

# Virilization in a Postmenopausal Female Due to Androgen Secreting Ovarian Dermoid Cyst

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ABSTRACT

Virilizing ovarian dermoid cysts are very rare. The source of androgen in these cysts may be tumors such as Sertoli–Leydig cell tumor or Leydig cell hyperplasia. A 52-year-old postmenopausal female with virilization was found to have an ovarian dermoid cyst on ultrasound. Her serum testosterone levels were elevated. Leydig cell hyperplasia within the dermoid cyst was found to be the source of androgen in this patient.

**KEYWORDS:** Dermoid cyst, Leydig cell, virilization

## INTRODUCTION

Ovarian tumors causing virilization are exceedingly rare and account for <1% of all ovarian neoplasms.<sup>[1]</sup> Leydig cell hyperplasia in the ovaries has also been implicated in some cases of virilization, especially in postmenopausal females.<sup>[2]</sup> Mature cystic teratomas (dermoid cysts) of the ovary are very rarely associated with androgen production.<sup>[3-9]</sup> We are presenting a case of virilization in a postmenopausal female where Leydig cell hyperplasia in a mature cystic teratoma was found to be the source of testosterone.

## CASE REPORT

A 52-year-old postmenopausal female presented with the complaints of hirsutism and temporal hair loss for the past 2 years. She was a multiparous female and had attained menopause 5 years back. On examination, she was found to have male pattern alopecia and facial hirsutism on her chin. Her external female genitalia was grossly normal in appearance, and her bimanual and rectovaginal examination failed to demonstrate any masses. Her serum total testosterone was elevated (360 ng/dL), whereas her serum levels of dehydroepiandrosterone sulfate (DHEA-S) was found to be normal. Transvaginal ultrasound showed a 5 cm × 5 cm right ovarian cystic mass with features suggestive of a dermoid cyst.

A provisional diagnosis of Androgen secreting ovarian tumor was made and the patient underwent laparotomy. Intraoperatively, 6 cm × 5 cm right ovarian cyst was present. The left ovary was buried under adhesions but

appeared normal. Uterus, omentum, and gut appeared normal. The patient underwent hysterectomy and bilateral salpingoophorectomy. Cut section of the right ovary showed hair, bone, sebaceous contents, and fat [Figure 1].

On microscopy, the representative sections from ovary showed derivative of all the three germ layers in the form of squamous and intestinal epithelium, mature benign glial areas and choroid plexus, fat, smooth muscle along with bone and marrow elements. In addition, there were numerous pockets and aggregates of mature Leydig cells admixed with the other elements throughout the cyst. These Leydig cells had eosinophilic cytoplasm, round nuclei with small nucleoli and were highlighted by the inhibin immunohistochemistry [Figure 2]. No tumor-like area of Leydig cells or any immature elements were seen even on extensive sectioning. The other ovary was unremarkable.

The patient had an uneventful postoperative course and blood testing 2 weeks after the surgery showed normalization of her serum testosterone level.

## DISCUSSION

Virilization in postmenopausal women may be due to increased androgen production by the ovary or adrenal

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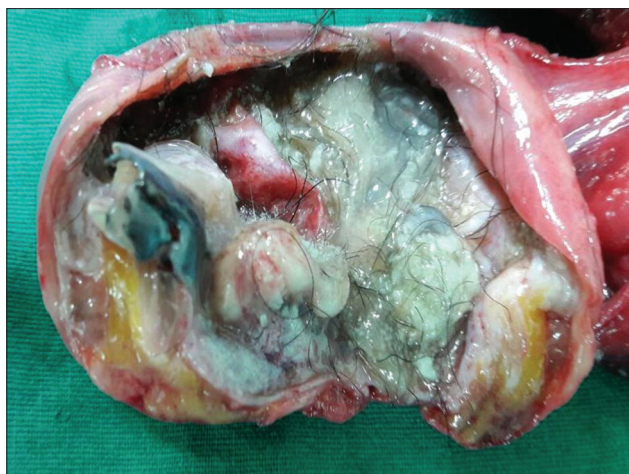
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**Figure 1:** Cut section of right ovarian dermoid cyst showing hair, bone, and fat

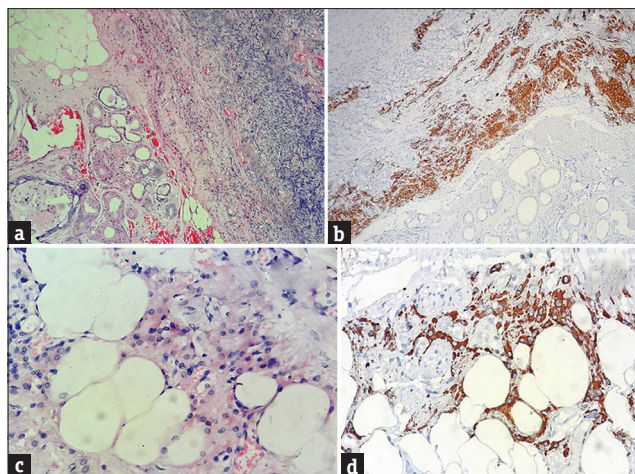
gland. The differential diagnosis of hyperandrogenism in a postmenopausal woman includes androgen-producing ovarian and adrenal tumors, Cushing's syndrome, partial congenital adrenal hyperplasia, and iatrogenic causes such as medication. Sertoli–Leydig cell tumors, Leydig cell tumors (hilar and nonhilar type), steroid cell tumors not otherwise specified (NOS), and gynandroblastomas are the usual androgen producing ovarian tumors.<sup>[1]</sup> Leydig cell hyperplasia is a rare cause of hyperandrogenism after menopause and can be the source of androgen even if the ovaries look normal on imaging studies.<sup>[2]</sup> In our patient, pre-operative diagnosis of mature cystic teratoma was made, but the source of androgens could not be identified. Histopathological examination revealed the source to be Leydig cell hyperplasia in the dermoid cyst.

A few cases of virilizing dermoid cysts have been reported where androgen-producing cells were found<sup>[3-8]</sup> or only elevated serum androgen levels and no source could be found.<sup>[9]</sup>

Hoffman *et al.* reported virilization in a 12-year-old girl with a huge dermoid cyst.<sup>[3]</sup> They identified a nest of Leydig cells in the dermoid cyst as the source of testosterone. Similar findings were reported by Wu *et al.* in a 55-year-old postmenopausal female with a layer of Leydig cells in the dermoid cyst.<sup>[4]</sup> The distinction between Leydig cell hyperplasia and Leydig cell tumor is based on the pattern and the size of Leydig cell nests, as described by the histological examination. Hyperplasia is usually nodular, but widely separated. A nodule of more than 1 cm is generally considered a Leydig cell tumor.<sup>[2]</sup>

Other androgen sources in a dermoid cyst implicated in virilization include Sertoli–Leydig cell tumor<sup>[5]</sup> and hilus-cell hyperplasia.<sup>[6]</sup>

Aiman *et al.* reported about a 73-year-old woman who presented with virilization and was diagnosed to have



**Figure 2:** (a) The appendageal structures in the lower left corner followed by the band of Leydig cells in the middle and the ovarian stroma in the right side (H and E,  $\times 100$ ). (b) Low power view of the corresponding 2a section with the Leydig cells highlighted by the inhibin stain (IHC for inhibin,  $\times 100$ ). (c) Lobules of mature adipose tissue with intervening Leydig cells (H and E,  $\times 100$ ). (d) Medium power view of the corresponding 2c section with the Leydig cells highlighted by the inhibin stain (IHC for Inhibin,  $\times 200$ )

bilateral ovarian benign cystic teratoma that contained only epithelial derivatives. They concluded that the hyperplastic ovarian stroma was the source of the excessive androgen production in that patient.<sup>[7]</sup> Brenner tumor within a dermoid cyst has also been reported to be the source of androgens in a postmenopausal female with virilization.<sup>[8]</sup>

Imaging studies and serum levels of androgens may help in identifying the source of androgen in women presenting with virilization. Normal serum levels of DHEA-S make adrenal origin as the source of androgens very unlikely. Androgen-producing ovarian tumors can be suspected if imaging of the pelvis, especially transvaginal ultrasound detects an ovarian mass. The diagnosis of Leydig cell hyperplasia has to be considered in all postmenopausal women with hyperandrogenism if imaging of ovaries is normal. Histopathological examination of the tumor is necessary to confirm the diagnosis.

Most of the postmenopausal women with Androgen-producing dermoid cyst have undergone hysterectomy and bilateral salpingo-oophorectomy. But as described above the source of androgen in these women has ranged from Leydig cell hyperplasia to Brenner tumor. In women with Leydig cell hyperplasia, bilateral oophorectomy is sufficient, whereas patients with potentially malignant tumors may require surgical staging.<sup>[2]</sup> Sertoli–Leydig cell tumors and especially steroid cell tumors NOS have malignant potential.<sup>[10]</sup> Frozen section intraoperatively may help us in deciding the appropriate management in these patients. Not offering frozen section to our patient was not a wise decision.

In our patient, the source of androgen was Leydig cell hyperplasia and she underwent hysterectomy and bilateral salpingoophorectomy which was sufficient. However if it had turned out to be a tumor with malignant potential then a complete surgical staging would have been required.

## CONCLUSION

Mature cystic teratomas can produce active hormones, although rarely. One has to keep in mind that Leydig cell hyperplasia may be the source of androgens in these patients and not necessarily an androgen producing tumor with malignant potential. Frozen section may help us in deciding the management of these patients.

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## Conflicts of interest

There are no conflicts of interest.

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