Pituitary and the ‘acute take’

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London
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Scope of lecture

The three presentations of pituitary disease
Case-based examples
Disorders of sodium
Manifestations of Pituitary Disease

Mass Effect
- headache
- hydrocephalus
- visual field defect
- cranial nerve palsy
- TLE
- csf leak

Hypopituitarism

Hyper-secretion
- Prolactinoma
- Acromegaly
- Cushing’s
- TSHoma
- Gonadotrophinoma
47 year old man admitted with angina

10 year history of diabetes and hypertension treated with iv heparin and nitrates discharged on oral nitrates, aspirin

1 day later
Returned to hospital complaining of headaches nitrates blamed, sent home

Next day
Returned to hospital complaining of headaches nitrates blamed, sent home

Next day
Returned to hospital complaining of headaches, right eye-closed diagnosis: right 3rd nerve palsy
Pituitary Apoplexy

CT with contrast

MR angiogram

MRI + contrast

Crushing central chest pain
Surgery postponed
Transferred to coronary care unit
No intervention
No heparin/anticoagulation

cerebral haemorrhage

Headache
Right 3\textsuperscript{rd} nerve palsy
Pituitary apoplexy
Scheduled for emergency transsphenoidal surgery
Pituitary Assessment

Cortisol & ACTH during CCU stay

**Attenuation**
- **ACTH** (ng/l)
- **Cortisol** (9 am) >1650 nmol/l (200-700)
- **ACTH** (9 am) 480 ng/l (<50)
- **fT4** 2.7 pmol/l (9-24)
- **TSH** 1.5 mU/l (0.4-5)
- **LH** <0.3 mU/l (1-10)
- **FSH** 0.9 mU/l (1-7)
- **Testosterone** 5.8 nmol/l (9-35)

Dexamethasone tests
Whispering corticotrophinoma

Hypertension and Diabetes Mellitus (10 years)
Hypercortisolaemia: Unequivocal, Severe, Persistent
Coexisting extreme elevation of plasma ACTH levels
Abnormal dexamethasone suppression test
Central hypogonadism and hypothyroidism

Conclusion
Apoplectic ACTH release
27 year old woman

Presented to neurologist
Headache

Coarse facial features
Sweating
Lethargy

OGTT GH nadir 23 ng/ml
IGF-I 850 ng/ml (173 – 333)

Vision normal
No sleep apnoea
Prolactin 1050 mU/l (RR <400 mU/l)

Acromegaly
What next?

2006
51 year old man
frontal headaches

Seen by neurologist

MR – lesion arising from clivus

Referred to neurosurgeon
transsphenoidal biopsy

Histology – prolactinoma with characteristics of carcinoma
December 2006
Reviewed by endocrinologist
Low libido
No galactorrhoea
Testosterone 2.6 nmol/l (92 ng/dl)
Cortisol 385 nmol/l (14.2 mcg/dl)
fT4 15 pmol/l (1.16 ng/dl)
TSH 1.8 mU/l
Prolactin >300000 mU/l (RR < 400)
   (>15000 ng/ml)

Prolactinoma

What next?

Started cabergoline & nebido
January 2009
- cabergoline 1.5 mg/week
- nebido 1 gm every 12 weeks
- prolactin nadir 3000 mU/l

What next?
June 2010

cabergoline 1.5 mg/week

prolactin 24000 mU/l

January 2009

2006

2010

2010

What next?

Cabergoline dose increased

Referred for trans-cranial debulking surgery
January 2011
attended Christie's
headache
facial numbness
prolactin 55000 mU/l
cabergoline 3.5 mg/week

March 2011
cabergoline 1.5 mg/day
Prolactin 19088 mU/l on
3-field radiotherapy 45 Gy in 25 fractions

What next?
November 2012
asymptomatic
cabergoline 1.5 mg daily
prolactin 1612 mU/l
fT4 9.1 pmol/l
TSH 2.57 mU/l
cortisol 223 nmol/l

annual echocardiogram
‘normal’

starting levothyroxine
Learning Points

- Measure prolactin in all peri-pituitary masses
- Recognise TSH deficiency
- High dose cabergoline
  - cardiac effects – annual echocardiogram
- Value of radiotherapy

<table>
<thead>
<tr>
<th>Date</th>
<th>Prostate (mU/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>January 2007</td>
<td>&gt;300000</td>
</tr>
<tr>
<td>January 2009</td>
<td>3000</td>
</tr>
<tr>
<td>January 2011</td>
<td>55000</td>
</tr>
<tr>
<td>November 2012</td>
<td>1612</td>
</tr>
<tr>
<td>March 2014</td>
<td>319 (16 ng/ml)</td>
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</table>
Causes of hypopituitarism (and mass effect)

- Pituitary and parapituitary tumours
- Trauma
- Radiotherapy
- Infarction (apoplexy)
- Infiltrations (sarcoid, histiocytosis, haemochromocytosis)
- Infections (TB, abscess)
- Sheehan’s (secondary to post-partum haemorrhage)
- Lymphocytic (ipilimumab) hypophysitis
- Empty sella (consequence of infarction or hypophysitis)

Pituitary adenomas & radiotherapy do not cause DI
53 year old man
Head & Neck tumour
External beam fraction
Nutrition via gastrostomy tube feeding

Admitted 3 weeks into 6 weeks of radiotherapy
nausea and vomiting
nil by mouth

Call to endocrinology:
serum Na 170 mmol/l
Urea 5.9 mmol/l
K 5.0 mmol/l
Creatinine 97 umol/l
Confused, drowsy
Not drinking
Pulled out infusion
Spent night sitting on floor

All medication had been stopped

**Past History**
Acromegaly – in remission
Transsphenoidal surgery
Hypopituitarism
hydrocortisone
levothyroxine
testosterone
oral desmopressin
**Management**

IV hydrocortisone infusion at 2-4 mg/hour

IV fluids – 200 ml/hour

Subcutaneous desmopressin 0.5 mg stat doses

2 hourly U&E

<table>
<thead>
<tr>
<th>Time (hours)</th>
<th>Serum Na (mmol/l)</th>
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<tr>
<td>48</td>
<td>130</td>
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</table>
64 year old man
Prostate cancer
Brachytherapy
External beam radiotherapy

Cystitis: asked to ↑ fluid intake

Endocrine referral
Na 116 mmol/l
Urea 4.2 mmol/l
K 4.8 mmol/l
Creatinine 87 umol/l

Idiopathic DI
DDAVP 10 mcg bd
therapy
↓ fluid intake
London Marathon April 2007

Hot day
completed marathon in 3 hr 30 min
collapsed at finish
died of hyponatraemia

2003
St Thomas’ admitted 14 patients with hyponatraemia
‘It is not about the sodium’

Hyponatraemia

Eunatraemia

Hypernatraemia

water

sodium
Causes of hyponatraemia

- Primary polydipsia: 20%
- Hypervolaemia: 32%
- Hypovolaemia: 35%
- SIADH: 4%
- Diuretic-induced: 7%
- Adrenal insufficiency: 2%

serum Na <130 mmol/L at the University Hospital of Würzburg
Neurological manifestations of symptomatic hyponatraemia vary

- Headache
- Irritability
- Nausea / vomiting
- Mental slowing
- Unstable gait / falls
- Confusion / delirium
- Disorientation

- Stupor / coma
- Convulsions
- Respiratory arrest

Symptomatic but less impaired; usually chronic

degree of symptomatology a surrogate for the duration

Life-threatening; usually acute

Adroogue NEJM 2000 342 1581
Ellison NEJM 2007 356 2064
## Signs and Symptoms of hyponatraemia

<table>
<thead>
<tr>
<th>Plasma Na concentration</th>
<th>Symptoms &amp; Signs</th>
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<tr>
<td>130 – 135 mmol/l</td>
<td>Usually asymptomatic</td>
</tr>
<tr>
<td>125 – 130 mmol/l</td>
<td>Anorexia, N&amp;V, abdominal pain, Disorientation, headaches</td>
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<tr>
<td>115 – 125 mmol/l</td>
<td>Agitation, confusion, hallucinations, impaired mental function</td>
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<tr>
<td>&lt;115 mmol/l</td>
<td>Seizures, coma</td>
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</table>
55 year old man
Small cell carcinoma of lung

SOB, anorexia, sweats, confusion

Na 110 mmol/l
Urea 4.5 mmol/l
K 4.6 mmol/l
Creatinine 51 umol/l

Euvolemic
Serum osmolality 226 mOsm/kg (275-295)
Urinary osmolality 611 mOsm/kg
Urinary Na  42 mmol/l

SIADH
Impact of Tolvaptan therapy in SIADH

Serum Na (mmol/l)

6th Feb 27th Feb 12th March
## Assessment of Hyponatraemia: not always due to SIADH

### Volume Status

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>&lt;20 mmol/l</th>
<th>&gt;20 mmol/l</th>
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<tbody>
<tr>
<td>Hypovolaemia</td>
<td>Tachycardia, hypotension, low JVP and CVP, decreased skin turgor, dry mucous membranes, elevated blood urea and plasma renin</td>
<td>GI losses: vomiting, diarrhoea, Mucosal losses: burns, Pancreatitis, Hypothyroidism, SIADH + fluid restriction, Cirrhosis, Cardiac failure, Primary polydipsia</td>
</tr>
<tr>
<td>Euvolaemia</td>
<td>Blood urea normal or low</td>
<td></td>
</tr>
<tr>
<td>Hypervolaemia</td>
<td>Peripheral, sacral and pulmonary oedema, ascites, raised JVP</td>
<td></td>
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### High output stoma

- Volume status
- Urinary Na
- Serum & urine osmolality
- Cortisol
- T4, TSH
Essential Diagnostic Criteria for SIADH

- Plasma osmolality <270 mOsm/kg
- Inappropriate urinary concentration (UOsm >100 mOsm/kg)
- Normal extracellular blood volume
- Elevated urinary sodium (>40 mmol/l) in presence of normal salt and water intake
- Exclude hypothyroidism & glucocorticoid deficiency
Using speed of onset of hyponatraemia secondary to SIADH to guide treatment

Hyponatraemia

- Acute
  - 3% saline ± diuretics
  - 24–48hr

- Gradual onset
  - > 48hr
  - Fluid restriction
  - Demoxycycline
  - Tolvaptan

Symptoms & Mental state

If the speed of onset is unknown, treated as though gradual onset
Fluid restriction

The higher the urine osmolality the less likely it is to work.
Can be harmful if urine osmolality is very high.

Useful tool: urine/plasma electrolyte ratio

\[
\frac{\text{Na}}{\text{Na}}_{\text{urine}} + \frac{\text{K}}{\text{Na}}_{\text{urine}} \quad \frac{\text{Na}}{\text{Na}}_{\text{serum}}
\]

<table>
<thead>
<tr>
<th>Ratio</th>
<th>Fluid restrict to:</th>
</tr>
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<tbody>
<tr>
<td>&gt;1</td>
<td>may worsen situation</td>
</tr>
<tr>
<td>0.5-1.0</td>
<td>&lt;0.5 L</td>
</tr>
<tr>
<td>&lt;0.5</td>
<td>&lt;1 L</td>
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</table>
Treatment of severe symptomatic hyponatraemia with 3% saline

IV infusion 150 mls 3% saline over 20 min

Check serum Na after 20 min while repeating an infusion of 150 mls 3% saline over the next 20 min

Repeat until the serum sodium has increased by 5 mmol/l

Infusion should be stopped:
- patient becomes asymptomatic
- serum Na is 120 mmol/L
- $\uparrow \geq 10$ mmol/L in 24 hours

Central pontine myelinolysis

Na$^+$ should be monitored every 2–4 hours

Verbalis AJM 2007 120 S1
Ellison NEJM 2007 356 2064
Monitoring Tolvaptan therapy

Competitively binds to the vasopressin V₂ receptor

stop fluid restriction and deoxycycline
starting dose **7.5 mg** oral
prescribe as a single dose
preferably administered in the morning
serum Na should be measured 6 hours after dose

**Over rapid Increase sodium:**
≥6 mmol/l during the first 6 hours
≥8 mmol/l during the first 6-12 hours
≥12 mmol/l within 24 hours
≥18 mmol/l within 48 hours
Conclusions

**Pituitary Disease**
- 3 manifestations - hyper, hypo & mass effect
- be aware of hypoadrenalism - measure cortisol

**Hyponatraemia**
- initial systematic assessment crucial
- avoid over-rapid correction
- use Tolvaptan with caution – starting dose 7.5 mg