It’s not all about numbers... Biochemistry quiz

Dev Datta
Biochemistry and Metabolic Medicine
Cardiff and Vale UHB
RCP/ SPW meeting, Cardiff
November 2017
Overview

• Interactive cases with voting
• Clinical biochemistry presenting through acute medical admissions
• Consider diagnostic approach and management
• Discussion after voting with learning points after each case
Case 1- Hypokalaemia

- 64 year old female
- Presented with LLQ abdominal pain 2/12 increasing abdominal pain, nausea, weight loss
- 25 year history of hypertension
- Previous episode of hypokalaemia attributed to diuretics
- Bendroflumethiazide 2.5mg OD
- Amlodipine 10 mg OD
- Rosuvastatin 20 mg OD
- Smokes 30 per day
- Drank 12-16 units alcohol/day; abstinent 3 months
- BP 166/90 mmHg
- No hypertensive retinopathy
- Normal CVS examination, no bruits
Lab Investigations

- Na 129 mmol/L*
- K 2.5 mmol/L*
- Creatinine 110 umol/L*
- Mg 0.82 mmol/L
- CRP 167 mg/L*
- WCC 22.8 x 10^9/L*
CT findings

• The CT appearance is consistent with acute diverticulitis of the proximal sigmoid with a small, associated collection which is probably too small for attempt of percutaneous drainage. The left adrenal is a little diffusely bulky. The right kidney is small and atrophic measuring 6.7cm in length. The left kidney is hypertrophied and of more normal appearance.
Progress

- Treated with IV antibiotics and oral K+
- Bendroflumethiazide stopped
- K+ 3.2 mmol/L

- 1 further similar admission, subsequent GI surgery
What additional laboratory investigation would you do next?

• Renin:aldosterone
• 24 hour urinary catecholamines
• Overnight dexamethasone suppression test
• Spot urine K+ / urine Cl-
• No further investigations required
Further investigations

- Aldosterone 2236 pmol/L **(100-450)
- Renin 2080 mu/L** (5.4-30)
- Aldosterone:Renin= 1 (<80 Conn’s unlikely)
Learning Points Case 1

• Mostly apparent GI/ Renal/ transcellular shift
• If the cause is not obvious....
• Check Mg, Ca, Bicarbonate
• If the cause is still not obvious....
• Check Urine K+ and Cl- and consider the BP
• Discuss interpretation and further investigations
Case 2

- 65 year old lady of Somali origin
- Noted to have hypercalcaemia
- Intermittent constipation
- Bilateral shoulder discomfort
- Obese, unintentional weight loss 6/12
- No localising symptoms
- Non smoker, no alcohol
• Type 2 DM
• Hypertension
• Dyslipidaemia

• Simvastatin, Lisinopril, Gliclazide, Metformin, Sitagliptin, Indapamide
Examination

- Obese
- No LN or clubbing
- Sinus tachycardia
- Late inspiratory crackles L lung base
- Obese abdomen
- Breast examination normal
Investigations

- Adjusted Ca 2.82 mmol/L*
- Phosphate 1.35 mmol/L
- ALP 103 U/L
- eGFR 81
- HbA1c 64 mmol/mol*
- PTH 0.5 pmol/L (1.6-7.2)*
- ACE 19 U/L (8-52)

- CA 12-5 65 U/mL* (<35) CA 19-9, CA 15-3, CEA normal
- FBC and electrophoresis normal
In the evaluation of hypercalcaemia....

- A detectable PTH, even if low, means that primary hyperparathyroidism remains probable
- PTH requests can be added on to the standard chemistry sample
- Sarcoidosis presenting with a normal ACE is common
- Measuring CA 12-5, CA 19-9, CA 15-3, AFP and CEA is an appropriate strategy to diagnose several common malignancies
Learning Points Case 2

• PTH is a very useful to test to establish the cause of hypercalcaemia
• There are differences in analysis between different laboratories
• Unconsidered measurement of ‘tumour markers’ can be misleading and potentially falsely reassuring
• Serum ACE is not sensitive for establishing a diagnosis of sarcoidosis
Case 3 23 yr old female

- New referral from primary care to MAU
- New diagnosis anorexia nervosa
- Long history of limited nutritional intake
- Went out for meal with mother just prior to admission
- Subsequently felt weak and unwell
- Admitted to MAU
Investigations

- **Albumin**: 33 g/L (33-50)
- **Adjusted calcium**: 2.12 mmol/L (2.2-2.6)
- **Magnesium**: 1.09 mmol/L (0.7-1.0)
- **Phosphate**: <0.21 mmol/L (0.8-1.5)
- **Sodium**: 141 mmol/L (133-146)
- **Potassium**: 2.3 mmol/L (3.5-5.3)
- **Urea**: 8.8 mmol/L (2.5-7.8)
- **Creatinine**: 72 umol/L (50-100)
What is the diagnosis?

• Refeeding syndrome
• Oncogenic osteomalacia
• Hyperventilation
• Electrolyte disturbance due to vomiting
Refeeding Syndrome

- Hypokalaemia
- Hypomagnesaemia
- Hypophosphataemia
- Thiamine deficiency
- Salt and water retention - oedema

Starvation / Malnutrition

Glycogenolysis, gluconeogenesis and protein catabolism

Protein, fat, mineral, electrolyte and vitamin depletion – salt and water intolerance

Refeeding (switch to anabolism)

Fluid, salt, nutrients (CHO major energy source)

- ↑ Glucose uptake
- ↑ Utilization of thiamine
- ↑ Uptake of K⁺, Mg²⁺ & PO₄³⁻

- ↑ Protein and glycogen synthesis

Insulin secretion
Phosphate Homeostasis

1400 mg/d

600 g PO4

1100 mg

200 mg

7000 mg

90% reabsorbed

Vitamin D

Stool 500 mg/day

Urine 900 mg/day

ECF

ICF

PTH
Phosphatoninins

+
Learning points Case 3

• Hypophosphataemia in inpatients is commonly due to redistribution

• There is often greater enthusiasm for ‘fixing numbers’ rather than understanding the mechanism

• In outpatients often related to primary hyperparathyroidism and vitamin D deficiency

• Refeeding syndrome can easily be induced in hospital inpatients
Case 4- Hypomagnasaemia

• JB 71 ♂
• Referred in view of recurrent hypomagnesaemia
• Has no current symptoms
• Didn’t ‘get on’ with oral Mg
• Several IV Mg infusions
PMH

- Laryngectomy for Ca 1999
- Laparotomy with subsequent burst abdomen following appendicitis 2007
- Lung resection for NSC lung Ca 2008
- Hypertension
- ?epilepsy
- Alcohol excess
Medication

- Calcium/Vitamin D
- Nifedipine 40mgs BD
- Dipyridamole 200mg BD
- Doxazosin 4mg OD
- Omeprazole 20mg OD
- Bendroflumethiazide 5mg OD
- Phenytoin
Biochemistry

• Mg 0.47 mmol/L**
• Na 135 mmol/L
• K 3.6 mmol/L
• Urea 4.2 mmol/L
• Creat 84 umol/L

• Adj Ca 2.32 mmol/L
• PO4 1.12 mmol/L
• Alb 33 g/L**
• ALP 83 IU/L
• ALT 12 IU/L
Assessment of hypomagnesaeemia

• Even if asymptomatic and no other significant electrolyte problems will require emergency assessment if Mg <0.5 mmol/L
• Hypokalaemia commonly causes hypomagnesaeemia
• Consider renal and GI loss or transcellular shift
• Is required in all patients taking a PPI
Adapted from Marshall and Bangert, 2008

Mg pool

12

0.1

0.2

100

96

7

4

mmol/ 24 hrs

Adapted from Marshall and Bangert, 2008
Consequences of hypomagnesaemia

• <0.4 mmol/L
• Anorexia, nausea, malaise, confusion
• Low K (Mg dependent Na/K pump)
• Low Ca (impaired PTH release)
• Association with cardiac rhythm disorders
Replacing magnesium intravenously

- 1 dose of 40 mmol IV magnesium can effectively replace total body magnesium in most cases
- Oral magnesium replacement is of no clinical utility
- Cardiac monitoring is an absolute requirement for magnesium replacement
- Determining the effectiveness of IV magnesium replacement is best achieved by measuring levels 1 hour post infusion
- A slow, body weight-adjusted, multiple infusion strategy for magnesium replacement is most effective
Learning points Case 4

• Consider hypomagnesaemia if hypokalaemia/hypocalcaemia present
• For inpatients, usually an issue in relation to GI loss
• Redistribution can be an issue for sick patients
• Address underlying cause and consider replacement
• Oral magnaspartate 10 mmol BD
• IV replacement- weight adjusted total Mg dose over 3-4 slow infusions, usually without cardiac monitoring
Case 5

23 yrs Female
2 days after taking recreational drug
Vomiting, mouth ulcers
GP prescribed metronidazole
Worse N&V, abdominal pain
Hyponatraemia (Na 125 mmol/L)
Admitted local DGH
Severe abdominal pain, agitation
Hyponatraemia (Na 113 mmol/L) – Dx SIADH, fluid restriction
Hypertension, tachycardia
Weakness, arms and legs
Neurology review – red-brown urine
What is the diagnostic test?

- Urine electrolyes and osmolality
- Serum CK
- Urine Porphobilinogen:creatinine (PBG)
- CT abdomen
- Urine metanephrines
Random urine, protected from light

Result: PBG:creat =72 (<1.5 umol/mmol)
Learning Points Case 5

• Acute Porphyria should be considered in the context of acute abdominal pain + motor neuropathy +- hyponatraemia
• Diagnostic test is urine PBG
• Discuss with National Acute Porphyria Service