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Case Report

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Postmenopausal lady with virilization: Diagnosis of a rare steroid cell tumor of the ovary

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Abstract

64 year old postmenopausal lady presented with features of virilization over last 5 years. Her Total Testosterone level was 22.2 nmol/l (0.52- 2.47 nmol/l) which is very high to be attributed to normal aging. Her past medical history was unremarkable except adequately controlled diabetes mellitus. Her DHEAS level was normal and did not have other hormonal abnormalities. Her transvaginal ultrasound scan showed a left ovarian tumor of 3 X 3 cm in size. She underwent a CECT abdomen and pelvis which also confirmed the left ovarian tumor without any malignant features or metastasis.

Total abdominal hysterectomy and bilateral salphingo - oophorectomy was performed. Histology confirmed left ovarian steroid cell tumour. Her Testosterone level came to the normal range with significant symptomatic improvement over few months.

Therefore, the virilization after menopause should be evaluated clinically and biochemically when necessary to exclude sinister causes like androgen secreting adrenal tumors. Steroid secreting benign tumors of the ovary is also an important cause of post-menopausal virilization. This may be missed during imaging due to the small size , non specific and variable features [1]. However the symptom improvement after identifying and removing this kind of benign tumors would remarkably improve the patient's quality of life.

Case history

64 year old female presented with progressive alopecia for 5 years. She was initially presented to Dermatologist for the treatment of alopecia. She also had other features androgen excess on direct questioning such as hirsutism. She denied masculine build and roughening of voice. She did not have features of Cushing syndrome or hypothyroidism. She was a known patient with Diabetes mellitus and on oral hypoglycemic medication. She was not on any other medication but has received treatment for her alopecia time to time. She is a mother of two children and her menopause was at 52 years of age. She denied any post menopausal complications such as post menopausal bleeding. She did not give a history suggestive of Polycystic ovarian syndrome when she was young. Her mother has had a ovarian carcinoma and father and brother had Diabetes Mellitus. She denied any exposure to topical testosterone.

On Examination, she had severe male pattern balding with increased terminal hairs in androgen dependent areas (upper lip, chin, lower abdomen, upper arm and upper thigh). There was no masculine build but clitoromegaly was present. Her voice was not deep. Her blood pressure was 130/80 mmHg. Abdominal examination was unremarkable. She did not have evidence of Diabetes complications such as food disease.

Management

Patient was referred to the Gynecologist for the excision of the ovarian tumour. She underwent Total abdominal Hysterectomy and bilateral salphingo – oophorectomy and made an uneventful recovery from the surgery. Pathological examination of the gross specimen showed (Figure 2) enlarged left ovary with a lobulated mass of 3 X 3 cm size. Cut surface showed yellow orange colour lobulated mass in the left ovary.

Histology of the tumour confirmed (Figure 3 & 4) a steroid cell tumour of the left ovary. Right ovary, uterus and fallopian tubes were unremarkable. Her post operative investigations got delayed due to the travel restrictions imposed due to the Covid 19 pandemic, to the patient's resident area. She started to experience reduction in hair loss, new hair growth with disappearance of frontal balding. She also experienced thinning of her facial hair. Her post operative 4 month testosterone level was 0.87 nmol/l (0.52 – 2.47) which is within the normal range.

Investigations

Test	Result	Normal range
Serum Testosterone level (Repeated and confirmed)	22.2 nmol/l (643.1 ng/dl)	0.52- 2.47 nmol/l
FSH	125.5mIu/ml	36 – 168 mIU/ml
LH	24.5 mIU/ml	14.4 – 62.2 mIU/ml
TSH	0.64 mIU/L	0.350 – 4.940 mIU/L
FT4	15.75pmol/l	6.44 – 18.02 pmol/l
ODST	38nmol/l	< 50 nmol/l
9 am Prolactin	150.03 mIU/L	73 – 407 mIU/L
DHEAS	75.6 micrograms/dl	35- 430 micrograms/dl
FBS	128 mg/dl	90 – 120 mg/dl
HbA1c	7 %	< 6.5%
Serum Sodium	138 mmol/l	136 – 146mmol/L
Serum Potassium	4.8 mmol/l	3.5 – 5.1 mmol/l

Imaging

Trans vaginal USS	Well demarcated , solid ovarian tumor measuring 2 x 2.9 cm in the right ovary .
CECT abdomen and Pelvis (figure 1)	Well defined , homogenously enhanced , solid soft tissue mass in the left adnexial region (2 x 3 cm size), ovaries not separately identified.

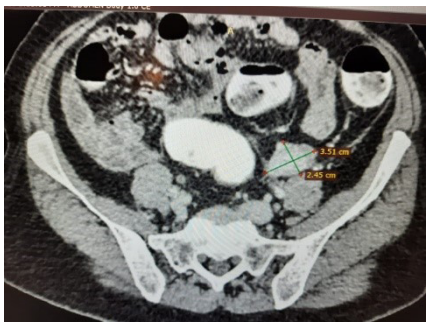

Figure 1: Well defined , homogenously enhanced , solid soft tissue mass in the left adnexial region (2 X 3 cm size), ovaries not separately identified.

Figure 2: Cut surface of the ovary showing yellow color lobulated tumor.

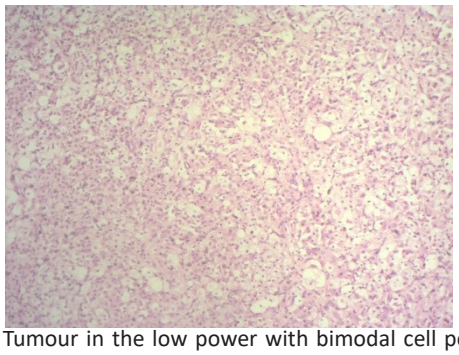

Figure 3: Tumour in the low power with bimodal cell population showing large, round to polyhedral cells with vacuolated cytoplasm as well as smaller cells which had eosinophilic granular cytoplasm. (H & E, X10).

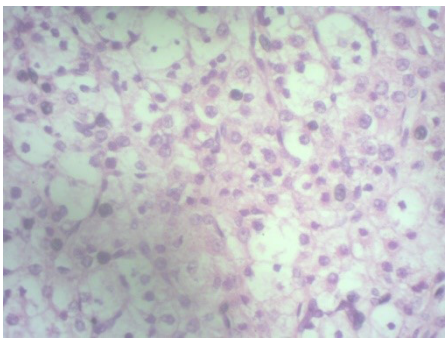

Figure 4: High Power showing polygonal tumor cells with central nuclei, prominent nucleoli and abundant cytoplasm (H &E, 40X).

Discussion

Our patient is case of post menopausal virilization which had a gradual onset over 5 year period. There are wide variety of causes for post menopausal virilization which can be categorized as tumorous and nontumourous. Post menopausal ovary remains hormonally active secreting a significant amount of androgens and comparatively low level of oestrogens [2]. High gonadrotrophins, specially LH, maintain this androgen secretion beside the absence of oestrogen [3]. This imbalance between Androgens and estrogens is further amplified by gradual reduction in SHBG level (increase free androgen index) and insulin resistance (insulin acting as co gonadotrophin). This relative androgen excess may lead to few androgenic symptoms like appearance of few terminal hairs on the face and decrease in body and scalp hair. However the level of Testosterone rarely exceeds 40 ng/dl (1.38 nmol/l) [4]. When this hyperandrogenic features are severe and onset is abrupt with rapid evolution of symptoms, ovarian or adrenal tumour secreting androgens should be suspected. When there is a tumour secreting testosterone, the total testosterone level is much higher (> 100 -140 ng/dl) or >3 folds of the upper limit of normal [5,6].

Non tumorous causes of post menopausal virilization includes, Polycystic ovary syndrome, Congenital adrenal hyperplasia, Ovarian hyperthecosis, Obesity, States of insulin resistance, Endocrinopathies (Cushing's syndrome, Acromegaly) and Iatrogenic causes such as Testosterone/DHEA supplementation, Antiepileptics (valproic acid and oxcarbazepine) and Danazol [5]. Tumourous causes includes Adrenal tumors (Androgen-secreting carcinomas, Androgen-secreting adenomas) and Ovarian tumors (Sertoli Leydig cell tumors, Hilus cell tumors, Granulosa theca cell tumors, Steroid cell tumours, Metastatic neuroendocrine/ gastrointestinal tumors and Cystadenomas) [5,6]. Ovarian steroid cell tumours are very rare functioning sex cord stromal tumours. It comprises <0.1% of all the ovarian tumours [6]. These were previously known as lipoid cell tumours. One third of these tumours are considered to be malignant and peak age of onset is 40 years [6]. However there are only few case reports of post menopausal women and children who had this tumour [7]. Our patient is a postmenopausal lady presented with symptoms of virilization. These tumors are devided into 3 subtypes depending on their cell of origin, stromal luteoma, leydig cell tumour and steroid cell tumour, not otherwise specified (NOS) [8]. Of these subtypes, the steroid cell tumours, NOS account for about 60% of steroid cell tumours [9]. These tumours commonly secrete Androstenidione, α-hydroxyprogesterone, and testosterone [7]. However, 6-23% have estrogenic manifestations such as menorrhagia, [3] postmenopausal bleeding, or even endometrial carcinoma [4]. 56-77% have symptoms of androgenic manifestations, such as hirsutism and virilization including acne, clitoral enlargement, deep voice, and alopecia as in our patient. 25% of these tumors are nonfunctioning and found only incidentally.

Our patient's Testosterone level was repeatedly high and it was in the tumourous range. However the onset of symptoms and the evolution of symptoms were gradual over 5 year period. She had significant frontal balding, increased body and facial hair and mild clitoral enlargement (1.5 cm X 2 cm). She did not have deepening if the voice or masculine habitus. She had Diabetes mellitus and was in oral hypoglycemic agents with a reasonable blood glucose control. Considering the clinical features and very high testosterone level, our differential diagnoses were ovarian hyperthecosis, adrenal tumour or ovarian tumour. Clitoromegaly and features of virilization should always direct the diagnosis towards ovarian hyperthecosis and Her FSH and LH were in the post menopausal range. Other hormone levels were within the normal range. Her DHEAS level and serum cortisol level was normal making an adrenal androgen production less likely. She underwent a transvaginal Ultrasound scan which showed a left sided ovarian tumour measuring 3 X 3 cm. She underwent a CT abdomen and pelvis according to the local availability. It confirmed the ultrasound finding and did not show any malignant features or metastasis.

Our patient was started on Spironolactone while she was waiting for surgery, knowing that the effects may take a long time to appear. This was a time that Covid 19 infection was rapidly spreading in the country. Therefore all the routine surgeries were delayed. After 2 months of clinical diagnosis, she underwent uncomplicated total abdominal Hysterectomy and bilateral salphingoophorectomy.

Pathological examination of the gross specimen showed (Figure 3) enlarged left ovary with a lobulated mass of 3 x 3 cm size. Cut surface showed yellow orange colour lobulated mass in the left ovary.

Histology of the tumour confirmed (Figure 4, Figure 5) a steroid cell tumour of the left ovary. Right ovary, uterus and fallopian tubes were unremarkable.

Therefore, the virilization after menopause should not be attributed to aging and it should be evaluated clinically and biochemically when necessary. The main reason for this evaluation is to exclude sinister causes like androgen secreting adrenal tumors. However the symptom improvement after identifying and removing this kind of benign tumors would remarkably improve the patient's quality of life.

References

1. Saida T, Tanaka Y, Minami M. Steroid cell tumor of the ovary, not otherwise specified: CT and MR findings. AJR Am J Roentgenol. 2007;188: 393-4.
2. Fogle RH, Stanczyk FZ, Zhang X, Paulson RJ. Ovarian androgen production in postmenopausal women. J Clin Endocrinol Metab. 2007; 92: 3040-3.
3. Sluijmer A V., Heineman MJ, De Jong FH, Evers JLH. Endocrine activity of the postmenopausal ovary: The effects of pituitary down-regulation and oophorectomy. J Clin Endocrinol Metab [Internet]. 1995; 80: 2163-7.
4. Haring R, Hannemann A, John U, Radke D, Nauck M, Wallaschofski H, et al. Age-specific reference ranges for serum testosterone and androstenedione concentrations in women measured by liquid chromatography-tandem mass spectrometry. J Clin Endocrinol Metab. 2012; 97: 408-15.
5. Markopoulos MC, Kassi E, Alexandraki KI, Mastorakos G, Kaltsas G. Hyperandrogenism after menopause. Eur J Endocrinol. 2015; 172: R79-91.
6. Swain J, Sharma S, Prakash V, Agrawal NK, Singh SK. Steroid cell tumor: a rare cause of hirsutism in a female. Endocrinol Diabetes Metab Case Reports. 2013: 8–11.
7. Bhagat R, Bodal VK, Gupta N, Garg P. Steroid cell tumour of ovary – A rare case report. J Clin Diagnostic Res. 2016; 10: ED06–7.
8. Kim YT, Kim SW, Yoon BS, Kim SH, Kim JH, Kim JW, et al. An ovarian steroid cell tumor causing virilization and massive ascites. Vol. 48, Yonsei Medical Journal. 2007: 142–6.
9. Li K, Zhu F, Xiong J, Liu F. A rare occurrence of a malignant ovarian steroid cell tumor not otherwise specified: A case report and literature review. Oncol Lett. 2014; 8: 770–4.