FRCPath Clinical Biochemistry

Part 2, Module 2, Paper 3 - Cases

Practice Questions

The following cases were used in the Autumn 2022 exam have been retired from the cases question bank and will not appear again in their exact current format. The topic areas remain very much in scope for future exams.

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February 2023

Section A – Cases

Case 1

A 43-year-old man was brought by ambulance to the Emergency Department having been found unconscious at home.

Arterial blood gases, on oxygen, showed:

H^+	78.1 nmol/L	(35 – 45)
pH	7.11	(7.35 – 7.45)
P_{CO2}	1.7 kPa	(4.27 – 6.40)
P_{O2}	30.7 kPa	(11.07 – 14.40)
Bicarbonate	4.1 mmol/L	(21 – 25)
Lactate	>20 mmol/L	(0.5 – 2.2)

(a) Classify this patient's acid-base status. (4)

Metabolic (1) acidosis (1) with partial (1) respiratory compensation (1)

Blood results of a sample analysed in the laboratory showed the following:

Sodium	140 mmol/L	(133 – 146)
Potassium	3.9 mmol/L	(3.5 – 5.3)
Chloride	111 mmol/L	(95 – 108)
Bicarbonate	6 mmol/L	(22 – 29)
Urea	3.4 mmol/L	(2.5 – 7.8)
Creatinine	87 µmol/L	(59 – 104)
Glucose	4.1 mmol/L	(3.7 – 6.0)
Lactate	2.0 mmol/L	(0.5 – 2.2)
Osmolality	323 mOsmol/kg	(275 – 295)
Ethanol	<10 mg/dL (i.e. <100 mg/L)	
Paracetamol	<3 mg/L	
Salicylate	<50 mg/L	

(b) Showing the formula used, calculate the osmolal gap and comment on the result. (4)

Calculated osmolality = 2 [Na] + [urea] + [glucose] = 2 x 140 + 3.4 + 4.1 = 287.5 mOsmol/kg.
Accept any recognised formula.
Osmolal gap = Measured osmolality – Calculated osmolality = 323-287.5 = 35.5 mOsmol/kg
There is a significant (increased) osmolal gap.
1 mark for formula; 1 mark for correctly calculated osmolality; 1 mark for calculation of osmolal gap; 1 mark for comment.

(c) Showing the formula used, calculate the anion gap and comment on the result. (4)

Anion gap = ([Na] + [K]) – ([Cl] + [HCO_3]) = (140 + 3.9) – (111 + 6) = 26.9.
Increased anion gap.
1 mark for formula; 2 marks for correctly calculated anion gap; 1 mark for comment. Accept any recognised formula.

(d) Suggest two additional tests that should be requested in this situation. (4)

Ethylene glycol (2) and methanol (2).

(e) Explain the discrepancy between the lactate results obtained on the point of care analyser and laboratory method. (4)

Metabolites of ethylene glycol (1) (glycolic acid (1) and oxalate (1)) interfere with the lactate method on the point of care analyser (1).

Case 2

A 61-year-old woman was referred to Acute Medicine by her General Practitioner after bloods showed severe hypokalaemia. The patient was known to have Type 2 Diabetes Mellitus and had noted that her glycaemic control had deteriorated recently. She had also noticed that she was bruising easily. She stopped smoking one year previously, having previously smoked 20-30 cigarettes per day.

Bloods taken on admission showed:

Sodium	144 mmol/L	(133 – 146)
Potassium	2.0 mmol/L	(3.5 – 5.3)
Chloride	98 mmol/L	(95 – 108)
Urea	8.6 mmol/L	(2.5 – 7.8)
Creatinine	83 µmol/L	(45 – 84)
Bilirubin	16 µmol/L	(<21)
AST	68 U/L	(10 – 45)
ALT	163 U/L	(9 – 55)
ALP	360 U/L	(30 – 130)
GGT	603 U/L	(8 – 33)
Protein	62 g/L	(60 – 80)
Albumin	38 g/L	(35-50)
Glucose	23.9 mmol/L	(3.7 – 6.0)

Arterial blood gases on air showed:

H^+	26.9 nmol/L	(35 – 45)
pH	7.57	(7.35 – 7.45)
P_{CO2}	5.2 kPa	(4.27 – 6.40)
P_{O2}	7.48 kPa	(11.07 – 14.40)
Bicarbonate	35 mmol/L	(22 – 29)

24-hour urine cortisol: 24373 nmol/24 hours (<165)

(a) Interpret this patient's arterial blood gas results. (4)

Hypoxia (1) with uncompensated (1) metabolic (1) alkalosis (1).

(b) What is the most likely reason for the patient's hypokalaemia? Describe the mechanism leading to hypokalaemia in this case. (3)

Cortisol excess (1) causing spillover activation of mineralocorticoid receptor (1) which leads to excessive renal excretion of potassium (1).

A chest radiograph showed a mass at the left lung hilum.

(c) What is the most likely diagnosis? (3)

Lung tumour (1) secreting ectopic ACTH (1) leading to Cushing syndrome (1)

The patient's condition deteriorated and metyrapone and spironolactone were commenced.

(d) Outline the mechanism of action of each of these drugs and how they will counteract the effects of the underlying disease process. (5)

Metyrapone: Competitive (1) inhibition of 11β-hydroxylation in the adrenal cortex (1) leading to inhibition of cortisol production (1).
Spironolactone: Aldosterone receptor antagonist (1) leading to reduced mineralocorticoid effect (1).

(e) In general, list five other causes of Cushing syndrome. (5)

Drugs (glucocorticoids)
Pituitary tumour (Cushing disease)
Adrenal hyperplasia
Adrenal tumours
CRH-secreting tumours
(1 mark per correct answer – accept any correct answers)

Case 3

A 24-year-old man was admitted to General Medicine with a recent history of lethargy and weight loss. Blood pressure was 95/70. Blood results showed:

Sodium	122 mmol/L	(133 – 146)
Potassium	5.9 mmol/L	(3.5 – 5.3)
Chloride	90 mmol/L	(95 – 108)
Urea	7.7 mmol/L	(2.5 – 7.8)
Creatinine	76 µmol/L	(59 – 104)
Osmolality	260 mOsmol/kg	(275 – 295)
TSH	<0.10 mU/L	(0.35 – 4.94)
Free T4	35 pmol/L	(9 – 19.1)

Urine sodium was 120 mmol/L.

(a) Interpret the thyroid function tests. (2)

Thyroid function tests consistent with hyperthyroidism. (2)

(b) What is the most likely cause of this patient's hyponatraemia? Explain your reasoning, and outline the mechanism leading to the hyponatraemia. (14)

Cause:
Addison's Disease/adrenal insufficiency (2) – likely to be autoimmune (2).
Reasoning:
Low serum osmolality excludes osmotic hyponatraemia or pseudohyponatraemia (2).
Low blood pressure suggestive of whole body sodium depletion (1). Disproportionately increased urea in keeping with suspected fluid depletion (1).
High urine sodium excretion indicates inappropriate renal sodium loss (2).
Patient is already known to have one autoimmune disease, so is at increased risk of having another autoimmune disease (2).
Mechanism:
Loss of aldosterone synthesis (1) leading to reduced renal sodium reabsorption (1).

(c) Which further tests should be carried out to confirm the diagnosis? (4)

Short (1) Synacthen Test (1) with ACTH on baseline sample (1).
Adrenal autoantibodies (1).

Case 4

A 30-year-old man was referred to Lipid Clinic. He had been noted to be gaining weight and to have abdominal bloating. His mother had recently been found to have hypercholesterolaemia, so his GP had checked a fasting lipid profile which showed the following results:

Total Cholesterol	8.4 mmol/L
HDL Cholesterol	1.9 mmol/L
Triglycerides	2.11 mmol/L
Calculated LDL Cholesterol	5.6 mmol/L
Non-HDL Cholesterol	6.5 mmol/L

(a) Write the formula most commonly used to calculate LDL cholesterol. (2)

LDL cholesterol = Total Cholesterol – HDL Cholesterol – Triglycerides/2.2

(b) State one situation in which calculation of LDL cholesterol is not valid. (1)

Hypertriglyceridaemia

(c) In order to ascertain if further investigation of the possibility of Familial Hypercholesterolaemia is appropriate, what additional pieces of clinical information would be helpful? (9)

Presence of tendon xanthomata (1) in patient or 1st or 2nd degree relative (1)
Family history of myocardial infarction (1) before age of 50 years in 2nd degree relative (1) or 60 years in 1st degree relative (1)
Family history of increased cholesterol (1) >7.5 mmol/L (1) in adult 1st or 2nd degree relative (1) or >6.7 mmol/L in child or sibling younger than 16 years (1)
(Also accept Dutch Lipid Clinics Network Criteria or Wales FH Service Criteria)

(d) What are possible pathological causes of a secondary hyperlipidaemia of the pattern shown in this patient? (4)

Primary (1) hypothyroidism (1)
Nephrotic syndrome (2)

(e) What drugs may cause a secondary hyperlipidaemia of the pattern shown in this patient? (4)

Thiazide diuretics, immunosuppressants, antiretrovirals, oestrogens & progestogens, steroids (max 4 marks for question).

Case 5

A 75-year-old man presented with general deterioration, increased confusion, recurrent falls and unsteadiness. He was treated for a urinary tract infection but was found to deteriorate rapidly, developing bilateral nystagmus, marked past-pointing, dysarthria and central ataxia. He had a complex medical history including epilepsy controlled with long-term phenytoin.

His pathology results showed

	Admission	
Creatinine	93 μmol/L	(59 – 104)
ALT	76 U/L	(9 – 55)
GGT	135 U/L	(8 – 33)
ALP	390 U/L	(30 – 130)
Bilirubin	180 μmol/L	(<21)
Albumin	21 g/L	(35 – 50)
Total Protein	48 g/L	(60 – 80)
Phenytoin	18 mg/L	Therapeutic range 5-20 mg/L
Plasma glucose	13 mmol/L	(3.7 – 6.0)

His symptoms resolved following a reduction in his phenytoin dose.

(a) Explain why. (8)

Phenytoin is 90% protein bound and displaced by bilirubin (2 marks)
The combination of low albumin and high bilirubin may cause an increase in the free phenytoin concentration, resulting in toxicity, despite the measured total phenytoin concentration being within the therapeutic interval. (6 marks)

(b) Name four anti-epilepsy drugs, apart from phenytoin, that commonly cause liver enzyme increases. (4)

Carbamazepine (or Eslicarbamazepine or Oxcarbazepine)
Phenobarbitone
Primidone
Valproate
Rufinamide
Topiramate
Do not allow: Ethosuximide, Gabapentin or pregabalin (only rare increases), Lacosamide (only a few patients on polytherapy have increases), Lamotrigine, Perampanel, Retigabine, Tiagabine, Vigabatrin, Zonisamide

(c) List four indications for therapeutic drug monitoring for phenytoin. (4)

Therapy initiation
IV therapy for status epilepticus
Unexpected deterioration in seizure control
Diagnosis of toxicity
When interacting drugs are added / withdrawn
Pregnancy
?compliance

(d) Comment on the significance of the plasma glucose concentration in this patient. (4)

Elevated glucose consistent with diabetes, requires repeat to confirm. Note that phenytoin has potential to elevated glucose. Mechanism proposed to be inhibition of insulin secretion.

Case 6

A GP rings you regarding a patient with deranged LFTs. She is 51 years old, has hypertension and is on Lisinopril, an ACE-inhibitor.

Total Protein	69	g/L	(60 – 80)
Albumin	45	g/L	(35 – 50)
Total Bilirubin	13	μmol/L	(<21)
Alkaline Phosphatase	53	U/L	(30 – 130)
ALT	81	U/L	(9 – 55)

(a) What would you ask about in the history? (4)

Alcohol; Obesity; T2DM; Hepatotoxic drugs; Risk factors for viral hepatitis

(b) Name two non-hepatic causes of raised ALT. (2)

Hypothyroidism
Polymyositis
Rhabdomyolysis (CK >1000; requires emergency admission)
Heavy exercise, weight lifting
IM injections

(NB Other pathology causing raised liver ALT but would also allow points for: Hyperthyroidism, CCF)

Looking back at previous results:

	23/01/2022	10/01/2022	06/12/2021	29/09/2020	19/08/2017
ALT	85	82	87	20	17

(c) There is nothing of significance in the history. In addition to transferrin saturation, name four further investigations or groups of investigations you would advise the GP to do to look for aetiology, and explain your reasons. (4)

- AST, GGT and FBC (MCV, platelets) - Alcohol
- HbA1c, glucose, lipids – T2DM, NAFLD
- Coagulation screen – Liver function
- TSH – Hypo and hyperthyroidism can cause raised ALT
- Ferritin – haemochromatosis
- Chronic viral hepatitis screen (Hep B surface antigen, Hep C antibody)
- Autoantibodies (AMA, ASmA, ANA, LKM) & Immunoglobulins; AIH, PBC
- Alpha-1-antitrypsin level
- Caeruloplasmin (usually if age <40 years)
- AFP
- USS of liver

(0.5 mark for each test and 0.5 mark for associated reason. Maximum 2 marks for tests and 2 marks for associated reasons.)

(d) What investigations may be helpful in deciding if the patient has liver fibrosis? (3)

NAFLD fibrosis score or FIB4
ELF testing
Fibroscan

The results of the tests you advised were all normal apart from:

Transferrin saturation 85.8 %

(e) List two causes of iron overload. (2)

Primary:
Haemochromatosis (AR)

Secondary to other conditions/iatrogenic factors:
Repeated blood transfusion (eg, beta thalassaemia, sickle cell anaemia)
Iron loading anaemias (eg, beta thalassaemia, sideroblastic anaemias, chronic haemolytic anaemia, aplastic anaemia)
Iron and iron containing supplements (enteral and parenteral)
Porphyria cutanea tarda (hepatic iron accumulation)
Alcohol increases iron absorption and causes raised ferritin and %IBC saturation.
High iron, transferrin, transferrin saturation, and serum ferritin can be seen in acute hepatic injury due to leakage of intracellular contents, and can incorrectly give the impression of iron overload.

(f) How may primary iron overload present? (2)

Asymptomatic
Fatigue
Weakness
Joint pains
Deranged liver enzymes
Cirrhosis
Erectile dysfunction
Arthritis (hands, 2nd and 3rd fingers)
Cardiomyopathy
Diabetes +/-bronzing of skin

(g) What further blood test might you suggest? What are the common mutations in primary iron overload? (3)

HFE genotyping
C282Y and H63D