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 confirmed 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 TTG IgA	Negative	
Anti Parietal Ab	Present at 1/100	
Intrinsic Factor	Equivocal	
Vitamin B12	177	ng/l
Testosterone	12.1	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' 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, which 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

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