Acute (Tubulo-) Interstitial Nephritis (TIN)

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Case 1

- 16 year old girl with intractable psychosis
- Started Clozapine
- Monitored closely
- 6 weeks later: AKI – Creatinine 200
How would you manage?

1. Withdraw drug and observe
2. Withdraw drug and give steroids
3. Withdraw drug and give plasma exchange
4. Continue on drug and give steroids
5. Continue drug and plasma exchange
Treatment:
Withdraw drug, Prednisolone

- After 3 days, creatinine 160
- After 10 days creatinine 90
Case 2

- 13 year old boy
- Obese
- 2 month history of macroscopic haematuria
- Creatinine 203 µmol/l
- UPC 152 mg/mmol; UAC 19.1 mg/mmol
- U Beta-2 microglobulin 53 mg/l (normal < 0.03)
- Generalised aminoaciduria
Given Prednisolone

6 weeks later, plasma creatinine 69
Acute Tubulo-Interstitial Nephritis

- Often called acute interstitial nephritis (AIN)
- Term AIN first used in 1898 by Councilman
  - PM findings of patients with diphtheria & scarlet fever
- Most common causes of acute interstitial inflammation are: Pyelonephritis and acute allograft rejection: Not discussed further
Councilman JEM 1998

An acute inflammation of the kidney characterized by cellular and fluid exudation in the interstitial tissue, accompanied by, but not dependent on, degeneration of the epithelium; the exudation is not purulent in character, and the lesions may be both diffuse and focal.
TIN

- Primary injury to tubules and interstitium
- No glomerular abnormality – but GN may be associated with TIN
- Clinical features:
  - AKI
  - Proximal tubular dysfunction
What proportion of AKI in children is due to TIN?

A. 5%.
B. 10%.
C. 15%.
D. 20%.
E. 25%.
Epidemiology

- True incidence unknown
- 10-25% AKI in adults
- 4-7% AKI in children
Aetiology

- Immunologically mediated
- Exact mechanisms poorly understood
- Three main precipitating events:
  - Drugs
  - Infection
  - Idiopathic autoimmune disease
- Inflammatory bowel disease
  - 19% of kidney biopsies
  - Mesalamine strongly associated with TIN
Aetiology: Drugs

- NSAIDS
- Antimicrobials, esp β-lactams
- Anticonvulsants
- Psychiatric
- Diuretics
Presentation

- “Classic triad” Fever, rash & eosinophilia
  - Present in 30%
- Low-grade fever, maculopapular rash, arthralgia, anorexia, nausea, vomiting, malaise
- AKI
- Proximal tubulopathy
Diagnosis

- Suspected clinically
- Confirmation requires biopsy
Treatment

- Remove precipitating cause
- Steroids
- Possible role for mycophenolate
- Many recover spontaneously
- May lead to CKD
TIN at GOSH

- 27 biopsy proven cases in 23 years
- 11 boys, 16 girls
- Age 8 months to 15 years; median 12 years
TIN at GOSH: Aetiology

- 12 (44%) history of drug exposure
- 1-12 weeks between drug and symptoms
- 8 (30%) had infection (6 respiratory)
- 13 (48%) no precipitating event found
TIN at GOSH

- Non-specific symptoms
- Anorexia, malaise, vomiting
- Proteinuria 96%
- One nephrotic range, rest mild - Median alb/creat ratio 16.5 mg/mmol (range 4.4-43.7)
- Micro-haematuria 78%
TIN at GOSH: Proximal tubulopathy

- Glycosuria 81%
- Potassium wasting 70%
- Phosphate wasting 62%
- Acidosis 27%
- LMW proteinuria 94%
- Ultrasound normal in 45%
- Rest had increase in size and/or echogenicity
TIN at GOSH: Renal Function

- Max plasma creat median 263 μmol/l
- Min eGFR median 20 (range 4.6-103)
- 4 required RRT
TIN at GOSH: Treatment

- 26 received steroids
- Renal function improved in all
- Median eGFR 76; 15 (55%) had eGFR < 80 at last follow-up
If a patient has TIN, who else should be consulted?

1. Oncologist
2. Ophthalmologist
3. Otorhinolaryngologist
4. Orthopaedic surgeon
5. Occupational therapist
Tubulo-interstitial nephritis with Uveitis

- Rare, though incidence unknown
- Median age 15
- Female to male ratio 3:1
- Uveitis occurs after onset of TIN in 60%
- Uveitis onset ranges from 1 month before to 3 months after TIN
- Renal prognosis good
- Uveitis may be more difficult to treat; relapses in 40%
Which drug to use for dyspepsia.

1. Proton pump inhibitor (e.g. omeprazole, lansoprazole)

2. H2 receptor antagonist (e.g. ranitidine)
Proton Pump Inhibitors

- Common cause of TIN
- Associated with progressive renal failure
10,482 participants in Atherosclerosis Risk in Communities Study

Increased risk of incident CKD (Adjusted HR 1.5, CI 1.14 – 1.96)

Adjusted HR compared with H2 receptor antagonists 1.35 (CI 1.17 – 1.55)

Twice daily dosing associated with higher risk than once daily
Veterans Affairs database
173,321 new PPI users and new 20,270 H2 receptor blocker users
Followed for 5 years
PPI users had higher risk of incident CKD (eGFR < 60) HR 1.22 (CI 1.18 – 1.26)
Graded response on duration of PPI
Summary

- TIN is an important cause of AKI and proximal tubulopathy
- Frequently drug induced or infection-related
- Requires biopsy for confirmation
- Mainstay of treatment is steroids
- Consider TINU – exclude uveitis
- PPI: common cause of TIN, increased risk of CKD