Ovarian steroid cell tumour: In search of a rare cause of hyperandrogenism despite uncertainty and surgical risk

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Introduction

Ovarian steroid cell tumours account for <0.1% of ovarian tumours.[1,2] They can be further differentiated into stromal luteomas, Leydig cell tumours and steroid cell tumours not otherwise specified (NOS).[2] These lesions typically remain smaller than can be reliably detected on ultrasound, CT or MRI, despite still producing clinically significant hyperandrogenic features. In patients with ovarian steroid cell tumours, virilisation is sudden, progressive, and understandably distressing. Between 25-45% of steroid cell tumours are associated with malignancy[3] and there is no specific non-invasive test to diagnose this condition. Adrenal tumours can also present in a similar fashion.[4] Diagnosis, therefore, usually follows elective bilateral oophorectomy.[5] Clinical uncertainty, medical and surgical risks may make decision to proceed with oophorectomy challenging and therefore could delay diagnosis and management.

Case Presentation

A 64-year-old woman was referred with a 4-year history of progressive scalp alopecia and hirsutism. She had a history of 4 vaginal births, 1 caesarean section, negative regular cervical screening and an unremarkable menopause at 52 years of age. She denied post-menopausal bleeding or constitutional symptoms. She preferred to manage her hirsutism with daily plucking. Additionally, she had autosomal dominant polycystic kidney disease and had required peritoneal dialysis prior to a right pelvic renal transplant and subsequent transperitoneal bilateral nephrectomies of native kidneys due to sepsis. Medical history was also significant for hypertension. She did not have insulin resistance nor diabetes. Regular medications included mycophenolate, tacrolimus, prednisone, Bactrim and four different antihypertensives.

Examination was significant for clitoromegaly. Her hairline had receded and there was hair thinning, particularly over the crown. Biochemically, she presented with DHEAS levels of 1.2-1.5umol/L, and testosterone levels of 5.1-5.7nmol/L. Dexamethasone suppression testing only showed a 25.5% reduction in testosterone (Table 1). Baseline creatinine remained in the hundreds.

Table 1: Chemical Pathology Hormone Investigations

Hormone Investigations	10/5/19	5/8/19 Pre-Dex[1]	7/8/19 Post-Dex[1]	26/8/20 Post-op[2]	Reference Ranges
Prolactin (mU/L)	204				58-416
FSH (U/L)		37	39	36	25-135
LH (U/L)		39	36	35	10-100
Testosterone (nmol/L)	5.7	5.1	3.8	<0.1	0.5-2.8
SHBG (nmol/L)	24	24	24	26	40-90
17-HPR (nmol/L)		1.2	0.1		<3.0
DHEAS (umol/L)	1.5	1.2	1.6	<0.2	0.5-5.0

[1] Pre and post 2-day low dose dexamethasone (0.5mg 6-hourly) suppression test.
[2] 13 days post laparoscopic BSO and Hysteroscopy D&C.

In September 2019, CT scanning showed an atrophic and irregular left adrenal. However, Nephrology, Endocrinology and Radiology Specialist opinions were that this was secondary to previous peri-operative adrenal haemorrhage and not consistent with an adrenal adenoma. Ultrasound showed 2.6mL right and 1.5mL left ovaries without masses and an endometrial thickness of 4.0mm. Repeat ultrasound in 2020 similarly showed unremarkable ovaries, however, also showed an endometrial thickness of 7.3mm.

An opinion from the advanced laparoscopic surgical team was sought. Given the surgical history and risk of adhesions, opinion was sought and a recommendation of laparoscopic bilateral salpingo-oophorectomy (BSO) and hysteroscopy, dilatation and curettage, over a hysterectomy and BSO, was made. Hysteroscopic findings were of an atrophic appearing endometrium. Laparoscopic exploration revealed an atypical left ovary with a patchy pearlescent cortex (Figure 1). Histological examination revealed a 10mm ovarian steroid cell tumour of the left ovary without malignancy (Figure 2) . Washings were negative for malignancy. Androgen levels reduced significantly by day 13. Hyperandrogenic features improved over a matter of weeks. She reported only managing facial hair once a week by her six week review.

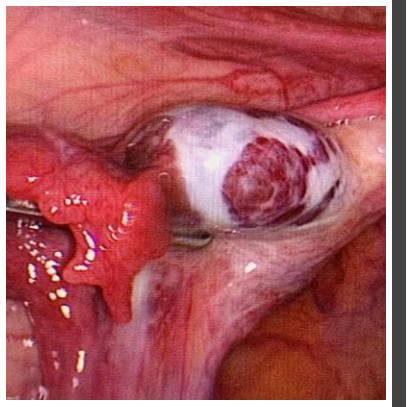

Figure 1: (Left) Atypical appearing and affected left ovary

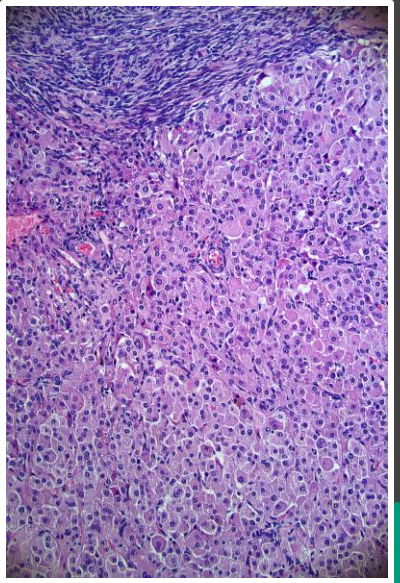

Figure 2: Sheets of monotonous steroid producing cells with uniformly eosinophilic granular cytoplasm form a smooth boundary with the darker spindled ovarian stroma. (haematoxilyn and eosin, x 400 (objective x 40))

Discussion

Sudden hyperandrogenism in postmenopausal women is rare. Ovarian hyperthecosis or androgen-secreting tumours are the most likely causes.[6] Ovarian hyperthecosis was not likely here; given suddenness, absence of insulin resistance and normal ovarian volumes.[6,7] Differentiating between adrenal and ovarian sources of androgen excess is challenging. The CT scan report may have directed suspicion towards the adrenals. Dexamethasone suppression testing show high sensitivity, but limited specificity, for the differentiation.[5] Overall, the literature suggests the combination of normal DHEAS, testosterone twice the upper limit of normal and <40% suppression with low-dose dexamethasone, is not only consistent with an androgen-secreting neoplasm, butthat it is most likely ovarian.[1,2,4,5] For diagnosis, treatment and risk of ovarian malignancy, bilateral salpingo-oophorectomy is indicated.[3,5,8] GnRH agonists have been demonstrated as a potential treatment for virilisation in poor surgical candidates and without needing to delineate the source of androgen excess prior.[4] Given this patient's surgical history and ultrasonographic features of endometrial hyperplasia, Nephrology and Advanced Laparoscopic Gynaecology opinions were gathered. Laparoscopic BSO and hysteroscopy D&C were performed by an Advanced Laparoscopic surgeon, allowing for surgical management of the most likely cause of androgen excess, whilst further characterising endometrial cancer risk before considering need for hysterectomy. BSO was successful and suspicion of endometrial malignancy was lowered. Hysterectomy has not been recommended. Histological findings of a 10mm left ovarian steroid cell tumour (NOS) without malignancy, confirmed the ovary as the cause, further supported by sudden improvement in symptoms and hormonal investigations.[4,5] Long-term gynaecology follow up will not be required.

Conclusion

Androgen secreting tumours of the ovary are rare, however, are important causes of sudden and progressive virilisation in women. Without radiological evidence of a specific lesion, uncertainty of the origins of androgen excess may persist. This case highlights the utility of serum testosterone, DHEAS and dexamethasone suppression tests in differentiating between ovarian and adrenal causes to support targeted operative intervention, even when significant surgical risk exists.

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