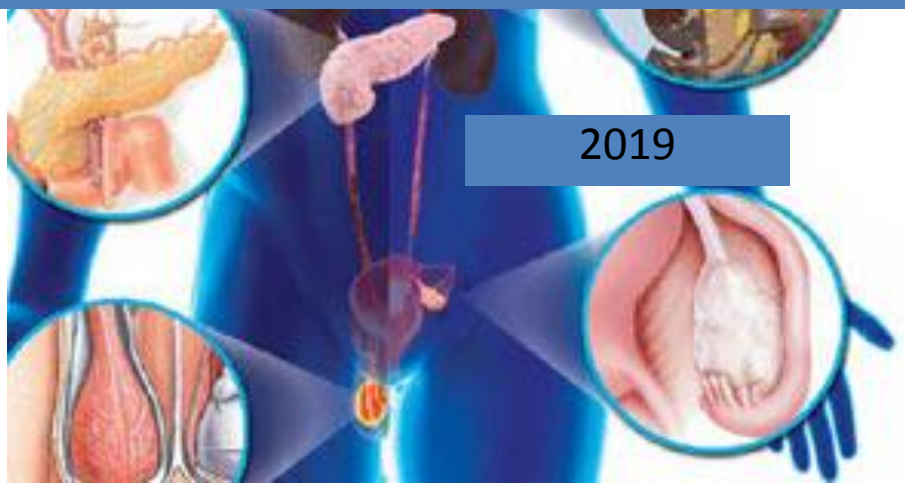
ENDOCRINE CASES

Felicity Kaplan



2019

Mr WO aged 18

- 4/7 n&v, dizziness, 1xdiarrhoea, extreme fatigue, vague abdo pain. Parents away.
- No relevant past history/travel/Rx
- O/E (7pm 27/10/11)
  - Apyrexial, unwell, dry, BM 5.8
  - P 96, BP 109/75
  - Abd mildly tender
  - Urine ketones ++

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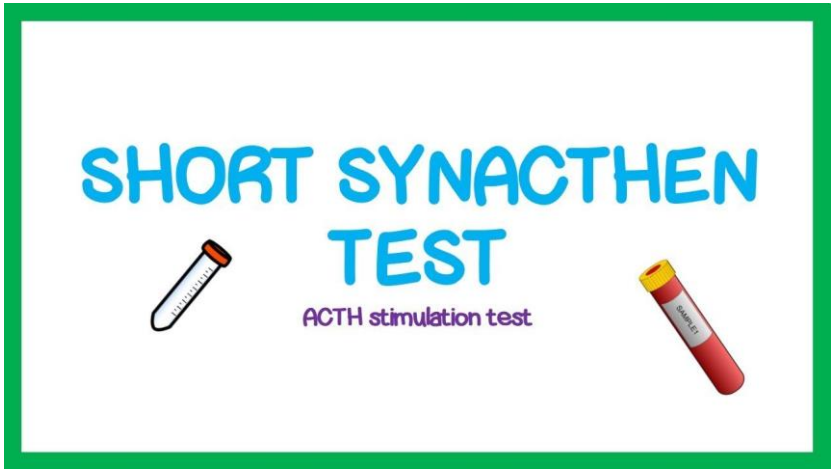
- Ix (27/10/11 at 7.50pm)
  - pH 7.55, pCO_2 1.9, pO_2 14.8, HCO_3 11.9
  - Glucose 4.5
  - Na 107, K4.5-5.6, creat 58, CRP 20, WBC 7.6
  - Amylase 67
  - CXR NAD

- Plan
  - IV saline, anti-emetics
  - uNa, uOsm
  - SST (1pm 28/10/11)
  - TFTs
  - Empiric IV hydrocortisone (9.30pm 28/10/11!)

- 31/10/11 call from lab
  - SST
    - 0 mins 93
    - 30 mins 103
    - 60 mins 91



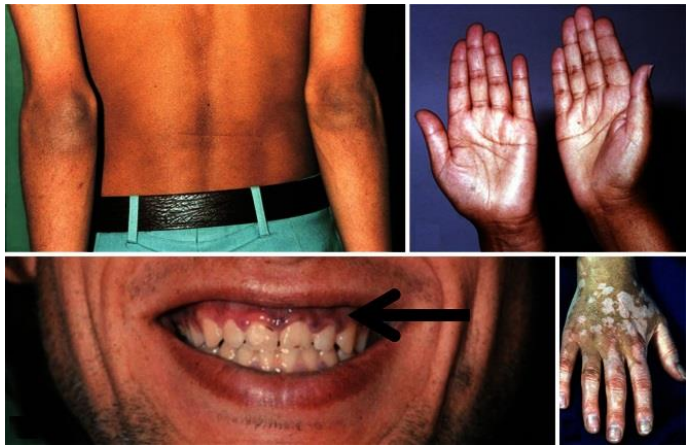
- Diagnosis Addisons disease

Lessons

- Addison's is potentially life-threatening
- Severe hyponatraemia is potentially lifethreatening
- Suspect in context of hyponatraemia
- Treat URGENTLY as Addison's until proven otherwise
- Random cortisol rather than SST initially
- Cover with antibiotics if concerned

Adrenal insufficiency

- Primary
  - Addison's (autoimmune)
  - Metastatic/sarcoid/amyloid
  - Haemorrhage
  - Infective
  - CAH
  - Drugs (ketoconazole, MTP)



Adrenal insufficiency

- Secondary
  - Reflects ACTH deficiency
    - Hypothalamic/pituitary pathology
    - Suppression of HPA axis by exogenous steroids

Mrs TS aged 51

- B/G
  - Nurse
  - Hemiplegic migraine
  - GORD
  - Depression
  - Recurrent hypoglycaemia (normal cortisol)
- Rx
  - PPI, fluoxetine, triptan

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- Admitted 6/2012
  - Sudden headache, sweating, palpitations
  - Vomiting, Lt leg tingling, blurred vision
  - Mum very ill
- Ex
  - well looking
  - BM 1.7, not hyperpigmented
  - BP 135/85, no postural drop
  - Neuro NAD

- Ix
  - Routine bloods all normal (Na 138)
- Mx
  - 50% dextrose and 10% dextrose infusion
  - Recurrent hypo’s
- Further Ix
  - Cortisol, insulin, C peptide, GH, SU when BM<2.5

- Results
  - BM 2.0
  - Lab glucose 2.1mmol
  - C peptide <94 pmol/l
  - Insulin 96 pmol/l
  - SU negative
- Interpretation?

- INSULIN ADMINISTRATION!!

Causes of hypoglycaemia

Ill or medicated individual
1. Drugs
Insulin or insulin secretagogue
Alcohol
Others (refer to UpToDate table on drugs that cause hypoglycemia)
2. Critical illnesses
Hepatic, renal, or cardiac failure
Sepsis (including malaria)
Inanition
3. Hormone deficiency
Cortisol
Glucagon and epinephrine (in insulin-deficient diabetes mellitus)
4. Nonislet cell tumor
Seemingly well individual
5. Endogenous hyperinsulinism
Insulinoma
Functional $_{\beta}$-cell disorders (nesidioblastosis)
Noninsulinoma pancreatogenous hypoglycemia
Post gastric bypass hypoglycemia
Insulin autoimmune hypoglycemia
Antibody to insulin
Antibody to insulin receptor
Insulin secretagogue
Other
6. Accidental, surreptitious, or malicious hypoglycemia

Insulinoma v factitious hypo's

Plasma marker	Insulinoma	SU	Insulin injection
Glucose	↓	↓	↓
Insulin	↑	↑	↑
C-peptide	↑	↑	↓

Mr PD aged 68 retired engineer

- B/G
  - Hypertension >25years
  - prone to hypokalaemia (lowest 2.5)
  - IHD/dyslipidaemia
  - Ex-smoker
- Rx for BP (endocrine clinic 6.2017)
  - Bisoprolol 10mg
  - Moxonidine
  - Losartan 100mg
  - Doxazosin16mg
  - Amlodipine 10mg
  - Spironolactone 12.5mg + K supps (normalised K)
  - A043755

- Ex
  - BMI 31.4
  - P60 reg
  - BP 134/84
  - Otherwise unremarkable

Investigations

- 24 hour urinary metanephrines normal
- 24 hour urinary cortisol 30
- calcium, FBC, CRP, LFT normal
- Na147, K 3.4, urea 6, creatinine 86, GFR 76
- **off spironolactone** aldosterone 344pmol/L, renin <2mU/L (ratio>90)
- $HbA1_c$ 31
- MRI adrenals – 17 mm left adrenal nodule, right adrenal gland normal

Management

- Wished to proceed to surgery (Mr Pullar) without further investigation
- Histology: ‘benign aldosteronoma’
- 4/12 Post-op
  - Rx doxazosin 4mg, bisoprolol 5mg, amlodipine 10mg
  - Off SPL, amlodipine, losartan
  - BP 112/74
  - K+ 5.0

Patients who should be referred to a specialist clinic in secondary care

- Patients with young-onset hypertension <40 years of age
- Patients with a suspected secondary cause of hypertension
- Patients with uncontrolled BP despite being prescribed ≥3 antihypertensive drugs
- Patients with multiple drug intolerances
- Patients with suspected non-adherence to medication

Mrs EH aged 51

- Known microprolactinoma on cabergoline
- Admitted 3.8.18 with severe Rt abdo pain, LOA, no significant LOW
- Tender RUQ
- Dx ?liver pathology/renal stones
- Ix
  - WBC 11.1, amylase normal, CRP 88, ALT 87, ALP 155, U&E normal, microscopic haematuria

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- **CT urinary tract**: no calculi, ? Colitis, indeterminate altered liver attentuation
- **CT abdo/pelvis with contrast**: 4.9x5.4x7.7cm mass from pancreatic neck toward liver hilum, the liver shows widespread low-attenuation lesions with rim enhancement suggestive of a large number of metastatic deposits, likely lymph node mets
- **CT thorax**: no mets

- BUT.. no significant loss of weight and CA199 normal
- Liver biopsy (USS guided):
  - Neuroendocrine carcinoma, likely pancreatic origin
- Referred to RFH neuroendocrine unit

Learning points

- Think of neuroendocrine tumour (NET) in patients with pre-existing endocrine condition/s

- Not all pancreatic lesions are pancreatic cancer

Mrs HL aged 55

- Known NET under RFH
- Partial pancreatectomy and splenectomy 2017
- Admitted 8/2018 unwell with hypokalaemia and abnormal TFTs (GP), recent onset diabetes (HbA1c 85)
  - K+ 2.0, Na 136 (no culprit drug)
  - TSH 0.22 fT4 2.1 fT3 <1.0
  - Glucose 6.9
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- Seen by endocrinologist
  - Pituitary profile requested
- Ix:
  - Cortisol 7000!
  - Prolactin normal
  - Hypog hypog
  - Pituitary MRI normal
  - ACTH awaited
- Progress; patient had episode of psychosis on ward

- D/W RFH urgently
  - Presumed ectopic ACTH…Rx metyrapone
  - Disease progression on recent PET (patient not yet aware)
- Worsening steroid psychosis
- ACTH 445ng/L!
- Urgent transfer to RFH ITU
- Rx Bilat adrenalectomy and chemo

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Steroid-induced psychosis as a manifestation of ectopic ACTH secretion from metastatic poorly differentiated neuroendocrine tumour

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Case Report

- 65 year old fisherman presented with altered mental status, agitation, generalised oedema, dyspnoea, liver impairment and severe persistent hypokalaemia (2.2 mmol/L).
- Past history: COPD, IPF (on steroids since May 2012), ex-smoker.
- Physical exam: deeply tanned, Cushingoid facies, severe proximal myopathy.
- Medications prior to admission: Prednisolone 40mg OD, Furosemide 40mg OD, Inhalers, Lanzoprasole.
- In a view of clinical and biochemical features of steroid access the Endocrine referral was made.

Investigations

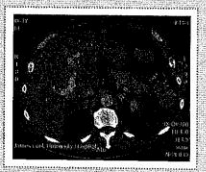
- Patient had following abnormal endocrine tests: cortisol-3118nmol/l, ACTH-632ng/l, total chromogranin A-480u/l, 5-HIAA-551umol/24h.
- CT Thorax/Abdomen showed multiple liver metastasis, pulmonary fibrosis, RUL nodule, enlarged parathracheal, subcarinal lymph nodes, bilateral adrenal hypertrophy.
- CT head/MRI of pituitary were normal.
- Liver biopsy confirmed the presence of poorly differentiated (very high Ki67 index-90%) small cell neuroendocrine tumour which positively stained for TTF1, CK7, CD56, AE1/3, chromogranin, synaptophysin.
- Positive staining for TTF1 and CK7 are sought to be in favour of primary lung lesion.
- The diagnosis of poorly differentiated metastatic small cell neuroendocrine tumour with ectopic ACTH secretion was made.

Initial Investigations	
K	2.2
Na	147
HCO3	40
Cl	103
Urea	7.8
Creatinine	77
ALT	179
ALP	145
GGT	745
Bilirubin	11

Case Resolution

- Patient was started on Metyrapone 1g 4 hourly. Ketoconazole 200mg OD was added later.
- His cortisol and liver function had initially improved and potassium normalised.
- Oncology team put him on three months course of carboplatin with etoposide. Further investigations suggested for ?Carcinoid in a form of Octreotide scan were not recommended by Oncology Department due to its relative insensitivity in the settings of poorly differentiated neuroendocrine tumour.
- Patient passed away just in four months since presentation despite intensive chemotherapy.

Patient's picture at presentation
Sunken eyeballs and fullness out of proportion



CT abdomen (centers point towards bilateral bulky adrenal glands)

Conclusion

We reported this case because of the interesting clinical presentation of an ectopic ACTH secretion exacerbated by exogenous steroid intake. This case also shows the importance of good differential diagnosis of hypokalaemia. Treatment options were limited due to the aggressive nature of the tumour.

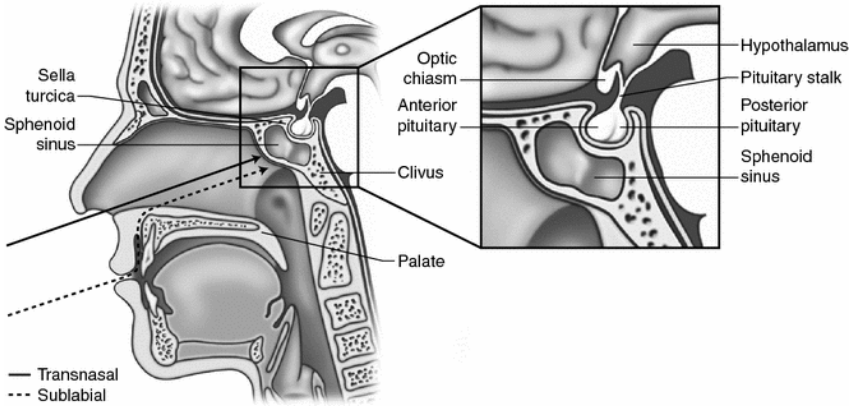
together we do the amazing

Learning points

- Discuss odd TFTs
- Think about underlying causes for sudden onset diabetes (esp slim patient)
- Worry about very low potassium levels if no drug culprit
- Remember that steroids (endogenous or exogenous) can cause psychosis

Mr GC aged 65 112992

- Investigated by GP for erectile dysfunction and fatigue



- Testo 3.6, LH 2.2
- TFT, cortisol, GH normal
- PRL 37000mIU/L!! (NR<324)
- MRI Nov 2017: large clival mass
  - There is large mass involving the clivus and the right side of the anterior pituitary. This extends onto the tuberculum sellae and also invades the right side of the cavernous sinus. The posterior pituitary is separately seen. The pituitary stalk is normal. Likely to be an intraclival-sellar macroadenoma.

- Rx CBG 2mg in divided doses– excellent response in 5m on MRI April 2018
- Normalised PRL, testo within 5m

Learning point

- Think of prolactinoma in patients with ED

- Prolactinomas (even macroprolactinomas) generally do not require surgery

Mr SS aged 46 Estate gardener

- Referred to endocrinology with hypogonadism
  - Testo 3.0, LH 1.2
- Known prediabetes, BMI 36, depression
- Sx
  - weight gain, fatigue…struggling with manual work, ED
- Ex
  - Clinical centripetal obesity, not otherwise Cushingoid; BP 142/87

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- Ix
  - U&E normal
  - TFT normal
  - Prolactin normal
  - cortisol 467, IGF1 normal
  - Pituitary MRI 8/18 normal
  - uCortisol 1503 nmol/24h (0-146)
  - Post 1mg DST cortisol 622nmol/L
  - ACTH: 53ng/L (high)
- Mx: referred to Barts for evaluation of pituitary Cushings

Learning points

- Think Cushings in patients with
  - obesity,
  - DM,
  - Hypertension
  - Depression
  - ED (oligo/amenorrhoea in women)

  - All of these are common but consider other clues eg weakness, unrelenting weight gain, bruising etc

Mrs YD aged 46

- Dec 2016 renal colic
- Referred to me with hypercalcaemia
  - aCa 2.93mmol/L, PTH 47pmol/L, high uCa 8.3mmol/24h, U&E normal, Vit D 26 - treated
- Dx: primary hyperparathyroidism

- Localising studies
  - USS possible 8mm Rt inferior adenoma
  - Sestamibi negative
  - SPECT CT Addenbrooke's 9/17 negative
    - IDEALLY WANT 2 CONCORDANT IMAGING MODALITIES
- Dexa normal

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- Referred to Mr Palazzo at Hammersmith as scans not concordant (1600 parathyroidectomies)
- **Feb 2018**: parathyroidectomy and Rt hemithyroidectomy (8mm lesion was thyroidal, and thyroid nodular); 2 small parathyroid glands removed
- Persistent hypercalcaemia!

- July 2018 Rt PUJ renal calculus: removal and stent
- Several other smaller right sided renal calculi
- 2 small calculi within the left kidney.

- 4D CT and sestamibi suggested left paraesophageal lesion at the thoracic inlet
- **Aug 2018** reoperative surgery
- No parathyroid adenoma found; left hemithyroidectomy, 2 further small parathyroids removed
- “The operation was very prolonged and incredibly disheartening”
- “ I'm afraid that she is one of a handful of patients that I will never be able to forget”
- “quite clearly she has a supernumerary parathyroid adenoma”

- what next?!
- cinacalcet is associated with hypercalciuria, making renal calculi even more likely
- fluorocholine PET (new modality): aortopulmonary window parathyroid adenoma

- **Dec 2018** reoperative thoracoscopic parathyroid surgery with cardiothoracic surgeon (their 12th such procedure – previously sternotomy)
- PTH fell intraop
- Postop Ca normal, exactly 2 years after initial presentation!

Learning points

- Can give vitamin D supplements in hyperparathyroidism
- PLEASE tell patients this can be a long tedious process with lots of tests!!

THANK YOU