

A case of very late onset Congenital Adrenal Hyperplasia?

S.J. Dickinson., T.A. Howlett & M.J. Levy

Department of Endocrinology, University Hospitals of Leicester NHS Trust

A 46 year old lady presented with a 4 year history of progressive facial hirsutism and increasingly irregular periods which stopped at the age of 44. She had no hallmarks of insulin resistance or polycystic ovarian syndrome, having never been overweight with regular periods following her menarche at the age of 12, having been on the oral contraceptive pill between the ages of 16 and 25. She had two children at the age of 18 and 24 and unsuccessful IVF at 36. There was no family history of diabetes and the only past medical history was Gilbert's syndrome. On examination she had moderately severe hirsutism on the face and chin and was not cushingoid in appearance. Her blood pressure was 136/83 and her BMI 23.3kg/m². The remainder of the examination was normal.

Tests showed normal electrolytes, elevated serum testosterone of 4.8 nmol/L (0.2-3.0) with a normal SHBG of 62 nmol/l (30-75), and elevated gonadotrophins (LH 47 iU/l, FSH 75 iU/l). Her thyroid function was normal. She had an elevated androstenedione level of >35 nmol/l (0.7-10.8) and 17-Hydroxyprogesterone (17OHP) of 41.9 nmol/l (1-10). On subsequent questioning she reported that she was a tall child and volunteered that she felt she always had a small vaginal introitus with clitoromegaly and a persistently very elevated libido.

Subsequent investigations showed an ACTH level of 20 ng/l (0-50). A low dose dexamethasone suppression test showed complete suppression of testosterone, androstenedione, 17-OHP and cortisol. A subsequent synacthen test showed a basal cortisol of 420 nmol/l rising to 533 nmol/l at 30 minutes, although the 17OHP response was not measured. Imaging of the ovaries and adrenals with ultrasound and CT showed no significant abnormalities.

Because of the suppressibility of 17OHP and androstenedione a diagnosis of very late congenital adrenal hyperplasia (CAH) was considered and the patient was started on reverse circadian prednisolone. Six weeks after starting treatment her androstenedione and 17OHP fell to within normal limits and she reported slowing in her hair growth and a reduction in her libido. Interestingly she reported significant hot flushes and apparent menopausal symptoms since starting steroids which she had not previously. Subsequent genotyping has shown a mutation in CYP21 (g.655A/C>G and g.1683G>T) compatible with non-classical late onset CAH.

Although the presenting history and initial testosterone level were suspicious of an adrenal tumour, the final diagnosis was CAH. The interesting aspects of this case are the late age of presentation and the fact that clinical presentation only occurred after cessation of periods. It is hypothesised that the fall in oestrogen levels at menopause may have unmasked previously undiagnosed CAH. The commencement of menopausal symptoms only after steroid suppression of androgens may also suggest that aromatisation of previously high androgen levels to oestrogen had hitherto protected her from menopausal symptoms. We would hope for a discussion about other possible differential diagnoses and whether there is a need for ovarian / adrenal venous sampling or whether the diagnosis of CAH is secure.