The Association for Clinical Biochemistry & Laboratory Medicine

Clinical Biochemistry Case 3 – Low cortisol

Patient: 53 y/o GP patient

Clinical details: Dizzy spells

Past medical history: Grave's disease

Results (Sample booked in 04.07.21 15:42):

- U&E, LFT, fasting plasma glucose – normal
- FT4 = 36.4 pmol/L (7.5 – 21.1 pmol/L)
- TSH = <0.01 mIU/L (0.34 – 5.6 mIU/L)
- Corrected calcium = 2.73 mmol/L (2.20 – 2.60 mmol/L)
- Cortisol = 38 nmol/L (9am range = 240 – 618 nmo/L)

Question 1: What further information would be useful to help decide whether this result requires urgent action?

- Time of sample collection ie. 9am/early morning sample? – Although it should be noted that a cortisol of 38 nmol/L would be considered low in a patient with intact cortisol production irrespective of the time of sample collection. The exception to this would be a midnight cortisol value, however a midnight sample collection time is extremely unlikely in this case given the GP location, clinical details and time of sample receipt.

- Does the patient have a history of steroid use either prescribed e.g. for asthma, eczema, pituitary or adrenal insufficiency or illicit eg. anabolic steroids for body building, herbal remedies?

- Has this sample been collected as part of a dexamethasone suppression test?

- Does the patient have any signs/symptoms of hypocortisolaemia? Do they have a previous history of cortisol insufficiency/treatment?

Question 2: List three possible causes of the low cortisol result.

- 9am sample for a dexamethasone suppression test
- Exogenous steroid use
- Primary adrenal insufficiency (Addison's disease) eg. caused by autoimmune disease, TB, adrenal haemorrhage, adrenal metastases
- Secondary adrenal insufficiency (hypopituitism) eg. caused by pituitary adenoma/carcinoma, pituitary haemorrhage, previous pituitary surgery
- Tertiary adrenal insufficiency (hypothalamic insufficiency) – unlikely given the critical requirement of cortisol production to sustain life
- Congenital adrenal hyperplasia

- Immunoassay interference – although not a commonly affected analyte therefore unlikely

Question 3: Taking into account the patient's test results, clinical details and past medical history, what is the most likely cause of the slightly raised corrected calcium result? Explain your answer.

It is difficult to determine the cause of the mild hypercalcaemia without further biochemical testing. However, the patient's overt hyperthyroidism is likely to be at least partially responsible for the observed increase. Hyperthyroidism is a recognised cause of hypercalcaemia. The exact mechanism is unknown, however it is believed due to due to a direct effect of the increased thyroid hormone concentrations on bone metabolism i.e. increased bone turnover.

Hypocortisolaemia is also associated with hypercalcaemia. The mechanism of this is related to the significant hypovolaemia observed in patients with cortisol deficiency (due to lack of action of ADH in the nephron and the accompanying significant renal fluid loss). Hypovolaemia results in a decreased GFR and subsequently increased tubular calcium reabsorption. It is unlikely that this is a significant contributor in this patient as their renal function and electrolytes are normal.

It is important that other common causes of hypercalcaemia are excluded in this patient, particularly primary hyperparathyroidism as this is the most common cause of hypercalcaemia in a GP population. PTH measurement is required to exclude/confirm this diagnosis.

Question 4: List 5 signs/symptoms of hypocortisolaemia.

- Nausea, vomiting, abdominal pain
- Diarrhoea
- Postural hypotension, dizziness, sweating, increased heart rate
- Palpitations
- Weakness, fatigue
- Muscle weakness
- Headache
- Hyperpigmentation (if primary adrenal insufficiency)