Solving a hairy problem

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Case history:
A 72 year old woman presented to our endocrine clinic with a 4 year history of hirsutism and acne. Previous investigations had revealed a raised testosterone level. This had been managed with cyproterone acetate which was discontinued after she developed a cerebral venous sinus thrombosis.

Her past medical history included breast cancer diagnosed in 1996, hypertension and a hysterectomy in 1998 for menorrhagia. She was not on medications commonly implicated in the development of hirsutism.

On examination she had thick hairs distributed over her face, shoulders and abdomen. In addition acne was noted over her back. There were neither pigmented striae nor any other features of Cushing’s. There were no clinical features of virilisation.

Investigation and methods:
Blood results revealed a persistently raised testosterone between 5.7 and 9nmol/l (NR 0.0 to 2.7). Her LH and FSH were 38.9 and 46.5 IU/L respectively. Her dihydrotestosterone was 1.27nmol/l (NR 0.0 to 1.0) and androstenedione was 5.5nmol/l (NR 4.0 to 10.2). A low dose dexamethasone suppression test (LDDST) demonstrated a cortisol level suppressed below 30 nmol/l at 48 hours with an insuppressible testosterone suggesting that the adrenals were not the cause of the patient’s hyperandrogenaemia. Her 17 hydroxyprogesterone (17-OHP) rose from 7.2 to 18.1nmol/l during a short synacthen test excluding congenital adrenal hyperplasia (CAH). An MRI scan of her pelvis demonstrated bilaterally small ovaries consistent with the menopause. To determine whether her ovaries were the source of her raised androgens we performed adrenal/ovarian vein sampling. All four veins were successfully catheterised and venous sampling revealed testosterone levels greater than 52.1 nmol/l her right ovary and 45.9 nmol/l in her left ovarian vein. This was compared to a testosterone of 5.5nmol/l in her right common iliac vein which strongly supports that the source of the raised androgens arose from both ovaries.

Results and treatment:
The patient went on to have a bilateral oophorectomy performed in July 2011. Her ovaries measured 25 x 12 x 10mm and 32 x 25 x 15 mm. The histology revealed bilateral stromal hyperthecosis. Post-operatively, the patient’s testosterone has improved to within normal limits (0.7nmol/l). At her most recent follow up she described an improvement in her hirsutism.

Conclusions and points of discussion:
Post menopausal hirsutism is common. The differential diagnosis includes polycystic ovarian syndrome (PCOS), Cushing’s syndrome, androgen secreting adrenal/ovarian tumours, CAH and hyperthecosis. Whilst a detailed history and biochemical testing is useful in excluding PCOS, Cushing’s and CAH, venous sampling is required to confirm either adrenal or ovarian sources of raised androgens. Plain imaging is a poor modality to localise ovarian tumours as
they are often undetected. It should also be noted that a LDDST has a 12% false negative rate at excluding adrenal androgen secreting tumours. Unfortunately venous sampling remains a technically difficult procedure and is very much operator dependent. A previous audit performed at St Bartholomew’s hospital demonstrated that in only 10 out of 32 venous sampling procedures were all four veins correctly catheterised. In our case successful venous catheterisation increased our confidence of an ovarian source of androgen secretion prior to exposing our patient to the risks of surgery.

The histology of our patient’s ovaries revealed an unusual cause for raised androgen secretion. Ovarian hyperthecosis is defined as the presence of luteinised stromal cells at a distance from the follicles. Whilst this condition is implicated commonly as a cause of hirsutism in premenopausal women it remains a rare cause after the menopause.