Case report: Delayed diagnosis of Addison’s disease and Autoimmune Polyglandular Syndrome Type 2 due to misinterpretation of short synacthen test

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Background

- Short Synacthen test (SST) is commonly used to confirm diagnosis of Addison’s disease.
- However, misinterpretation can happen in inexperienced hands and this can lead to potentially adverse outcome.
- We present a case in which a diagnosis of Addison’s disease was missed as his SST was misinterpreted due to background hydrocortisone injection being administered to the patient.
- This patient was also found to have Autoimmune Polyglandular Syndrome Type 2 (APS-2) after further tests were performed.

Case Study

- A normally fit and well 28-year-old Caucasian man presented to hospital with a few days history of general malaise and a syncopal episode.
- On admission, patient was hypotensive and tachycardic.
- Admission bloods showed hyponatraemia, hyperkalaemia, acute kidney injury and raised inflammatory markers.
- The diagnosis of Addison’s disease was suspected.
- Patient was given hyperkalaemia treatment, intravenous fluids, antibiotics and hydrocortisone.
- Patient markedly improved over the next few hours.
- On the day after, SST was performed without holding off patient’s morning dose of hydrocortisone.
- Therefore, his SST results showed high cortisol levels.
- This was misinterpreted as ruling out adrenal deficiency.
- He was hence discharged without hydrocortisone replacement.
- Two weeks later, patient was re-admitted to hospital with similar presentation.
- SST was repeated before patient’s morning dose of hydrocortisone.
- This time, it demonstrated flat response and finally patient’s diagnosis of Addison’s disease.
- Patient was started on oral hydrocortisone and fludrocortisone.
- Patient’s blood test also showed evidence of autoimmune hypothyroidism.
- Further blood tests were performed to screen for other conditions associated with APS-2.
- Patient was also found to have probable underlying pernicious anaemia.

Investigations

| First admission | Cortisol (on admission) | 164   |
|                | 9am Cortisol (before ACTH injection) | 1655  |
|                | Cortisol (30 mins after ACTH injection) | 1655  |
|                | Sodium | 127   |
|                | Potassium | 6.7   |
|                | Urea | 23.3  |
|                | Creatinine | 319   |
|                | CRP | 206   |

| Second admission | Cortisol (on admission) | 73   |
|                | 9am Cortisol (before ACTH injection) | 97   |
|                | Cortisol (30 mins after ACTH injection) | 93   |
|                | Cortisol (60 mins after ACTH injection) | 90   |
|                | ACTH | 1180  |
|                | Sodium | 117   |
|                | Potassium | 5.0   |

Other blood tests

- Free T4: 9.6 pmol/l
- TSH: 22.17 mU/l
- Anti TPO Ab: >910 IU/ml
- Anti Adrenal Ab: Positive
- Anti Islet Cell Ab: Negative
- Anti GAD Ab: Negative
- Anti TgIgA: Negative
- Anti Parietal Ab: Present at 5/100
- Intrinsic Factor: Equivocal
- Vitamin B12: 777 ng/l
- Testosterone: 22.1 nmol/l

Discussion

Interpretation of Short Synacthen Test

- A SST diagnoses adrenocortical insufficiency by the impaired functional capacity of adrenal cortex to synthesize cortisol after the subject is given a dose of ACTH.
- Adrenal insufficiency is excluded by an incremental rise in cortisol of >200 nmol/L and a 30 min value >600 nmol/L.
- Clinicians fell into the pitfall of misinterpreting the result as the patient’s morning hydrocortisone dose was not omitted before SST was performed.
- This should never happen as a diagnosis of Addison’s disease can be missed as a result of this.

Type 2 Autoimmune Polyglandular Syndrome

- Type 2 APS (APS-2), which is also known as Schmidt’s syndrome, is the most common form of polyendocrine syndrome.
- It is characterised by the presence of Addison’s disease along with autoimmune thyroid disease and/or type 1 diabetes.
- Affected individuals may also have problems with other endocrine organs and common features include primary hypogonadism, myasthenia gravis, coeliac disease and pernicious anaemia.
- Screening for autoantibodies may be helpful in assessing disease risk as the relevant autoantibodies are frequently detectable years before disease onset.
- Screening for other associated conditions allow early identification of underlying condition which could be asymptomatic initially.

Conclusion

- Addison’s disease is a rare endocrinological disorder, often presents with non-specific symptoms.
- Due to its insidious onset, patients’ first presentation can be with life-threatening Addisonian crisis.
- Therefore, it is paramount to correctly perform and interpret SST results to prevent missing the diagnosis of Addison’s crisis in clinical practice.
- As Addison’s disease can co-exist with other autoimmune conditions, screening for other autoimmune disorders should be performed to enable early identification of any other underlying conditions.

References