



# Diagnosis of Leydig Cell Tumour following presentation with virilization and ovarian hyperthecosis

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## BACKGROUND

Leydig cell ovarian tumour is a rare sex cord-gonadal stromal tumour which constitutes less than 0.5% of ovarian tumours<sup>1</sup>. These cancers appear at all ages but most of the cases concern women in the perimenopause. Leydig cell tumours are difficult to diagnose as they are often difficult to detect despite multiple different imaging studies<sup>2</sup>.

## CASE

Our patient was 54 years old at the time of presentation and working as a specialist nurse. She had no relevant gynaecological history. Her last period was 3-years ago when she was developing symptoms of hirsutism. She had undergone a bariatric gastric sleeve surgery in October 2020 with a BMI of 31.4 at referral. Her medical history included Type 2 diabetes and hypertension.

She had been seen by the endocrine team 8 months prior to referral to the Gynaecology team and diagnosed 3 years ago with ovarian hyperthecosis after a full work up to exclude ovarian and adrenal causes when presenting with symptoms of virilisation.

She was commenced on GNRH analogue therapy Zoladex 10.8mg every three months from March 2020 which did not suppress testosterone levels significantly. She continued to experience male pattern hair growth and heightened sex drive. On general examination, there was evidence of hair thinning in the scalp area. Her abdomen showed evidence of increased hair growth despite using topical creams and epilation to keep under control.

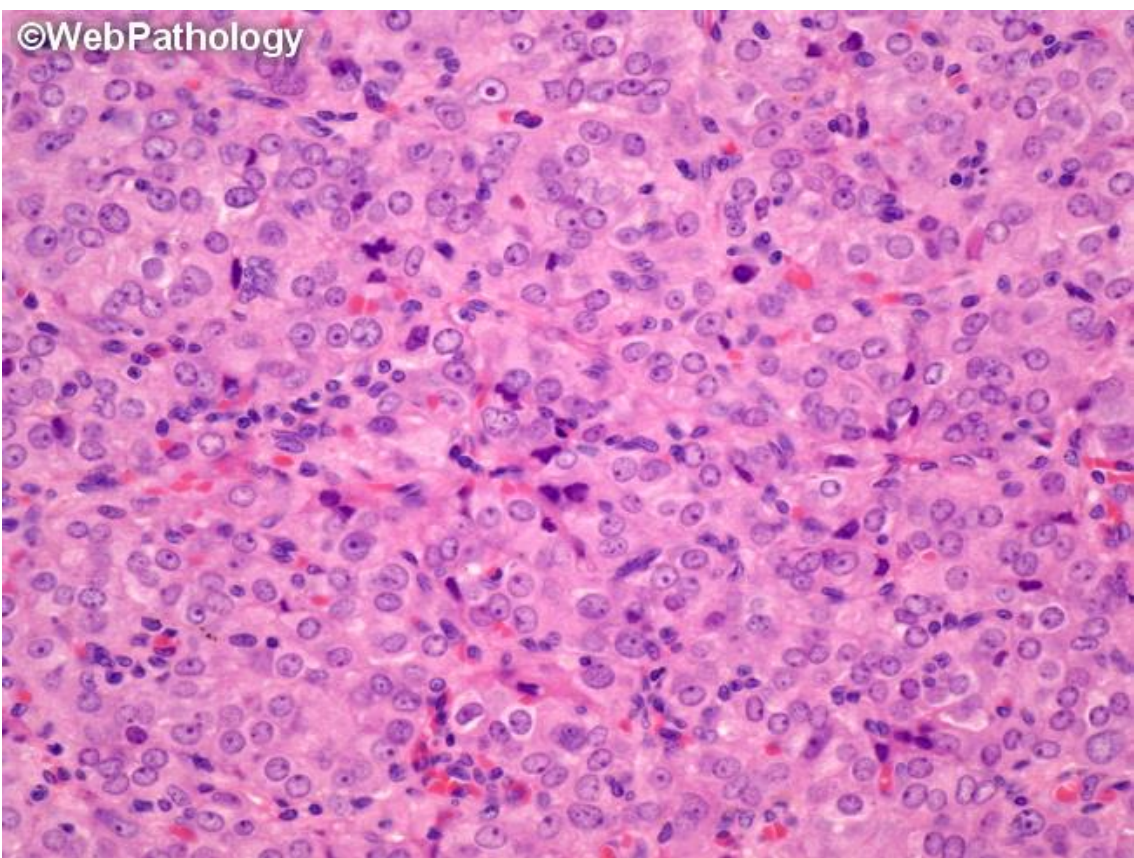
A transvaginal scan showed a retroverted uterus. Ovaries were seen with calcifications bilaterally. There were no evidence of any cystic changes and Doppler signals were negative. CT abdomen confirmed no adnexal masses and no significant abdominal or pelvic lymphadenopathy. MRI scanning was also negative. There was no identified ovarian abnormality on any imaging modality.

Following appropriate counselling, the patient opted to have laparoscopic bilateral salpingo-oophorectomy. Despite a challenging laparoscopy due to her body habitus and dense intraabdominal adhesions the procedure was uneventful, and she was discharged home as a day case. One of the ovaries showed a 12mm un-encapsulated tumour. There was no obvious nuclear atypia or mitosis, and this was confirmed as benign. Further immunostaining studies were undertaken, and a supplementary report confirmed the presence of Leydig cell tumour.

## INVESTIGATIONS

|                                           | 11/10/19 | 25/11/19 | 6/2/20<br>Pre-<br>zoladex | 5/5/20<br>Post-<br>zoladex | 18/08/21 | 07/12/21 | Laparoscopic bilateral Salpingoophorectomy<br>13/10/22 | 02/12/22 |
|-------------------------------------------|----------|----------|---------------------------|----------------------------|----------|----------|--------------------------------------------------------|----------|
| Androstenedione (normal range 0-6 nmol/L) | 2        | 1.5      |                           |                            | 1.2      | 1.7      |                                                        | 1.1      |
| DHEAS (normal range 1-12 umol/L)          | 2.7      | 1.6      |                           |                            | 1.8      | 1.9      |                                                        |          |
| Estradiol (normal range 72-529pmol/L)     | 903      |          | 146                       |                            | 53       |          |                                                        |          |
| FSH (normal range 3-10 u/L)               | 7.7      |          | 13.4                      |                            | 3        |          |                                                        |          |
| LH (normal range 2-13 u/L)                | 14.1     |          | 14.2                      |                            | <0.1     | 0.1      |                                                        |          |
| Testosterone (normal range <1.6nmol/L)    | 10.3     | 11.9     | 8.4                       | 5.6                        | 6.9      | 8.4      |                                                        | 0.4      |
| Free Androgen index (normal range <4.6)   |          | 49.6     |                           |                            | 15       | 20       |                                                        | 0.8      |

## HISTOLOGY



Leydig cell tumour composed of diffuse sheets of uniform round or polygonal cells with abundant eosinophilic cytoplasm resembling mature Leydig cells. The nuclei are round, uniform, and variably-sized and have prominent central nucleoli. Cytologic atypia is absent and the mitotic activity is not increased. The tumor cells are surrounded by delicate vasculature<sup>4</sup>.

### References:

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## DISCUSSION

Hyperandrogenism refers to the condition in which excessive androgens are found circulating in the female body. Clinical manifestations range from hirsutism and acne to virilization (including androgenic alopecia, voice deepening, clitoral enlargement, breast atrophy, increased muscle mass )and emotional distress

Common causes of hyperandrogenism are polycystic ovarian syndrome, congenital adrenal hyperplasia, Cushing’s syndrome, and ovarian tumours. Presence of virilization in a post menopausal woman increases the possibility of an underlying androgen secreting ovarian or adrenal tumour and work up must actively exclude these.

Androgen secreting ovarian neoplasms are rare and account for 5% of all ovarian tumours. Common androgen secreting ovarian tumours include Leydig cell neoplasm, stromal luteoma, Sertoli-Leydig cell tumour and ovarian hyperthecosis. Most often, women present with virilization, raised testosterone level and bilateral salpingo-oophorectomy being indicated after ruling out adrenal neoplasm.

Leydig cell tumour is a member of the sex cord stromal tumour group of ovarian and testicular cancers arising from Leydig cells. While the tumour can occur at any age, it occurs most often in young adults, mainly in males, usually at 5-10 years of age. Children present with precocious puberty, one third of females develop progressive masculinisation which is preceded by anovulation, oligomenorrhoea, amenorrhoea and defeminisation, acne, hirsutism, deepening voice, clitoromegaly, temporal hair recession and an increase in musculature. Ovarian Leydig cell tumours generally occur in postmenopausal women with virilising symptoms, are almost always unilateral, rarely malignant<sup>3</sup>.

## LEARNING OUTCOMES

Our case reports a rare ovarian tumour, which was not detected on ultrasound scan or CT scan. As symptom control was not achieved with the trial of Zoladex, a surgical approach in the form of bilateral laparoscopic salpingo-oophorectomy was required both for diagnostic and therapeutic purposes.

Therefore, in postmenopausal women with high androgen levels of unknown aetiology, a high index of suspicion to the possibility of such rare ovarian tumours despite negative imaging should prompt clinicians to consider oophorectomy when there is no evidence of adrenal tumour.