Cushing's syndrome

She was really relieved to be feeling better from her polymyalgia but “I don’t mean to complain doctor, but I have just put on so much weight, especially around my face, and my skin gets all bruised!”. Here Cushing’s syndrome is discussed as part of the BMJ easily missed series (BMJ 2013;346:f945).

Cushing’s syndrome statistics

- 1% of the general population take glucocorticoids and of these 10% will develop Cushing’s.
- Endogenous Cushing’s is rare but in secondary care clinics for refractory hypertension and diabetes, prevalence was 0.6% and 0.5%, respectively.

What causes Cushing’s syndrome?

Cushing’s syndrome is a consequence of chronic exposure to excess glucocorticoids regardless of their origin.

- Endogenous, e.g. cortisol-producing adrenal tumours or ACTH-producing pituitary tumours.
- Exogenous, e.g. glucocorticoid tablets, inhalers, nasal sprays and skin creams (more common!).

Why is it missed?

The mean time to diagnosis from first presentation with suggestive symptoms is 6y! It is missed because it evolves slowly over time and its symptoms are a great mimic for other more common conditions that we regularly see, e.g. obesity, menopause, depression, hypertension, etc.

I think we are more likely to detect it in those taking oral steroids, but those on topical preparations and those with endogenous Cushing’s need a higher degree of suspicion to spot!

Why does it matter?

Because of significant morbidity and mortality!

- Untreated Cushing’s has a 50% mortality at 5y – predominantly from cardiovascular disease and infections.
- Myopathy.
- Congestive cardiac failure.
- Osteoporosis.
- Menstrual irregularity and infertility.
- Mood disturbance.

How do we diagnose it?

In the history, look for multi-system disease – a study of 700 patients with Cushing’s found the following prevalence of symptoms:

<table>
<thead>
<tr>
<th>Symptoms/conditions suggestive of Cushing’s syndrome</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight gain</td>
<td>97%</td>
</tr>
<tr>
<td>Depression</td>
<td>62%</td>
</tr>
<tr>
<td>Subjective muscle weakness</td>
<td>29%</td>
</tr>
<tr>
<td>Headache</td>
<td>47%</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>50%</td>
</tr>
<tr>
<td>Refractory diabetes</td>
<td>50%</td>
</tr>
<tr>
<td>Refractory hypertension</td>
<td>74%</td>
</tr>
</tbody>
</table>

Basically, we need to think about it! Physical examination is also important – the features that have the best discriminatory value between obesity and true Cushing’s are shown in bold:

- Easy bruising.
- Purple striae.
- Objective muscle weakness.
- Plethora.
- Hirsutism or scalp thinning.
- Central obesity, moon face, buffalo hump and supraclavicular fat pads.
- Signs of cardiac failure.
- Hypertension.

**Investigations**
- If you have a strong suspicion of endogenous Cushing’s, refer to secondary care. You may want to consider a primary care screening test:
  - 24h urinary cortisol (if normal eGFR)
  - Late night salivary cortisol (if available)
  - Overnight 1mg dexamethasone suppression test – take 1mg dexamethasone at 2300h and measure serum cortisol at 0900h – if <50nmol/L excludes (>95% sensitivity).

However, all of these can give frequent false positives and negatives – refer if in doubt!
- Blood tests including random cortisol, LFTs, cholesterol and glucose are not helpful in confirming or excluding the diagnosis.
- If a patient is taking exogenous steroids, biochemical confirmation is not possible and diagnosis should be made on the basis of history and examination.

**Management**

Depends on the cause!
- Exogenous Cushing’s should be managed by reducing the oral steroid dose as soon as is clinically possible.
- Endogenous Cushing’s requires surgical resection of the pituitary, adrenal or ACTH-producing tumour

**Cushing’s syndrome**

- Be aware of it!
- Consider the diagnosis in patients with weight gain, muscle weakness, easy bruising and osteoporosis – especially if they have refractory hypertension or diabetes.
- If endogenous Cushing’s is suspected, refer to endocrinology.
- If exogenous Cushing’s occurs aim to reduce dose of glucocorticoids as soon as clinically possible – this may involve referral to consider steroid sparing agents!

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Exeter Thur 6 Oct
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London Sat 8 Oct
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London Wed 19 Oct
Nottingham Thur 20 Oct
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London
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- The Telephone Consultation Course (location) .............................................................   (date).........................
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