An unusual presentation of 17alpha hydroxylase deficiency

Authors: Florian Wernig[1], Maura Moriarty[1], Jeannie Todd[1], Francis Lam[1], Gill Rumsby[1]
1 Dept of Endocrinology, Imperial College Healthcare NHS Trust, London

Case History

- 26 year old Afghani female
- Parents - consanguineous relationship
- Family Hx otherwise unremarkable

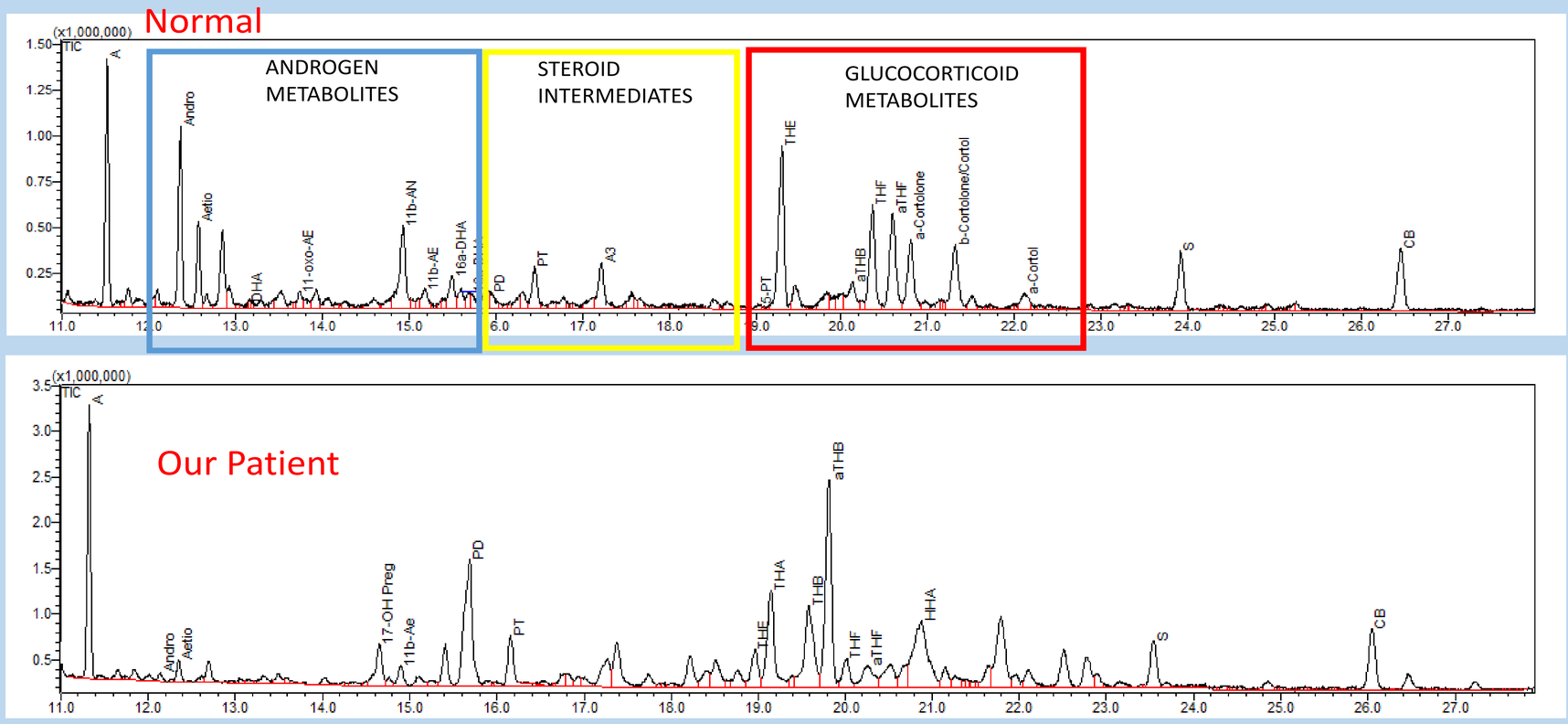
- Primary amennorhoea age 14
  Normal breast development
  Reduced body hair

- Lost to medical follow up
- Spontaneous menarche age 18
  Regular menstrual cycle

- Represented for investigation of 3 year hx
  Primary Infertility age 24

Investigations:	
Blood Pressure	Normal
U&E	Unremarkable
Cortisol	35 nmol/L
17-OHP	2.1 nmol/L (< 9.6)
Short Synacthen Test	Peak Cortisol 139 nmol /L No rise in 17-OHP
DHEAS	<0.4 µmol/L (0.7 – 11.5)
Testosterone	<0.5 nmol/L (<2.0)
Oestradiol	325 pmol/L
17-OHP	2.1 nmol/L (< 9.6)
LH	5.4 IU/L
FSH	6.7 IU/L
Renin	2.3 nmol/L (0.5 – 3.1)
Aldosterone	<60 pmol/L (90 – 700)

24 hour Urine Steroid Profile



Urine Steroid Profile Result

- Decreased cortisol metabolites
- Raised Corticosterone and progesterone
- Increase in 17-hydroxyprogesterone metabolites

Suggestive of partial 17 hydroxylase deficiency and 17,20 lyase deficiency

Aldosterone metabolites absent
- Raises added possibility of aldosterone synthase deficiency

Clinical Course

Commenced on prednisolone 3mg daily
- No change in sense of well being

IVF commenced
- Previous attempts at induced ovulation unsuccessful
- Ovarian stimulation (with gonadotrophins) and oocyte retrieval
- First cycle unsuccessful

- Genetic testing showed confirmed a 3bp deletion (p.Phe54del)This is reported to have approx. 37% of normal activity of 17 hydroxylase
- Activity of 17,20 lyase is estimated at 8% of normal

- Aldosterone synthase genetic testing was negative

17 alpha hydroxylase deficiency accounts for less than 1% of all patients diagnosed with congenital adrenal hyperplasia. Almost 100 mutations in the CYP17A1 gene causing 17-hydroxylase/17,20-lyase deficiency (17OHD) have been described. CYP17A1 is expressed in both the adrenals and gonads. Hallmarks of 17OHD include hypertension, hypokalaemia, primary amenorrhoea and absence of secondary sexual characteristics. Clinical characteristics vary depending on the activity levels of 17 hydroxylase. Most patients with 17OHD remain infertile.

Given the low estimated 17,20 lyase activity levels a more severe clinical presentation would have been expected. The urine steroid profile suggests an additional aldosterone synthase deficiency in this patient and is the most likely reason for the absence of the classical features of hypertension and hypokalaemia. This has not been identified on genetic testing but the possibility of an alternative mutation exists.

Discussion:
What, if any, options are available for this lady to assist fertility?
Is there a role for long term steroid replacement? If yes, what is the most appropriate option in her case

References:
Marsh, C.A. and Auchus, R.J., 2014. Fertility in patients with genetic deficiencies of cytochrome P450c17 (CYP17A1): combined 17-hydroxylase/17, 20-lyase deficiency and isolated 17, 20-lyase deficiency. *Fertility and sterility*, *101*(2), pp.317-322.

BES2016 1--EP
Adrenal and steroids
Florian Wernig
DOI: 10.3252/pso.eu.BES2016.2016
Poster presented at: SfE BES 2016