Endocrine Emergencies 101 for Nurses with a paediatric twist

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Introduction

• Non diabetic endocrine emergencies rare

• Consider clinical situations that require immediate attention and the need for specialist referral

• Mix of clinical scenarios and what we see in paediatrics
Case study 1

• 3/52 baby
  o 2nd opinion
  o ? Future management

• Born at term
• Weight 4.53kg
• Non-consanguineous parents
• No family history
Case study 1

- Ante-natal USS
  - Boy
- Baby born
  - Male SOR assigned
  - Given a male name
- Post natal check
  - No testes in scrotum
- Urgent USS...
- DIAGNOSIS?

- Normal bladder and kidneys
- No testes or ovaries
- Chromosomes
  - 46XX
- Bloods
  - ↑ 17OHP
    - 101.9nmol/L (NR: 0-5nmol/L)
- Local Paediatrician
  - 21OHD CAH
  - Hydrocortisone and Fludrocortisone
Referral to tertiary centre

- Parents very anxious
  - Genital reconstructive surgery
- Referral into the DSD MDT
- On examination
  - Prader V in Prader scoring system
46XX CAH

- Baby will have been exposed to excess male hormone in-utero
- The genitalia will look like a boy’s:
  - Labia will fuse to look like a scrotum
  - Clitoris enlarges and looks like a penis
- Can sometimes be so severe, sex assignment is difficult
  - Need karyotype
  - Will still have normal internal structures
  - Surgery may be needed to correct outer appearance
  - CONTROVERSIAL

- Exposure to prenatal androgens and Prader 3 virilisation at birth
- Same baby at age 8 weeks at the time of genital reconstruction, showing some regression of virilisation after starting steroid treatment
- Another baby girl with a more severe form of 21OHD, leading to more severe virilisation (Prader IV)
Further investigations

• Repeat Pelvic USS
  o No testes
  o Ovaries seen

• Review of management, including intensive support and input from CNS

Change from hydrocortisone suspension to tablets
Medication review

- Stay on same dose of Fludrocortisone
- Hydrocortisone suspension tds
  - 2/2/3mg
- Changed to hydrocortisone 10mg tablets
  - 1.25mg qds
  - Guidance given on crushing and mixing with water, breast milk
  - Dosage titrated against BSA calculations
    - Side effects of underdosing → androgenisation
    - Side effects of overdosing → Cushings
    - Regular bloods
- Intensive emergency management training
  - x 3 emergency hydrocortisone packs prescribed and administered
CORTISOL DEFICIENCY

Steroid replacement therapy

4. Mix a crushed 1/2 of a tablet with the 2/3s of cooled boiled water.

5. Then draw up 1 ml of the mixture into a 2 ml syringe.

6. Give by mouth as shown by ward nurses.

Where are they kept and what do they do?

The adrenal glands sit on the top of the kidneys in the back of the body. Each gland produces most of two hormones. These are:

- Cortisol, with which it influences the way your body uses food for energy
- Aldosterone, with which it influences how much salt your kidneys retain and how much urine the kidneys produce

What happens if there is too little cortisol in the body?

- The body does not use food properly because there is not enough cortisol
- Loss of appetite
- Weakness
- Headache
- Sleepiness, forgetfulness, and irritability
- Loss of muscle and joint pain
- Loss of body weight
- Type 2 diabetes

What happens if there is too much aldosterone?

- Body conserves salt
- Body conserves water
- Water retention
- Swollen ankles
- High blood pressure

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How to give an emergency injection of Effortrol®

- Mix a crushed 1/2 of a tablet with the 2/3s of cooled boiled water.
- Then draw up 1 ml of the mixture into a 2 ml syringe.
- Give by mouth as shown by ward nurses.
What is a DSD?

- Congenital conditions in which development of chromosomal, gonadal or anatomic sex is atypical

  - True genital ambiguity
    - 1 in 5000 / 1 in 4500 births

  - Genital anomalies
    - 1 in 300 births
Classification of DSD

- **46,XY DSD (under virilised genetic male)**
  - Disorders of testicular development
    - Ovotesticular DSD
  - Disorders of androgen synthesis / action
    - CAIS
  - Others
    - Hypospadias

- **46,XX DSD (over virilised genetic female)**
  - Disorders of ovarian development
    - Ovotesticular DSD
  - Androgen excess
    - CAH

- **Sex chromosome DSD (variable)**
  - Turner syndrome
  - Klinefelter syndrome
  - Mixed gonadal dysgenesis
Case study 2

January 2001

February 2002
Case study 2

- Facial appearance
  - ‘Moon face’
- Weight gain
  - Truncal obesity
  - Buffalo hump
- Skin
  - Thin and fragile
  - Stretch marks
- Muscle weakness
- Mood disturbance
- Menstrual disturbance
- Hypertension
- Related excess androgen production

- Growth failure in children
- Abnormal virilisation
Abnormal virilisation in a 6.2 yr old prepubertal boy with Cushing’s disease
Rapid progression of severe paediatric Cushing’s disease in an 6.2 yr old boy
Age 6 years

- 2 year history of rapid weight gain
- Purple striae
- Depressive state
- Growth failure
- Hypertension 135/55
- Virilised
  - G3 P2 Prepubertal testes
- Raised liver enzymes
- Abdominal U/S
  - Enlarged fat laden liver
  - Enlarged adrenals
Endocrine investigations?

- Urinary free cortisol
  - 1098 nmol/24h (NR 40 – 340)
- Midnight cortisol
  - >1650 nmol/l (NR <50)
- Low dose dexamethasone suppression test
  - Failure to suppress cortisol (>1650 nmol/l)
- Adrenal androgens
  - Raised:
    - Androstenedione 36.3 nmol/l (NR <1.0)
    - DHEA-S 1.4 μmol/l (NR <0.5)
    - Testosterone 8.1 nmol/l (NR <0.8)
Next steps?

Pituitary surgery?

Adrenalectomy?
Pituitary surgery plan

• Control the hypercortisolaemia
• Stabilise the child’s general condition
• Treatment was initiated with **ketoconazole** 200 mg 8-hourly, but discontinued after 6 weeks due to deteriorating liver function
• **Metyrapone** 250 mg 8-hourly was substituted but was not tolerated even when given by naso-gastric tube, because of persistent nausea and vomiting

The serum cortisol remained elevated at
> 1,250 nmol/l
What happened next?

• The child’s general condition deteriorated rapidly with hyponatraemias secondary to persistent vomiting, inadequate nutritional support and incipient respiratory failure.

• The decision was taken to transfer the child to a PICU and to stabilise his condition in preparation for bilateral adrenalectomy.

  o **Life saving procedure!**
How could his hypercortisolaemia be controlled prior to surgery?
Severe Cushings - Etomidate

- Etomidate
  - IV anaesthetic agent
  - Suppresses corticosteroid synthesis
- Adrenal suppression
Control of hypercortisolaemia with adrenolytic therapy - IV Etomidate
Finally.. Progress!

- Post-operatively, the patient made good progress.
- Serum cortisol pre-hydrocortisone was <20 nmol/l, indicating removal of all adrenal tissue, and he recovered steadily on replacement therapy of hydrocortisone 5 mg three times daily and fludrocortisone 50g twice daily.
Case study 3 – 13 week old baby girl

- Admitted for poor feeding
  - Born at 41 weeks
  - Weighed 3.4kg
  - Mother was 29 years of age
  - Hypoglycaemic at 24 hours
  - Phototherapy for jaundice

  - 6 weeks
    - Not fixing and following
  - 10 weeks
    - Small optic discs
    - Absent electroretinogram response to light

- On examination
  - Pale
  - Still
  - Weight 5.36 kg (-1.05 SD)
  - Length 60.5cm (0.21 SD)
  - Hypotonic
  - Roving nystagmus

- Likely diagnosis?
- What further assessment is needed?
Septo Optic Dysplasia

- Corpus callosum
- Septum pellucidum
- Optic nerves
- Pituitary
**Why?**

- Nystagmus
- Failure to fix and follow
- Neonatal hypoglycaemia
- Jaundice
  - Optic Nerve Hypoplasia
  - Hypopituitarism

- Cranial ultrasound
- MRI
  - Absence of septum pellucidum
- Bloods
  - T4
  - TSH
  - Random cortisol
  - Electrolytes
What would the results show?

<table>
<thead>
<tr>
<th>Test Description</th>
<th>Value</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum sodium</td>
<td>163 mmol/L</td>
<td>135 - 145 mmol/L</td>
</tr>
<tr>
<td>Urine osmolality</td>
<td>132 mOsm/kg</td>
<td>NR 500 – 800 mOsm/kg water</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Large values = concentrated urine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lower values = dilute urine</td>
</tr>
<tr>
<td>Random cortisol</td>
<td>220 nmol/L</td>
<td>NR &gt;500 nmol/L</td>
</tr>
<tr>
<td>Peak cortisol on standard synacthen test (ACTH 250mcg)</td>
<td>1269 nmol/L</td>
<td></td>
</tr>
<tr>
<td>Free T4</td>
<td>13.9 pmol/L</td>
<td>NR 10-20 pmol/L</td>
</tr>
<tr>
<td>TSH on stimulation test</td>
<td>0 mins 3.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>30 mins 26</td>
<td></td>
</tr>
<tr>
<td></td>
<td>60 mins 33 mU/L</td>
<td>NR 0.5 – 5 mU/L</td>
</tr>
<tr>
<td>Peak GH on stimulation</td>
<td>Low normal 8 µg/L</td>
<td>NR &gt;7 µg/L</td>
</tr>
</tbody>
</table>
TRH test

- TRH 7 mcg/kg slow IV injection over 3 mins
- Interpretation
  - In normal people, a rise in TSH at 20 mins with a fall at 60 is seen
  - In hypothalamic hypothyroidism
    - TSH increases at 20m, and continues to rise at 60
  - In hypothyroidism 2° to hypopituitarism
    - No change in TSH level
What do the results mean?

What treatment should the baby have?
Further diagnosis and treatment

- Baby has diabetes insipidus
- Hypothalamic hypothyroidism
- No cortisol deficiency

**WHY?**

- DDAVP
  - 25mcg daily initially
- Thyroxine
  - FT4 falls to 8.9pmol/L at age 5 months

**What happens next with the baby?**
Baby unwell again

- Admitted acutely unwell to the ER
  - Poor perfusion
  - Mottled and cold peripheries
  - Capillary glucose 1.3mmol/L (NR 4-7)
  - Sodium
    - 167mmol/L
  - Lab glucose
    - 2.2mol/L
  - Treatment?
    - IV fluids
    - DDAVP dose adjusted
    - DI difficult to control
      - Sodium fluctuating between 130 and 156 mmol/L

What is the explanation for the poor progress?
ACTH deficient

- DI cannot be properly controlled with cortisol deficiency
  - Latter required for water excretion
- Peak cortisol on synacthen was exaggerated as low dose was not used
- IM injection after time 0
  - < 6/12: 62.5mcg
  - 6/12 – 2yrs: 125mcg
  - > 2yrs: 250 mcg

- Random cortisols during illness were never >500
- Baby started on hydrocortisone
  - When on full replacement
    - DI stabilised
- Height
  - Remained on 10th centile
  - Age 5 years
    - Fell to 3rd centile
    - GH therapy commenced
Comments on Case Study 3

- Difficulty in diagnosing adrenal insufficiency
- Important role of cortisol in water balance
- Evolving pattern of GHD in SOD
  - Normal levels often found in infancy
Baby aged 10 days referred to the paediatric endocrine clinic

Fit and well
  - Beginning to feed poorly
  - Slightly jaundiced

What could be the indication for referral?

Congenital hypothyroidism
Congenital hypothyroidism

- All babies screened at 5 days of life
  - Guthrie Test - TSH
    - Sleepiness
    - Poor feeding
    - Constipation
    - Goitre
    - Oedema
    - Jaundice

- Treatment:
  - Thyroxine tablets
    - 100 mcg / m2 / day
Screening

- Guthrie card at 5-8 days – detects TSH
- Notification if positive TSH >20mU/L
- Start treatment within 24 hours
- If borderline TSH 6-19.9mU/L - repeat
- Thyroid isotope scan usually performed
  - Assess size and site of gland
Technetium scan
Flow sheet false positive

Blood spot 26mU/l

<table>
<thead>
<tr>
<th>Date</th>
<th>TSH</th>
<th>Free T4</th>
<th>Free T3</th>
<th>Thyroxine dose (mcg)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>13/8/2015</td>
<td>7.43</td>
<td>20.7 (12.5-24.6)</td>
<td>-</td>
<td>-</td>
<td>Rpt 2/52</td>
</tr>
<tr>
<td>27/8/2015</td>
<td>5.2</td>
<td>19.2</td>
<td>-</td>
<td>-</td>
<td>Discharge</td>
</tr>
</tbody>
</table>
## Flow sheet double borderline

1\textsuperscript{st} blood spot 9.8mU/l; 2\textsuperscript{nd} spot 10mU/l

<table>
<thead>
<tr>
<th>Date</th>
<th>TSH</th>
<th>Free T4</th>
<th>Thyroxine dose (mcg)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>30/5/2015</td>
<td>26.2</td>
<td>15.3 (12.5-24.6)</td>
<td>-</td>
<td>Started 25mcg OD</td>
</tr>
<tr>
<td>12/6/2015</td>
<td>6.1</td>
<td>18.7 (9-19.6)</td>
<td>25 mcg OD</td>
<td>Continue</td>
</tr>
<tr>
<td>31/7/2015</td>
<td>19.2</td>
<td>14.0</td>
<td>25 mcg OD</td>
<td>Increase to 35mcg OD</td>
</tr>
<tr>
<td>1/10/2015</td>
<td>0.6</td>
<td>23.6</td>
<td>35mcg OD</td>
<td>Reduced to 30mcg OD</td>
</tr>
<tr>
<td>2/2/2016</td>
<td>3.4</td>
<td>15.3</td>
<td>30mcg OD</td>
<td>Continue</td>
</tr>
<tr>
<td>1/4/2016</td>
<td>1.2</td>
<td>19.2</td>
<td>30mcg OD</td>
<td>Continue</td>
</tr>
<tr>
<td>2/6/2016</td>
<td>2.2</td>
<td>16.7</td>
<td>30mcg OD</td>
<td>Switched to tablets 37.5/25 mcg OD</td>
</tr>
</tbody>
</table>
Congenital Hypothyroidism

- Defects in T4 synthesis
- TRH and TSH deficiency
- TSH receptor defect
- Maternal disease
  - Drugs
- Trisomy 21

- Thyroid dysgenesis
  - Missing
  - Ectopic
  - Underdeveloped
Thyroid gland development – 4-7 weeks

- Thyroglossal duct degenerates between 7-10 weeks
- Thyroid reaches its end location anterior to the trachea by week 7
- If parts of the duct remain the person may also have a pyramidal lobe
  - 50% of the population
- Ectopic thyroid tissue left behind during migration
  - Common but asymptomatic
  - Parts of the duct may persist
    - Midline, movable cyst in the child
- Thyroid tissue left behind during migration
Treatment and follow up

**Treatment**
- Thyroxine
  - 25-50 mcg daily (10mcg/kg/d)
  - Crushed tablet or solution
  - NOT suspension
- Neonates have higher normal range fT4
- Maintain in upper half of normal range

**Follow up**
- Development, hearing and growth
- Often subtle speech delay
- Detect those with transient neonatal hypothyroidism
- Decision on withdrawal at 3 years
Case study 5

- Presentation of newborn baby
  - Tachycardic
  - Irritability
  - Restlessness
  - Hypertensive
  - Exophthalmos
  - Periorbital oedema
  - Goitre
Neonatal thyrotoxicosis

- Caused by trans-placental transfer of maternal TSH receptor antibodies
  - Stimulates the foetal and neonatal thyroid gland
- May occur in infants with mothers of some degree of hyperthyroidism

- Usually simply biochemical
- Signs and symptoms
  - Goitre
  - Tachycardia
  - Arrhythmias
  - Hypertension
  - Cardiac failure
  - ↑ appetite
  - Weight loss
  - Diarrhoea
  - Irritability
  - Exophthalmus
At 26 weeks’ gestation when there is a maternal history of Graves’ disease:

- Measure TSH receptor antibody level

  - < 350%
    - Monitor fetal heart rate and growth
      - < 160 beats/min, Consider periumbilical blood sampling for diagnosis
      - > 160 beats/min
  - 350%–500%
    - Monitor fetal heart rate
  - > 500%
    - Diagnose fetal hyperthyroidism; treat with propylthiouracil, 100 mg/d
Case study 7

- 14 year old Asian girl
  - 6 week history
    - Polyuria
    - Polydipsia
    - Weight loss

- Grandfather developed diabetes in his 50s and takes tablets

- On examination
  - Overweight
  - BMI – 98 / 99%ile
  - Pink stretch marks
  - Acanthosis nigricans
  - Blood glucose
    - 26mmol/L (468mg/dL)
  - Not acidotic
  - Urine
    - 3+ glucose
    - Moderate ketones

- Diagnosis?
- Investigations?
- Treatment?
Type 2 diabetes

- High risk ethnic group
- Family history
- Acanthosis
- BMI – obese
- Ketonuria
  - Unusual, but does occur in a 3rd of cases

- Because of the weight loss and ketonuria
  - Difficult to diagnose between Type 1 and Type 2 diabetes
Investigations to confirm?

- Islet cell and GAD antibodies
  - GAD test
    - Blood test to measure whether the body is producing a type of antibody which destroys its own GAD cells
      - Negative in Type 2
      - Positive in Type 1

- C-Peptide
  - Reflects amount of natural insulin that the child is producing
    - Normal or increased in Type 2
    - Low in Type 1
Treatment

• Results of bloods may take some weeks...
  
  o High blood glucose
  o Ketosis
    • Basal bolus regime of insulin
    • Dietary treatment and good exercise regime very important
  
  o When ketosis has resolved
  o Blood glucose lowered

  • Metformin gradually introduced
    o Gradually increase
    o Decrease then stop insulin
National Child Measurement Programme

- Measures and records the height and weight of over one million children each year in the UK
  - Reception age (4-5 years)
  - End of primary school age (10-11 years)

- Principally to assess weight and obesity levels in schools

- Parents can opt out
Prevalence of excess weight among children in the UK – 2014 / 2015

One in five children in Reception is overweight or obese (boys 22.6%, girls 21.2%)

One in three children in Year 6 is overweight or obese (boys 34.9%, girls 31.5%)
Obesity prevalence by ethnic group: Year 6

NCMP 2014/15

Child obesity: BMI ≥ 95th centile of the UK90 growth reference
Causes of increasing childhood obesity

- **Genes**
  - Monogenic
  - Polygenic
  - Co-morbidity genes

- **Environment**
  - Quality of food supply
  - Food convenience
  - Food industry
  - Price
  - Activity
Food industry

- £600 million spent last year marketing high sugar products to children
- Advertising – traditional and new
  - Advergames
    - Promoting material to websites
  - Characters
  - Social media
- Sponsorship of events, programmes and infrastructure
Management of Type 2 Diabetes

- Education
- Behavioural changes
- Dietary management
- Glycaemic monitoring
- Pharmacological therapy
  - Decrease insulin resistance
  - Increase insulin secretion
  - Slow post prandial glucose absorption

• Biguanides
  - Metformin
  - Acts on insulin receptors in liver, muscle and fat tissue
  - Long term use – associated with 1 – 2% reduction in HbA1c

• Insulin
  - Small doses can be effective

• Sulphonylureas
  - Increase insulin secretion
    - Useful when there is residual beta cell function
Paediatric Emergencies

• Some more urgent than others
  o Urgent treatment
  o Urgent referral

Differences between adults and paediatrics?

- DSD
- Diabetes
- Cushing's
- Neonatal thyrotoxicosis
- SOD
- CH
References


