The Association for Clinical Biochemistry & Laboratory Medicine

Clinical Biochemistry Case 1 – Raised testosterone in a female patient

Patient: 25 y/o female GP patient

Clinical details: Trying to conceive

No significant past medical history.

Results:

- U&E, LFT, bone profile, fasting glucose, HbA1c, TSH and ferritin – normal
- Testosterone = 5.3 nmol/L (<3.1 nmol/L)

Question 1 – What are the possible causes of a raised testosterone in a female patient?

Broadly the causes of a raised testosterone in a female patient can be divided into three categories: increased production by the ovaries, increased production by the adrenal glands and disorders causing increased concentrations of SHBG.

Increased production by the ovaries:

- Polycystic ovarian syndrome (PCOS) – the most common cause of increased testosterone concentrations in female patients
- Androgen-secreting ovarian tumours

Increased production by the adrenal glands:

- Congenital adrenal hyperplasia – late onset 21-hydroxylase deficiency
- Androgen-secreting adrenal tumours
- Cushing's syndrome

Increased concentration of SHBG:

- Hyperthyroidism
- Increased oestrogen concentrations – physiological ie. pregnancy or exogenous oestrogens eg. combined oral contraceptive pill or hormone replacement therapy
- Anorexia nervosa
- Liver failure

Methodological:

- Interference in immunoassays from other androgens – these may be physiological androgens or drugs

Question 2 – What action would you take (if any)?

A testosterone concentration ≥5.0 nmol/L in a female patient is more likely to be associated with one of the more sinister causes of a raised testosterone eg. androgen-secreting tumours or CAH. Therefore this testosterone result does require further action from a clinical perspective.

Step 1 – Result to be phoned to the patient's GP for further discussion.

Questions for the GP

- Why has the testosterone been requested?
- What was the patient's presenting complaint?
- Did the patient present with signs/symptoms of hyperandrogenism eg. hirsutism, virilisation, hair loss (in an androgenic pattern), oligo- or amenorrhea?
- Over what time scale did these signs/symptoms develop? – significant symptoms of hyperandrogenism (particularly virilisation) which have developed over a short time frame are suggestive of androgen-secreting tumours
- Is the patient taking any drugs which might interfere with our testosterone assay?
- Does the patient have any signs/symptoms consistent with the metabolic syndrome?

Step 2 (if required) – Confirmation of the testosterone result by an alternative methodology (LC-MS/MS)

Step 3 (dependent on patient presentation) – Referral to Endocrinology

Question 3 – Suggest three further tests (other than those listed below) which would be useful in the investigation of this patient. These may be laboratory or non-laboratory tests.

- SHBG
- βHCG
- Ovarian ultrasound scan
- 17-hydroxyprogesterone
- Androstenedione and DHEAS
- CT/MRI scan
- (24 hour urine steroid profile)
- (24 hour urine free cortisol or overnight dexamethasone suppression test)

Results of further hormone testing:

- LH = 0.6 IU/L
- FSH = 0.74 IU/L
- Oestradiol = 3081 pmol/L
- Prolactin = 705 mIU/L (70 – 566 mIU/L)

Question 4 – What diagnosis are these results consistent with?

Abnormalities: suppressed gonadotrophins, increased oestradiol and hyperprolactinaemia

These biochemical abnormalities, alongside the patient's increased testosterone concentration and clinical details, are consistent with a diagnosis of pregnancy.

Question 5 – Is further investigation required? Please explain your answer.

Assuming that the pregnancy is confirmed with βHCG testing (either urine or serum) the raised testosterone concentration does not require any further investigation. Increased testosterone in pregnancy is a physiological biochemical change caused by the increased SHBG levels associated with high oestradiol concentrations. In this case the majority of the 'extra' testosterone is bound to SHBG and is therefore not physiologically active.