renal artery stenosis is not uncommon and may cause hypertension and renal failure
- Diabetes insipidus commonly causes urinary symptoms although the renal and ureteral systems are normal
- The management of complications (infections, bleeding, pain) is crucial