Revise Nephrology

www.revisenephrology.com.au

For More info contact

Dr. Surjit Tarafdar

Email: surjit.tarafdar@gmail.com

1st set of Pre-MCQs Answers 2023

1 B. Contrast nephropathy usually presents earlier (2-5 days) and the recovery too is quick. The duration (3 weeks) and mottled rash on legs is pointing towards cholesterol atheroemboli.
Some points about cholesterol atheroemboli:

- Cholesterol crystal embolization to the kidneys
- Usually after coronary angiography (commonest cause), renal angiography or cardiovascular surgery
- AKI several weeks later (sometimes within 1-2 weeks)
- Urine bland
- Cyanosis or discrete gangrenous lesions in the toes with intact peripheral pulses (blue toes), livedo reticularis and focal neurologic deficits, orange plaques in the retinal arterioles (Hollenhorst plaques)
- May be accompanied by-eosinophilia, eosinophiluria, and hypocomplementemia
- Supportive therapy and secondary prevention of CV disease with aggressive lipid lowering therapy suggested

2 D. While the K is high and HCO3 is low, the first line management of these conditions will be medical management- note that according to the stem the patient has just presented to ED. Pericardial rub in a patient with AKI is an indication for dialysis.
The usual indications for dialysis include:

- Hyperkalemia refractory to medical management
- Metabolic acidosis refractory to medical management
- Fluid overload refractory to medical management
- Pericarditis
- Uremic symptoms

3 D. While choice a (Penicillin related acute interstitial nephritis) can develop in this patient, the question wanted us to think of the most likely cause of this patient's AKI. AKI is a relatively common complication of therapy with the aminoglycoside antibiotics, with a rise in the plasma creatinine concentration of more than 44 to 88 mmol/ or 50 percent increase in plasma creatinine concentration from baseline seen in 10 to 20 percent of patients. Also, one would expect presence of white blood cells as well as eosinophils in the urine as well as eosinophilia in AIN.
Some points about aminoglycoside toxicity:

- Aminoglycosides freely filtered across glomerulus and partially taken up by the proximal tubular cells
- Gentamicin levels inside PTC cells 100 to 1000 times serum levels
- Non-oliguric AKI due to ATN usually occurs 5-10 days after treatment
- Once daily dosing better from the nephrotoxicity perspective: higher peaks for shorter periods and prolonged period of very low exposure may allow for more efficient handling and excretion

- Hypomagnesaemia, hypocalcaemia and hypokalemia may be seen due to tubular defects

4 B. Add hydrochlorothiazide. Patient is already on optimal doses of ACEI and CCB.

The first line management of renal artery stenosis (RAS) is most often medical, while fibromuscular dysplasia (FMD) patients are often treated with revascularization procedures. In RAS, revascularization is only offered (in conjunction with medical therapy) in the following group of patients:
a) Short duration of blood pressure elevation prior to the diagnosis of renovascular disease
b) Failure of optimal medical therapy
c) Intolerance to optimal medical therapy
d) Recurrent flash pulmonary oedema
e) Otherwise, unexplained progressive renal insufficiency

Renovascular hypertension is one of the most common causes of secondary HTN. There are two common clinical variants of renovascular HTN: atherosclerotic RAS and FMD. About 80% of renovascular HTN cases are due to atherosclerotic disease and 20% are related to FMD. HTN appearing in younger individuals (i.e., children or young adults) is suggestive of FMD, while atherosclerotic renal artery stenosis should be suspected in recent onset of HTN in previously normotensive individuals above the age of 55 years. Other situations where renovascular HTN is suspected are resistant or malignant HTN, more than 1.5 cm discrepancy in the kidney sizes, episodes of unexplained flash pulmonary oedema and a rise in serum creatinine of more than 30% after initiating an angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB).

5 E. Nothing to suggest AIN/Conn's syndrome /pheochromocytoma/SLE. With AIN, there is usually a background of new drug exposure and NO association with hypertension, Conn's syndrome (primary aldosteronism) will usually have the associated hypokalaemia and/or metabolic alkalosis and pheochromocytoma generally has the classic triad of headaches, palpitations, and sweating.
With SLE would expect haematuria/proteinuria, i.e., some sort of glomerular involvement.
While GORD/Raynaud's/peripheral telangiectasia are pointing towards systemic sclerosis (SS0, with regards to renal involvement in SS, severe and life-threatening renal involvement (scleroderma renal crisis) develops in approximately 10 to 15 percent of patients. It is far more frequent in patients with diffuse cutaneous systemic sclerosis (dcSSc) than limited cutaneous systemic sclerosis (lcSSc) and almost invariably occurs in the early stages of the disease. This form of renal involvement is characterized by:

- Abrupt onset of marked or malignant hypertension (although some patients remain normotensive)
- Acute onset of oliguric renal failure
- GN not seen (so no haematuria) or proteinuria if present is usually mild
- Microangiopathic haemolysis anaemia and thrombocytopenia

A note on serology in SS

- Anti-deoxyribonucleic acid (DNA) topoisomerase I (Scl-70) antibodies are generally associated with dcSSc and a higher risk of severe interstitial lung disease (ILD)

- Anticentromere antibody (ACA) is usually associated with lcSSc; only 5 percent of patients with dcSSc have ACA

- Anti-RNA polymerase III antibody found in patients with dcSSc and generally associated with rapidly progressive skin involvement as well as an increased risk for scleroderma renal crisis.

6 B. All diuretics act by inhibiting the tubular reabsorption of Na^+. In case of loop and thiazide diuretics, with more Na^+ flowing to the distal nephron, the tubular cells reclaim some of the excess Na^+ leading to decrease in luminal positivity. The tubular cells try to compensate for this by secretion of the positively charged K^+ and H^+ into the lumen. Also, intravascular volume contraction because of diuretics causes activation of the renin-angiotensin-aldosterone system (RAS) which in turn leads to urinary K^+ and H^+ losses under the influence of aldosterone.

7 E. Primary hyperaldosteronism should always be suspected in the hypertensive patient with hypokalaemia and metabolic alkalosis (although more than half the patients are normokalemic) who is not on thiazide or loop diuretics. Aldosterone leads to reabsorption of Na^+ in the collecting duct and the resulting tubular negativity aids in the excretion of K^+ and H^+. It is important to remember though that as other parts of the renal tubules will try to compensate, the hypokalaemia and alkalosis is often not very florid with patients often presenting with low normal potassium and high normal bicarbonate in the presence of HTN.

8 C. Type 2 RTA is due to a proximal tubular defect in the reabsorption of $HCO3^-$ leading to urinary loss of $HCO3^-$ and normal anion gap metabolic acidosis with hypokalaemia. The absorption of HCO3- in this segment is linked to the coupled exchange of H^+ and Na^+. As this reabsorption of Na^+ is linked to the reabsorption of glucose, amino acids, phosphate and uric acid, the patient may present with glycosuria, hypophosphatemia and hypouricemia (due to urinary losses) and this condition is termed as Fanconi syndrome.

9 A. Bartter syndrome and Gitelman syndrome are autosomal recessive disorders characterised by hypokalemic, metabolic alkalosis and low-normal blood pressure. Bartter syndrome is usually seen in perinatal period or childhood while Gitelman syndrome is mostly a disorder of adulthood with hypomagnesaemia being a striking feature in the latter. The prevalence of Gitelman syndrome is 1 in 40,000 compared with 1 in 1,000,000 for Bartter syndrome.

The tubular defects in sodium reabsorption in Bartter and Gitelman syndrome are almost identical to those seen with chronic ingestion of loop and thiazide diuretics respectively, i.e., inhibition of sodium reabsorption in the TAL and DCT respectively with the resultant diuresis and volume contraction.

The combination of secondary hyperaldosteronism (due to volume contraction) and increased distal delivery of Na^+ causes increased secretion of K^+ and H^+ leading to the characteristic hypokalaemia and metabolic alkalosis. Blood pressure is on the lower side in both the conditions due to Na^+ loss and resultant volume contraction. In addition, Bartter syndrome is characterised by increased renal release of vasodilator prostaglandins due to increased NaCl uptake into the macula densa cells at the end of the thick ascending limb of the loop of Henle, contributing to the low blood pressure.

Conditions associated with metabolic alkalosis and/or hypokalaemia- Can be further sub-divided into two groups depending on the blood pressure:

Low-normal BP

- Bartter syndrome
- Gitelman syndrome

High BP

- Primary hyperaldosteronism (Commonest cause in this group)
- Liddle syndrome
- Chronic liquorice ingestion
- Apparent mineralocorticoid excess
- Familial Hyperaldosteronism

In Liddle syndrome the apical Epithelial Na^+ channel (ENAC) which is normally under the control of aldosterone is mutated and reabsorbs Na^+ independent of the aldosterone levels (the mutation causes higher than normal activity). As feedback, both the plasma renin activity and aldosterone concentration are low.
Renal artery stenosis leads to activation of renin-angiotensin-aldosterone system due to the decreased renal artery blood flow; the high aldosterone can lead to urinary loss of K^+ and H^+ leading to metabolic alkalosis and/or hypokalaemia.

10 D. PAN is a systemic necrotizing vasculitis that typically affects medium-sized muscular arteries with characteristic absence of involvement of veins, smaller arteries or capillaries and is ANCA negative. Absence of capillary involvement rules out the possibility of glomerulonephritis which is associated with glomerular capillary involvement.

11 E. While peripheral neuropathy may be seen in up to 75% of cases with PAN, gastro-intestinal symptoms with abdominal pain or blood in stool may be seen in up to 40%. Hypertension and orchitis may be seen in 35% and 20% cases respectively. Pulmonary involvement is uncommon in PAN.

PAN presentation

• Systemic features- fever/malaise	• 80%
• Peripheral neuropathy	• 75%
• Arthralgia/myalgia	• 60%
• Skin- livedo reticularis,purpura	• 50%
• Kidney- AKI due to infarct/bleed	• 50%
• GI- abdominal pain, PR bleed	• 40%
• Hypertension	• 35%
• Orchitis	• 20%
• Stroke	• 20%
• Cardiomyopathy, pericarditis	• 10%

12 A. The pathogenesis of PTLD in post-transplant patients is mostly related to B cell proliferation induced by infection with Epstein-Barr virus (EBV) in the setting of immunosuppression. In most parts of the world, 90 to 95 percent of adults show serologic evidence of EBV infection. Acute EBV infection leads to a polyclonal expansion of B cells harbouring the virus. In the immunocompetent, these virally infected B cells elicit a T cell response that eliminates the vast majority of the infected B cells. However, a small population of the virally infected B cells downregulate viral antigen expression and thus escape immune surveillance.

The incidence of PTLD is highest in the first year after transplantation, probably due to the more intense immunosuppression in this period (which suppresses the T cell response). The incidence of PTLD is much greater in heart transplant recipients probably due to the more intense immunosuppression in this group of patients. While there is some evidence linking the use of tacrolimus to PTLD, mycophenolate and alemtuzumab use do not seem to be associated with higher incidence of PTLD.

13. C Causes of AKI in patients with liver disease are:

- AKI associated with infection e.g., sepsis, SBP- 46%
- Pre-renal AKI- 32%
- HRS- 13%
- Parenchymal renal disease e.g., glomerulonephritis – 9%

14. C Idiopathic MN is common in Caucasian males and quite uncommon in children. C3 nephritic factor is involved in the pathogenesis of Mesangiocapillary GN (MCGN). More than 70% of idiopathic MN have circulating auto-antibodies against phospholipase A2 receptor 1(PLA2R1) located on the surface of podocytes. The characteristic abnormality on light microscopy is diffuse global capillary wall thickening due to subepithelial immune-complex deposition which appears as “spikes” in silver methenamine stain. Patients with sub-nephrotic range proteinuria are treated with ACEI or ARB alone and immunosuppressive therapy is only indicated in those with persistent high-grade proteinuria > 4 g/daily despite the use of ACEI or ARB. FSGS is the commonest cause of nephrotic syndrome in people of African origin.

15. D Renal involvement in amyloidosis most often presents as asymptomatic proteinuria or clinically apparent nephrotic syndrome. Proteinuria is seen in more than 75% of patients with AL or AA amyloidosis (the two commonest forms of amyloidosis).