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(CASE REPORT)

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CASE REPORT: AN INTERESTING CASE OF A MIDDLE-AGED WOMAN DIAGNOSED WITH ISOLATED ACTH DEFICIENCY CO-EXISTING WITH NON-FUNCTIONING ADRENAL INCIDENTALOMA IN A DISTRICT GENERAL HOSPITAL IN THE UK.

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ABSTRACT

We describe here a a woman who presented to the Endocrine Clinic in 2015 at the age of 50 years in a wheelchair with extreme lethargy, chronic pain and low morning Serum Cortisol. The patient had a Glucagon Stimulation Test. The results hinted towards Cortisol and Partial GH (Growth Hormone) deficiency. This was followed by an IGF-1 (Insulin like Growth Factor-1) estimation which was low and also had a SST (Short Synacthen Test) with base line ACTH (Adrenocorticotrophic Hormone) with the results showing a normal Plasma ACTH level and low morning Cortisol with inadequate response to Synacthen. The IGF-1 result later normalised. Two years later, the patient had a CT abdomen followed by CT adrenals with contrast done which showed a left adrenal adenoma which biochemically proved to be non-secretory. Thus, this middle-aged woman had Partial Isolated ACTH deficiency and left sided non- functional (non-secretory). adrenal incidentaloma. This case report of the combination of the two entities is unique as this is unlike the recent report of Isolated ACTH deficiency co-existing with mild autonomous Cortisol secreting Adrenal Incidentaloma (MACS).

Keywords: Cortisol, Growth Hormone, Glucagon, Synacthen, Incidentaloma

1 INTRODUCTION

Isolated ACTH deficiency is a rare condition with the aetiologies though unclear, include autoimmune process, congenital causes, physical trauma and pituitary tumour. It causes nonspecific symptoms like lethargy and weight loss and if not diagnosed early (no specific test available and therefore the diagnosis is difficult), it can lead to adrenal crisis (1-3).

An adrenal incidentaloma is an unsuspected adrenal mass ≥1 cm found on imaging while investigating for other pathology. It is most commonly a benign non-functioning adenoma (80-85%) but still requires evaluation for hormone excess and malignancy. It is found in 3% of abdominal CT scans at around 50 years of age; increases to 7-10% after age 70. The types are Non-functioning benign adenomas (80%), Mild autonomous cortisol secretion (MACS, 5–30%),

Pheochromocytoma, Aldosterone-producing adenoma or Conn's syndrome, Adrenocortical carcinoma (2–5%) and. Metastases (ref: 4-6). Our case was of the first variety- a non-functioning benign adenoma.

At the age of around 50 years, having either of the two lesions is rare and having both co-existent together is extremely rare and unique.

2 CASE REPORT

A 50-year-old woman was referred in 2015 to the Endocrine Clinic with fatigue and low morning Cortisol and high Prolactin. She had a background history of chronic fatigue syndrome (Myalgic Encephalomyelitis), to the extent that she sometimes needed a wheelchair and also came to the outpatients in a wheelchair. She had chronic pain. She had galactorrhoea which might have been a side effect from the Duloxetine she was taking and the initial blood test showed a raised Prolactin that changed to a normal Prolactin later on and there was a normal MRI pituitary scan. Thyroid Function was normal. However, the 9 o'clock Cortisol was below normal (170 nmol/L; N: 200-500) and this was the reason for the request a Glucagon Stimulation Test to see if there was any underlying deficiency of Cortisol or Growth hormone.

This is a less reliable test of somatotroph and corticotroph function than the Insulin Tolerance Test (ITT) but much safer. It is an excellent alternative in patients who cannot tolerate hypoglycaemia because of epilepsy, ischaemic heart disease or hypopituitarism. The false negative rate for cortisol response is 30%. Only 4-8 % of normals do not show an adequate rise in GH: this is usually in patients over 50.

Table 1: Glucagon Stimulation Test

Glucagon injection 1mg I/M Time	GH (ug/L)	Cortisol (nmol/L)	Plasma Glucose (mmol/L)
9.00	2.3	134	4.7
11.15	0.2	235	5.9
11.45	2.1	274	4.2
12.15	2.7	286	3.2
12.45	0.6	278	3.4
13.15 14.45	0.1 <0.1	209 217	4.0 4.4

Interpretation: For the Glucagon Stimulation test to be valid the blood glucose is expected to drop to 3.33 mmol/l – 3.44 mmol/L or 60-62 mg/dl (initial drop followed by a rise), the cut off for GH is 3 ug /L, Peak Cortisol is expected to be >440 nmol/L. Cortisol secretion during a Glucagon Stimulation Test is related directly to the pharmacological and stress effects of glucagon rather than depending on a specific drop in blood sugar. On the other hand, optimal GH release is strongly linked to reaching an adequate blood glucose nadir below 3.33 mmol/L

The following tests were carried out as there was a hint of Cortisol Deficiency and +/- Growth Hormone Deficiency (GH reached nearly 3 or 2.7ug/L when the Plasma Glucose was 3.2 mmol/L)

IGF-1 (Insulin like Growth Factor-1) was 58 ng/ml (N: 94- 252); IGF-1 is the primary mediator of growth hormone action, and serum IGF-1 measurement serves as the key screening test for growth hormone disorders. However, nutritional interventions should be the first-line approach before considering Growth Hormone replacement therapy in most cases of low IGF-1 (as IGF-1 is a sensitive marker for nutritional status). In this patient it normalized later. The other three IGF-1 results were normal. They were as follows: 102 ng/ml (N: 94-252) in 2015 and in later years 94.8ng/ml (N: 44.7-216- range changed) and 113 ng/ml (44.7-216)

Table 2: Short Synacthen Test

Cortisol (nmol/L) **0 hr expected > 170-200 nmol/L; after Synacthen test rise is expected to be > 200 nmol/L on top of the base line level**	**0 hr** **166**	**30 mins after 250 mcg of Synacthen I/M** **445**	**60 mins after 250 mcg of Synacthen** **485**
ACTH ng/L (N: 0-46)	12		

Interpretation: The conclusion was Isolated ACTH Deficiency (in Primary Adrenal deficiency or Addison's disease ACTH is supposed to rise with low Cortisol; whereas low to normal ACTH with Low Cortisol is suggestive of ACTH deficiency.

For her isolated ACTH Deficiency, she was commenced on Hydrocortisone 5mg orally twice and remained stable on that.

MRI of head and Pituitary was repeated in 2017 and compared to the one in 2015

Multi-sequential Non enhanced MRI of the Brain was performed. Findings: Comparison made with MRI done in 2015. The right parietal periventricular white matter lesion, axial flair was slightly larger with hyperintense rim compared to the previous scan. The remaining frontoparietal white matter focal T2 high signal intensities are unchanged compared to the previous scan. No interval new brain lesion. No acute abnormality on DWI. No hydrocephalus was identified. Impression: MR features of demyelinating disease.

The patient was referred to a Neurologist and Multiple Sclerosis was ruled out after various investigations.

Later in 2022, the patient had a repeat MRI of the pituitary gland without intravenous contrast. Findings and conclusion: No focal pituitary lesion. The suprasellar and parasellar structures were normal. A few bilateral frontoparietal white matter T2 high signal foci unchanged compared to the MRI done in December 2017. No interval new lesion.

In the year 2017, the patient for pain abdomen had a CT abdomen and pelvis, which picked up a left adrenal lesion- this was followed by an adrenal washout scan

Report: Left adrenal lesion 1.5 cm, with density (Hounsfield units) and absolute washout (>60%) and relative washout (>40%) were consistent with a benign adenoma. The Functional tests were carried out for the left adrenal Incidentaloma (benign tumour picked up incidentally). They were as follows:

Table 3: Functional Test results for adrenal tumour

Plasma Metanephrines **(N: <0.33 nmol/L)**	**Plasma Normetanephrines** **(N: <1.07nmol/L)**	**Aldosterone** **(N: <630pmol/L** **Renin (N: 0.3-2.2 nmol/L/hr)**	**Aldosterone Renin ratio** **(N: <1020)**	**Morning Cortisol (N: 200-500 nmol/L)**	**Free Androgen Index** **(N: <4.6)**	**Female Testosterone** **(N: <1.6 nmol/L)**	**Androstenedione** **N: < 6.0 nmol/L}**	**IgF-1** **GH** **(done as extra tests)**
0.17	0.60	Aldosterone:289 Renin:0.4	723	147	0.88	0.5	<1.0	IGF1:113 ng/ml (N); GH: 2.3 ug/L

Interpretation: The adrenal adenoma is non- secretory.

Also, IGF-1 which is a measure of GH deficiency was shown to be normal.

The patient therefore was diagnosed with: Isolated ACTH deficiency, Left adrenal adenoma (1.5 cm on CT scan in 2017/18) and Myalgic Encephalomyelitis (chronic fatigue syndrome).

She was maintained on Hydrocortisone 5mg twice daily

In 2024, the patient underwent a Day Cortisol Profile at PIU (Planned Investigation unit).

Table 4: Result of Day Cortisol Profile

Time	**9.00**	**10.05**	**12.05**	**14.05**	**16.45**
Cortisol (N: 200-500 nmol/L)	170	856 (after taking morning Hydrocortisone)	394 (took the second tablet of Hydrocortisone)	183	123
ACTH (N: 0-46 ng/L)	35				

Action: The plan was to increase her Hydrocortisone to 5mg on waking, 5mg at 2pm and 5mg at 5pm.

The Day Cortisol Profile was repeated in December 2025

Table 5: Day Cortisol Profile

Time	**8.30**	**9.30**	**11.30**	**13,30**	**16.45**
Cortisol (N: 200-500 nmol/L)	92	438 (after 1st dose of Hydrocortisone)	263	458 (after 2nd dose)	567 (after 3rd dose at 16.00)
ACTH (N: 0-46 nmol/L)	14				

Action: To maintain the patient on Hydrocortisone 5 mg thrice daily.

When I last spoke to the patient in 2026, the patient was continuing with: Hydrocortisone 5mg orally thrice daily. Vitamin D with Calcium tablets (for bone protection), Omeprazole (as proton pump inhibitor) and artificial eye drops and artificial saliva as the patient had dry eyes and dry mouth.

3 DISCUSSION

When a patient presents with lethargy and weight loss, even if the patient has Fibromyalgia or CFS/ME, it is worth doing tests for Cortisol deficiency in the form of Morning Cortisol or SST with a base line ACTH. Low Cortisol and raised ACTH favour Addison's disease or Primary Adrenal Deficiency where a low/normal ACTH in the presence of low Cortisol will favour ACTH deficiency or secondary hypoadrenalism. This will require evaluating the remaining Pituitary function in the form of Prolactin, Thyroid Function Tests, IGF-1, Gonadotrophins and doing MRI scan of Pituitary. However, an ITT or Glucagon Stimulation test may also be necessary, to begin with, in evaluating the Hypothalamo-Pituitary- Adrenal Axis function. Along with ACTH deficiency, our patient initially could have had partial GH deficiency (however IGF-1 was low on one occasion, the other three were normal). The patient was never treated with GH replacement. It is required to diagnose Adrenal deficiency- Primary (Addison's disease) or Secondary (ACTH deficiency) early because of the risk of the patient developing Adrenal Crisis.

Adrenal Incidentaloma is rare at the age of around 50 years and is usually benign as was in our case. The benign criteria include a size of <4cm, density on non-contrast scan < 10 Hounsfield units (10-20 HU also considered benign with size < 4cm), an adrenal absolute washout of >60% and relative washout > 40% on contrast scan. The functional tests include Plasma or Urine Metanephrines and Normetanephrines (to look for Pheochromocytoma), Aldosterone and Renin particularly if the serum Potassium is low (to look for Primary Hyperaldosteronism/Conn's syndrome), measurement of serum DHEA-S, androstenedione, 17-hydroxyprogesterone, 11-deoxycortisol, as well as testosterone in women and oestradiol in men and postmenopausal women can give clear indication of the adrenocortical nature of the adrenal mass (point towards adrenocortical Carcinoma) and Overnight Dexamethasone suppression test to rule out autonomous Cortisol secretion (4-6). This was not done in our case as the patient had Cortisol deficiency

Our patient had two uncommon co-existing conditions- Isolated ACTH deficiency and left adrenal non-functional Incidentaloma. Literature Review shows: An adrenal incidentaloma co-existing with isolated ACTH deficiency has been reported as a rare clinical condition where an adrenal mass secreted mild, autonomous cortisol (MACS), while the pituitary gland failed to properly produce ACTH (7). But an adrenal non -functional (non-secretary) incidentaloma at middle age in a woman with ACTH deficiency is very rare and unique, perhaps not reported before.

4 CONCLUSION

Our patient was put on Hydrocortisone after being diagnosed with ACTH deficiency early following presentation to the Endocrine Clinic. She also has been warned of the sick day rules, informed of carrying a steroid card, medic alarm bracelet, hydration salts and hydrocortisone injections and has been taught the technique to self -inject in case of an impending emergency adrenal crisis. With regards to the adrenal incidentaloma, she has been re-assured. This article aims to help the society, including the Non-Endocrine Doctors in understanding that patients with increasing tiredness, lethargy, loss of appetite and loss of weight may need investigation by an Endocrinologist to rule out Cortisol deficiency (primary or secondary) and also that patients having an adrenal incidentaloma picked up on CT Thorax, Abdomen and Pelvis, done for diagnosing another pathology, should be referred for further Endocrine Investigations including functional assessment.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Consent of the Patient was taken for submission of the article for publication

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