A Peculiar Case of a Dog Bite

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INTRODUCTION

We present a case of ectopic-ACTH syndrome, a rare cause of Cushing’s syndrome, where initial presentation of dog bite proved to be misleading and when a diagnosis of Cushing’s syndrome was made, despite extensive diagnostic procedures, finding the source of ACTH secretion, was challenging.

PRESENTATION

59-year-old male, ex-borry driver and a current smoker presented to Emergency Assessment Unit (EAU) in April 2012:
- Reported history of generalised facial and ankle oedema since a dog bite 6 weeks back, for which had received penicillin.
- Treated as angioedema (Prednisolone and antihistamine) and discharged.

PMH:
- November 2011 - Investigations (OGD & Colonoscopy) organised to investigate abdominal pain & altered bowel but patient failed to attend appointments.
- 2005 - Lung lesion on CT Thorax – Benign lung pulyp on histology

Short EAU assessments (5-between 08/05/2012 & 11/06/12) with progressive symptoms
- Worsening anasarca
- Breathlessness on exertion
- Noted to have mild hypertension, hypokalaemia, few high random blood glucose levels

Differential diagnosis of Nephrotic syndrome; Congestive Heart Failure; Comt’s syndrome and Vasculitis considered and ruled out by doing relevant investigations
- Also, recorded on couple of occasions to have “Cushingoid facies”

Furosemide, Spiranolactone initiated and referred to Endocrine outpatient clinic for further investigations.

Readmitted 15/06/2012 with
- Definite cushingoid appearance, new established diagnosis of diabetes & hypertension and persistent hypokalaemia
- Started on Metformin & Insulin
- Urgent inpatient investigations for Cushing’s syndrome organised.

INITIAL ENDOCRINE INVESTIGATIONS

- Low dose dexamethasone suppression test

<table>
<thead>
<tr>
<th>Cortisol (in nmol/l)</th>
<th>Baseline</th>
<th>48 hrs Post-Dex</th>
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<tbody>
<tr>
<td>Cortisol</td>
<td>2203</td>
<td>2318</td>
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<tr>
<td>ACTH (ng/l)</td>
<td>-</td>
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Given short history of progressive symptoms-

Ectopic ACTH-syndrome suspected

- ACTH-precurors (POMC): 610 p mol/L (N<100)
- ACTH (different lab)=13 ng/l (<50)

OTHER INVESTIGATIONS

- TFT and Prolactin - normal
- IGF-1 (<25 mcg/l)
- LH, FSH - low
- MRI pituitary – normal
- Calcium - normal
- High PTH (919 ng/l)
- Low Vitamin D levels (6.9 ug/l)
- Urinary 5-HIAA - normal
- Plasma metanephrine - normal

INVESTIGATIONS- IMAGING & HISTOLOGY

CT scan and MRI abdomen
- Metastatic liver lesions; bilateral adrenal gland enlargements/multiple nodules; no pancreatic lesions
- Lung lesion on CT Thorax
- Tumours causing the ACTH precursors in the ACTH assay or that a dependent Cushing's syndrome is suspected, but ACTH is not in the diagnostic range, and in fact as dexamethasone increase tumour secretion of glucocorticoids increase tumour secretion of ACTH.

SEARCH FOR THE PRIMARY

LIVER BIOPSY:

Metastatic neuroendocrine tumour (Ki67 25%); Grade 3 CDX2 positive – suggested primary sites:
1. Stomach
2. Small intestine
3. Possibly pancreas

NM OCTREOTIDE SCAN:

Findings not typical for somatostatin receptor +ve disease

UPPER GI ENDOSCOPY:

Candidiasis; No lesion

FASTING GUT HORMONES – ELEVATED

CART = 469 p mol/L (<85)
Chromogranin A = 247 p mol/L (<60)
Chromogranin B = 216 p mol/L (<150)

IMAGING & HISTOLOGY

PET Scan:

High metabolic activity within the tail of pancreas, bilateral adrenal lesions and liver suspicious of malignancy

TREATMENT

- Bilateral adrenalectomy; splenectomy; tail of pancreas resection
- Transarterial chemoembolisation being considered

REFERENCES

1. Wechsberg BL, Mundloska RB et al; Ectopic ACTH syndrome. Endocrine Reviews 15(7):727-787
5. White A, Rig DW et al; Cushing’s syndrome due to phaeochromocytoma secreting the precursors of adrenocorticotropin. J Clin Endocrinol Metabol 90: 457-471

DISCUSSION

Ectopic ACTH syndrome caused by Pancreatic Neuroendocrine tumour (NET) secreting ACTH precursors

POST-OPERATIVE

- On Hydrocortisone and Fludrocortisone
- Received appropriate vaccinations; long-term antibiotics prophylaxis
- Off metformin, insulin, anti-hypertensive agents, diuretics
- Repeat CT scan showed increasing size of liver metastatic lesions- transarterial chemoembolisation being considered.

CONCLUSION

Short progressive history, association of new diagnosis of hypertension and glucose intolerance, unexplained hypokalaemia should raise the index of suspicion for ectopic ACTH-precursor syndrome.

When an ectopic ACTH-dependent Cushing’s syndrome is suspected, but ACTH is not in the diagnostic range, and in fact as dexamethasone increase tumour secretion of glucocorticoids increase tumour secretion of ACTH. This is important to remember when interpreting dexamethasone suppression tests.