RENAL MEDICINE

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FINAL YEAR MEDICINE

CONTENTS

CASE 1

You are a foundation doctor working in the emergency department. Your patient, a 17-year-old male, is admitted generally unwell with vomiting and abdominal pain. His mother, who has accompanied him to the emergency department, reports he has not been well for some time, experiencing tiredness and excessive thirst.

His observations are as follows: respiratory rate 32 breaths per minute, saturations 96% on room air, heart rate 94 beats per minute, blood pressure 112/65 mmHg, temperature 36.9°C, capillary blood sugar 32 mmol/L.

On examination, you note the patient has dry mucous membranes and reduced skin turgor. He also has a 'fruity' smell to his breath.

You decide to perform an arterial blood gas, the results are as follows:

pH	7.32	(7.35 - 7.45)
pCO2	4.9 kPa	(4.7 - 6)
PO2	12 kPa	(11 - 13)
HCO3	17 mEq/L	(22 - 26)
Na+	143 mmol/L	(133 - 146)
Cl-	100 mmol/L	(95 - 108)

What is the most likely diagnosis and describe the ABG findings

METABOLIC DISTURBANCES

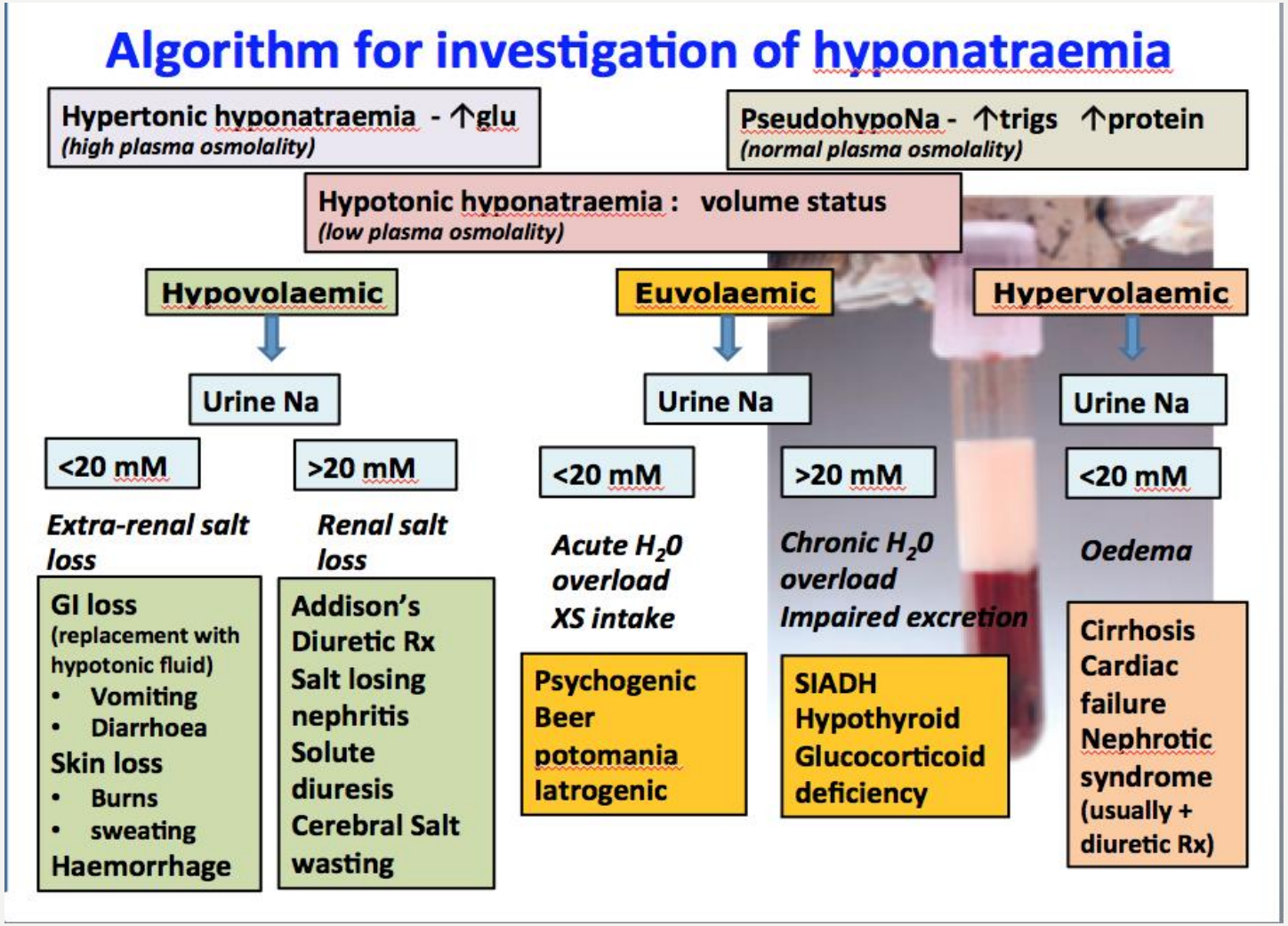
- Metabolic Acidosis (raised anion gap) → Lactate (shock, hypoxia), ketones (DKA, Alcohol), Urate (renal failure), Acid poisoning (Salicylates, Methanol)
- Metabolic Acidosis (normal anion gap) → GI Bicarb loss (diarrhoea, fistula), Renal Tubular Acidosis, Drugs (e.g. Acetazolamide), Addison's disease
- Normal anion gap approx. 8-14

- Metabolic Alkalosis → Vomiting/Aspiration, Diuretics, Hypokalaemia, Liquorice, Primary Hyperaldosteronism, Cushing's Syndrome

FLUID + ELECTROLYTE IMBALANCES

- In what cases would you see an increase in ECF?
- What clinical signs would make you think a person is fluid overloaded?
- How would you manage a patient who is fluid overloaded?

HYPONATRAEMIA



HYPONATRAEMIA

- Px → anorexia, nausea, malaise, headache, irritability, confusion, weakness, low GCS, seizures (if severe), HF/oedema, high risk of falls in elderly
- Ix → U+E, Urine + plasma osmolalities, urine Na (off diuretics), Urine dip, TSH, Cortisol
- Mx → Treat underlying cause, check all electrolytes + diuretic use, fluid restriction, loop diuretics, slow infusion hypertonic saline

HYPERNATRAEMIA

- Fluid loss without adequate replacement (D+V)
- Inappropriate fluid replacement (iatrogenic)
- Diabetes Insipidus
- Osmotic Diuresis e.g. DM (large urine volume and osmolality)
- Primary Hyperaldosteronism → suspect if high BP, low K+, High bicarb

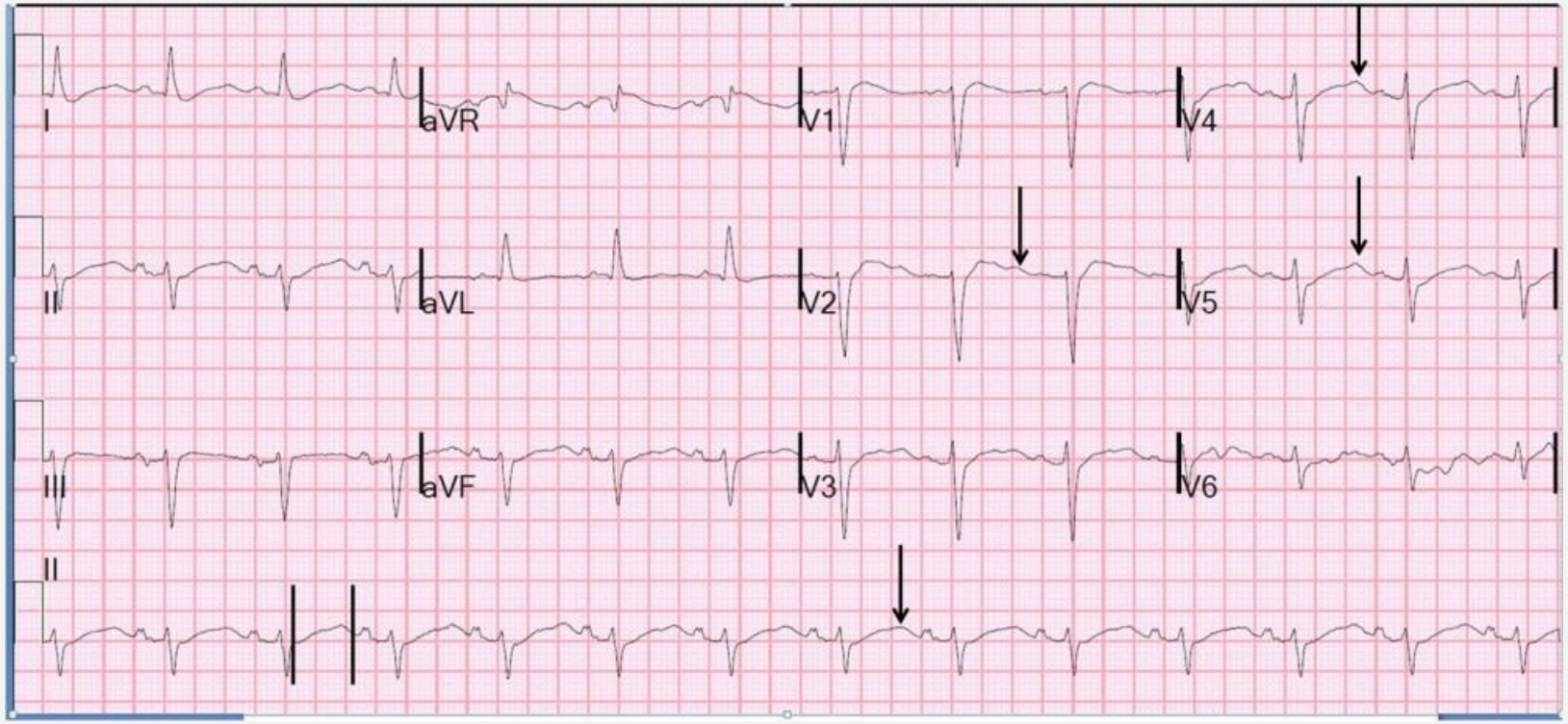
- Mx = Give water orally or 5% IV Dextrose solution, 0.9% IV saline if hypovolaemic slow infusion

HYPOKALAEMIA (K+ <3.5)

- Diuretics - especially Loops + Thiazides
- Primary Hyperaldosteronism
- Prolonged D+V
- Pyloric Stenosis
- Renal Tubular Failure
- Rectal Villous adenoma, intestinal fistula, Cushing's syndrome, Burns/skin defects, Alkalosis, liquorice abuse

- Px = Ask, muscle weakness, hypotonia, hyporeflexia, cramps, tetany, palpatations, risk of arrhythmia, constipation
- Mx = Oral Sando-K x2/8hrs + review after 3 days (>2.5mmol/l), IV Slow K+ infusion (max 10mmol/hr) (<2.5mmol/l) and treat Mg imbalance

HYPOKALAEMIA ECG



ECG = Small/inverted T waves, prolonged PR interval, U Waves, ST Depression

HYPERKALAEMIA (K+ >5)

- Why is hyperkalaemia important to manage?
- AKI, Metabolic Acidosis, Addison's Disease, Rhabdomyolysis, massive blood transfusion, Drugs (K+ sparing drugs, ACEis, Ciclosporin, Heparin, BBs)
- Px → Fast, irregular pulse, chest pain, weakness, palpitations, light headedness
- ECG Findings → Tall tented T waves, PR prolongation, small p waves, wide QRS, VF
- Mx → Treat underlying cause, Dietary restriction, avoid drugs, give loop diuretic if suitable, calcium resonium
- **Emergency Mx** → IV Calcium Gluconate (cardioprotective), IV Insulin/Dextrose, Nebulised salbutamol, Calcium Resonium

ACUTE KIDNEY INJURY (AKI)

- Rapid decline in renal function (hours-days) → raised serum creatinine and reduced urine output
- Stage 1 = **1.5x** rise within 48 hours or urine output <0.5ml/kg/hr for 6-12 hours
- Stage 2 = **2x** rise within 48 hours or urine output <0.5ml/kg/hr for >12 hours
- Stage 3 = **3x** rise within 48 hours or urine output <0.3ml/kg/hr for >24 hours (or anuria for 12 hours)
- RFx = >65, previous AKI, CKD, HF, CLD, Diabetes, Cognitive impairment, sepsis, hypovolaemia, oliguria, nephrotoxic drug use, cancer/cancer treatment, immunocompromised, toxins (herbal remedies)
- Most seen in the elderly

PRE-RENAL AKI

- **Lack of perfusion to the kidney**
- Local hypoperfusion → Renal Artery Stenosis, Renal Vasoconstriction (drug induced – ACEis, ARBs, NSAIDs)
- Systemic hypoperfusion → Hypovolaemia (D+V, Haemorrhage, Burns, Pancreatitis), Reduced Cardiac Output (HF, Cirrhosis, Sepsis, Drugs), Systemic Vasodilation (Sepsis, Drugs)
- Renal Hypoperfusion → Reduced eGFR → Increased Sodium reabsorption in attempt to **retain fluid** → LOW urine sodium + HIGH urine osmolality
- Raised Urea:Creatinine ratio as urine becomes so concentrated that urea spills into circulation through reabsorption

RENAL AKI

- **Structural damage to the kidney**
- Toxins + Drugs → Antibiotics, Contrast, Chemotherapy
- Tubular → Acute Tubular Necrosis
- Glomerular → GN, Autoimmune (SLE, HSP, Drugs, Infection)
- Interstitial → Drugs (NSAIDs, ARBs, Abx, Metformin, Statins), Interstitial Nephritis, Lymphoma Infiltration
- Vascular → Vasculitis, Thrombosis, Atherosclerosis

POST-RENAL AKI

- **Obstruction causing backflow/stasis of urine in the urinary tract**
- Renal Stones
- Blocked Catheter
- BPH/Prostate cancer
- GU Tumours/masses
- Neurogenic bladder

HOW TO ASSESS AKI

- Px = Dehydration (dry mucous membranes, weak pulse, reduced skin turgor), N+V, low urine output, pruitus, confusion, fatigue, drowsiness, falls in elderly
- Ix = Assess fluid status clinically (including urine output), **Urinalysis** (Dipstick, MC+S), **Bloods** (FBC, U+E, LFTs, CRP, Calcium, Myeloma screen), ABG, **Imaging** (Renal/Bladder US)
- Metabolic Disturbances = Hyperkalaemia, Metabolic Acidosis, Hyponatraemia, Hypocalcaemia, Hyperphosphataemia
- Mx = A-E, treat what is treatable; Fluids, Antibiotics, Hyperkalaemia, Relieve obstruction
- Monitoring → U+E, urine output, fluid balance, weight
- Unknown/Severe cause of AKI → Get senior help

INDICATIONS FOR DIALYSIS

- Refractory **Pulmonary Oedema**
- Persistent **Hyperkalaemia** (>7mmol/l)
- Severe **Metabolic Acidosis** (pH 7.2)
- **Uraemic complications** → Encephalopathy, Uraemic Pericarditis
- **Drug** Overload

5 STEPS IN MANAGING AKI

1) Assess Fluid Status
2) Stop Nephrotoxic Drugs
3) Urine Dip
4) Ultrasound
5) Monitor bloods daily

AKI CASE SCENARIO

1) A 35 year old male was in a RTA and on admission if found to have mildly raised urea and creatinine . His potassium levels are 5mmol/l
2) A 70 year old female with COPD and HF presents with an acute exacerbation of COPD. She has a mild AKI on admission and her potassium levels are 6.5mmol/l. She is on multiple medications, including Spironolactone which you have withheld.

Which patient would require close monitoring and daily bloods?

ACUTE TUBULAR NECROSIS

- Ischaemic/Nephrotoxic injury to the renal tubular epithelial cells → cell death/detachment from the basement membrane → tubular dysfunction
- Most common cause of AKI
- Ischaemia → Systemic hypoperfusion (trauma, surgery, dehydration, haemorrhage, burns, sepsis, D+V), local hypoperfusion (cold ischaemia during renal transplantation, renal surgery, renal artery stenosis)
- Nephrotoxins → Aminoglycosides, Radiocontrast agents, Lead, NSAIDs, Myoglobin (Rhabdomyolysis), Myeloma, Raised Uric acid
- Px = AKI sx, muddy brown casts in urine
- Ix = AKI tests + CK, Uric acid, urine studies (**high** urine sodium, low osmolality), Urea:Cr ratio, ABG, Renal US
- Supportive Management (fluids, stop nephrotoxins, correct electrolyte imbalance)

ACUTE INTERSTITIAL NEPHRITIS

- **Acute inflammation** of the renal tubulo-interstitium due to **hypersensitivity** reactions to drugs, autoimmune conditions or infection
- Drugs = Antibiotics (Penicillin, Rifampicin, Cephalosporins, Fluroquinolones), NSAIDs, Allopurinol, Furosemide, PPIs, Cancer Drugs (mAbs)
- Infections = HIV, Hantavirus, Staphylococci
- Systemic Disease = SLE, Sarcoidosis, Sjogren's
- Px = Fever, Rash, Arthralgia, Mild renal impairment, oedema, hypertension, **eosinophilia**
- Ix = Urine Dip (sterile pyuria + white cell casts), FBC, U+E, Urea:Cr Ratio, ANCA, ANA, ds-DNA, Complement profile, Renal US/biopsy
- Mx = Supportive; stop nephrotoxins, fluid restriction, monitor electrolytes, diuretics, oral corticosteroids (2 weeks oral prednisolone; if no response to supportive treatment)

CHRONIC KIDNEY DISEASE (CKD)

- Impaired renal structure/function or eGFR <60ml/min for >3 months
- Causes = Hypertension, DM, CVD, Obesity, GN, PMH AKI, Nephrotoxic drug use, obstructive disease, FHx, Multisystem Disorders (SLE, Vasculitis, Myeloma)

CKD stage	GFR range
1	Greater than 90 ml/min, with some sign of kidney damage on other tests (if all the kidney tests* are normal, there is no CKD)
2	60-90 ml/min with some sign of kidney damage (if kidney tests* are normal, there is no CKD)
3a	45-59 ml/min, a moderate reduction in kidney function
3b	30-44 ml/min, a moderate reduction in kidney function
4	15-29 ml/min, a severe reduction in kidney function
5	Less than 15 ml/min, established kidney failure - dialysis or a kidney transplant may be needed

HOW TO ASSESS CKD

- Px (approx. stage 4) = Fatigue, anaemia sx, oedema, N+V, pruitus, cramps, bone pain, reduced appetite/sleep, taste disturbance, polyneuropathy, polyuria, oliguria, nocturia, anuria
- Ix = Urine Dip (if 1+ blood arrange MSU), Bloods (FBC, U+E, eGFR +/- calcium, vit D, phosphate, PTH only if eGFR <30), Albumin Creatinine Ratio (ACR; >3mg/mmol in 3 months), Renal US

CKD MANAGEMENT

- Lifestyle Advice (weight loss, smoking cessation)
- BP Control → Offer Lisinopril/Losartan if DM/HTN + raised ACR (look up specifics), aim <140/90, or <130/80 if DM/ACR >70
- Treat reversible causes (obstruction/drugs/optimise comorbidities),
- Secondary Prevention → Antiplatelet and Bisphosphonates
- Symptomatic treatment → iron/B12/folate for anaemia, $NaCO_3$ for metabolic acidosis, loop diuretics for oedema
- Dialysis for stage 5 CKD/end-stage renal failure
- Complications → Anaemia, Renal Osteodystrophy, CVD, Protein malnutrition, Metabolic acidosis, Hyperkalaemia, Pulmonary oedema, Neuro complications, Uraemic complications (platelet dysfunction, pericarditis, encephalopathy

INFECTIONS OF THE URINARY TRACT

- Lower UTI → Urethritis, Cystitis, Prostatitis
- Upper UTI → Pyelonephritis, Renal Abscess
- Uncomplicated = Normal renal tract and function, usually E. coli
- Complicated = Congenital/acquired abnormality, catheter, young male, pregnancy, recurrent infections, reduced renal function, virulent organisms (Klebsiella, Proteus, Enterococcus, Pseudomonas)
- RFx = Female, sexual intercourse, exposure to spermicide, pregnancy, menopause, DM, immunosuppression, renal tract obstruction

HOW TO ASSESS URINARY INFECTIONS

- Px (uncomplicated) = LUTS (dysuria, frequency, urgency, nocturia, haematuria), suprapubic discomfort, low-grade fever, malaise, cloudy urine
- Px (pyelonephritis) = Fever, loin pain, rigors, N+V, flank pain, myalgia, flu-like illness, costo-vertebral angle tenderness, LUTS, confusion/falls in elderly
- Ix = Urine Dip/MC+S, Bloods (FBC, U+E, CRP, Cultures if unwell), Imaging (Renal US), Urology referral
- Start treatment if 3 or more symptoms OR 1 severe symptom without further testing
- Uncomplicated Mx = Nitrofurantoin/Trimethoprim (women 3 days, men 7 days)
- Pyelonephritis Mx = IV Co-amoxiclav + Gentamicin 10-14 days
- Pregnancy = Nitrofurantoin (1st/2nd trimester), Trimethoprim (3rd trimester) 7 days
- Catheter = send CSU, Gentamicin 7 days (only treat if symptomatic)

HYPERTENSION + THE KIDNEY

- Hypertension can lead to changes in renal vasculature over time → intimal thickening, glomerular sclerosis, shrinking of kidneys, fibrinoid necrosis (malignant hypertension)
- Bilateral Renal Disease (chronic GN, reflux nephropathy, analgesic nephropathy) → Activation of RAAS + Salt and water retention
  - Mx = ACEis + ARBs (aim BP <140/90)
- Unilateral Renal Disease (Renal Artery Stenosis, unilateral reflux nephropathy)
  - Screen for RAS if HTN/CKD + evidence of atheroma, >30% rise in creatinine after starting ACEi/ARB, abdominal bruit, recurrent flash pulmonary oedema in absence of cardioresp disease
  - Ix = U+E, Lipids, Glucose, Urinalysis, Aldosterone:Renin ratio, Duplex US (>50% stenosed), Gd-enhanced MRA, **CTA**, Angiography
  - Mx = ACEi/ARB, Statin, antiplatelet, renal artery stenting, reconstructive vascular surgery, nephrectomy
- Other Causes = Nephrotic syndrome, CKD, Polycystic Kidneys, Obstructive uropathy

DIABETES + THE KIDNEY

- Diabetic Nephropathy = most common cause of CKD
- Annual screening for all diabetics → ACR (morning urine sample) for microalbuminuria (3-34mg/mmol) or macroalbuminuria (>34mg/mmol) or eGFR<60 – persistent for >3 months
- Caused by extent and duration of HTN + hyperglycaemia
- What Investigations findings would point you towards diabetic nephropathy?
- Mx = Optimise glycaemic control, dietary protein restriction, ACEi/ARB if microalbuminaemia
- BP aim <140/90 or <130/80 if end-organ damage
- Look out for renally excreted drugs = Metformin, glibenclamide

NEPHROTIC SYNDROME

- Proteinuria (>3g/24hr) + Hypoalbuminaemia (<30g/l) + Oedema
- Complications
  - Antithrombin III Deficiency (+ Protein C/S) → high risk of **thrombosis**
  - Thyroxine Binding Globulin Deficiency → low **total** thyroxine levels (normal free thyroxine)
  - Low Immunoglobulins + Complement proteins → high **infection** risk
- Others = hypocalcaemia, hyperlipidaemia, AKI

CASE 2

A young mother brings her 5 year old son to the Emergency Department. She mentions her son has had 2 days of swelling on his legs, scrotum and around his eyes. She continues to tell you that he is generally tired and his urine is noted to be frothy. Boys mother has noticed a cough which has persisted. No past medical history except for eczema and asthma.

Renal biopsy: no abnormalities can be seen on light microscopy, however, electron microscopy reveals abnormal podocytes (fused).

- **What is the most likely diagnosis?**
- **What investigations do you want to do?**
- **What is your management plan?**

NEPHROTIC SYNDROME – MINIMAL CHANGE DISEASE

- Most common cause of nephrotic syndrome in children
- Causes = Idiopathic, NSAIDs, Rifampicin, Hodgkin's lymphoma, Thymoma, EBV
- 1/3 only one episode 1/3 infrequent relapses, 1/3 frequent relapses
- T-cell and cytokine mediated damage to basement membrane → raised glomerular permeability to serum albumin
- Normal BP
- Ix = Renal Biopsy (in adults); fusion of podocytes on EM
- Mx = Steroids, Cyclophosphamide

CASE 3

A 42-year-old woman presents to her GP with a 3-month history of fatigue and fluid retention. She has a 4-year history of systemic lupus erythematosus but has not been taking any regular medication for the past 14 months, and has a positive family history of type 1 diabetes. On examination, her eyes appear puffy and swollen.

Her blood results show low total T4 (other TFTs normal), and low serum TPO antibodies

- **What is the most likely diagnosis?**
- **What investigations do you want to do?**
- **What is your management plan?**

MEMBRANOUS GLOMERULONEPHRITIS

- Most common cause of GN in adults – activation of complement by immune deposits, involving basement membrane
- Px = nephrotic syndrome, proteinuria, CKD
- Causes = Idiopathic (antiphospholipase 2 antibodies), Infections (Hep B, malaria, syphilis), Malignancy (Lung cancer, lymphoma, leukaemia), Drugs (NSAIDs, gold, penicillamine), Autoimmune (SLE, Thyroiditis, RA)
- Ix = Renal Biopsy; BM thickening + sub-epithelial deposits of IgG/C3 ('Spike and bone')
- Mx = ACEi/ARB, Corticosteroids, Cyclophosphamide, anticoagulation if high risk
- 1/3 resolve spontaneously, 1/3 remain proteinuric, 1/3 develop end-stage renal failure
- Good prognosis = Female, young age, asx proteinuria at presentation

FOCAL SEGMENTAL GLOMERULOSCLEROSIS

- Scarring of the glomerulus
- Causes = Idiopathic, IgA Nephropathy, Reflux Nephropathy, HIV, Heroin, Alport Syndrome, Sickle-Cell
- Ix = Renal Biopsy; **Focal + segmental sclerosis, hyalinosis** on light microscopy, **effacement of foot processes** on EM
- Mx = Steroids +/- immunosuppressants
- Poor prognosis – 2/3 progress to end-stage renal failure

PATIENT COMES INTO CLINIC – NEPHROTIC SYNDROME?

1) Urinalysis
2) Bloods = U+E, eGFR, serum albumin
3) ACR spot test (>250 = nephrotic proteinuria)
4) Refer for renal biopsy to distinguish cause

Mx = Fluid/salt restriction, diuretics, stop exacerbating drugs, treat infection, ACEi/ARB, Immunosuppressants (Steroids, Cyclophosphamide)

NEPHRITIC SYNDROME + GLOMERULONEPHRITIS (GN): RAPDLY PROGRESSIVE GN

- Rapid loss of renal function, formation of epithelial crescents in glomerulus
- Causes = Goodpasture's syndrome, Wegener's Granulomatosis, SLE, Microscopic polyarteritis
- Px = Haematuria, HTN, red cell casts, proteinuria, oliguria, sx of underlying cause
- Ix = FBC, U+E, eGFR, Urine dip, Renal biopsy, anti-GBM Ab
- Mx = Treat underlying cause

NEPHRITIC SYNDROME + GN: IGA NEPHROPATHY

- Most common cause of GN, macroscopic haematuria 1-2 days after URTI
- Mesangial deposition of IgA immune complexes
- Association with alcoholic cirrhosis, coeliac/dermatitis herpatiformis, HSP
- Px = Young male, macroscopic painless haematuria, usually 1-2 days after URTI
- Ix = Renal Biopsy (mesangial proliferation), IgA + C3 deposits on immunofluorescence
- Mx = Conservative if mild, ACEi if HTN, Prednisolone if proteinuria

NEPHRITIC SYNDROME + GN: ALPORT SYNDROME

- Inherited X-linked dominant mutation in gene encoding type IV collagen → abnormal glomerular basement membrane
- More severe in males, presents in childhood
- Px = microscopic haematuria, progressive renal failure, bilateral sensorineural deafness, lenticonus, retinitis pigmentosa
- Ix = Renal biopsy (splitting of lamina densa on EM), Genetic testing

NEPHRITIC SYNDROME + GN (MIXED NEPHROTIC + NEPHRITIC)

- Diffuse Proliferative GN → Classic post-strep picture in a child, px with nephritic syndrome/AKI, most common renal disease in SLE
- Membranoproliferative GN → Mesangiocapillary GN, diagnosed on biopsy
  - Type 1 (90%) = Cyroglobulinaemia, Hep C, subendothelial + mesangial deposition of immune complexe (tram-track)
  - Type 2 (Dense deposits) = Lipodystrophy, Factor H deficiency, persistent activation of complement alternative pathway, Renal Biopsy shows dense deposits on EM
  - Type 3 = Hep B + C
- Post-streptococcal GN → young child, 7-14 days after group A strep infection (usually strep pyogenes), immune complex deposition in glomeruli (IgG, IgM, C3), Px = headache, malaise, nephritic syndrome, proteinuria, LOW C3, raised ASO titre

  - Renal Biopsy; endothelial proliferation + subepithelial humps from lumpy immune complex deposition

  - Immunofluorescence shows granular/'starry sky' appearance

THANK YOU

ANY QUESTIONS?

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