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CASE REPORT

# Adrenal Incidentaloma Camouflaging an Ovarian Leydig Cell Tumour: A Look Beneath the Surface

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## Introduction

Hyperandrogenism is one of the most common endocrine disorder affecting around 7% of the women in their reproductive years [1]. Clinical presentation ranges from acne, hirsutism, menstrual irregularities to frank virilization. Congenital adrenal hyperplasia, ovarian hyperthecosis and androgen-secreting neoplasms are few disorders, which can lead to virilization. Androgen-secreting tumours are the least common cause of hyperandrogenism and may originate from either adrenals or ovaries [1]. Androgen-secreting leydig cell tumour in an ovary is very rare [2]. Small size of such tumours make it difficult to diagnose them by routine imaging procedures. Presence of both adrenal and ovarian tumours in a female with androgen excess is a condition which is diagnostically very challenging. Here, we report our experience in diagnosis and management of one such case.

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## Case Report

A 46-year old female was referred to Endocrinology department for virilization work up. She developed amenorrhea at the age of 40 years. A year later, she noted progressive hair growth over sideburns followed by upper lip and chin, chest, back, thigh and abdominal region. She used to shave hair off her upper lip and chin once a week. There was neither any history of deepening of voice nor loss of weight and appetite. She attained menarche at 15 years of age and had regular cycles till 23 years of age, following which she developed irregular menstrual cycle requiring oral contraceptive pills. She had primary infertility and conceived at 37-years of age by in-vitro fertilization technique and gave birth to a full-term male child with elective caesarean section. She was diagnosed with diabetes mellitus and hypertension at age of 45 years.

On examination, she had temporal balding and grade 3 acanthosis nigricans at neck. Her body mass index was 32 kg/m$^2$ and blood pressure was 150/100 mm Hg. Her modified Ferriman-Gallwey score was 11. She did not have any clinical features suggestive of Cushing's syndrome or Acromegaly. No mass was palpable on abdominal examination and gynecological examination was normal except for clitoromegaly. Hormonal evaluation revealed serum testosterone levels of 418 ng/dl (*N*: 14–76). Her serum thyroid stimulating hormone 3.9 mIU/L (*N*: 0.5–5.5), free thyroxine 1.2 ng/dl (*N*: 0.89–1.76), cortisol 15.5 µg/dl L (*N*: 4.3–22.4), adrenocorticotropic hormone 40.9 pg/ml (*N*: 1–46), luteinizing hormone(LH) 1.5 IU/L (*N*: 1.9–12.5), follicle-stimulating hormone (FSH) 3.8 IU/L (N: 2.5–10.2), and prolactin 13 ng/ml (*N*: 2.8–29.2) were within normal range. Transvaginal ultrasonography (TVS) of pelvis was done, which was unremarkable. She underwent computed tomography (CT) of abdomen and pelvis which revealed a well-defined $2.7 \times 2.2 \times 1.8$ cm hypodense lesion in the right adrenal gland (Fig. 1). It was showing an average attenuation value

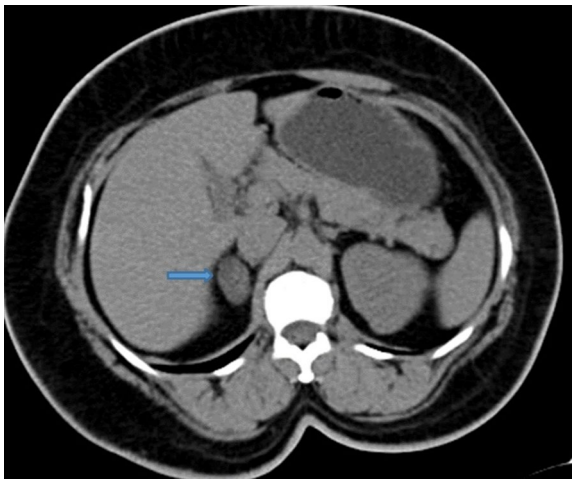

**Fig. 1** Computed tomography of abdomen showing an adrenal adenoma in right side

of 6 HU with significant post-contrast enhancement with absolute and relative washout values being 83% and 71% respectively, suggestive of adrenal adenoma. Uterus and ovaries were normal in size and morphology. In view of adrenal mass, she was subjected to further hormonal evaluation. Her serum dehydroepiandrosterone-sulfate (DHEAS) 17 µg/dl (*N*: 29.7–182.2) was not high indicating that the adrenal is not the source of androgen in our patient. Additionally, overnight dexamethasone suppression test, plasma aldosterone concentration and plasma renin activity were normal ruling out Cushing's syndrome and Conn's syndrome respectively.

At this point of time, occult ovarian tumor was thought as the possible source of androgen secretion due to the normal hormone work up for adrenal tumor. However, she underwent laparoscopic right sided adrenalectomy as there was no other obvious source of androgen secretion. The histopathological examination was suggestive of adrenal adenoma. However, her testosterone level remained elevated even after adrenalectomy, mandating laparoscopic exploration of bilateral ovaries. As no focal mass was identified in ovary and uterus was normal during exploration, bilateral oophorectomy was done. Histopathological examination revealed the presence of leydig cell tumour in the left ovary. On gross examination, the tumour was well-circumscribed 1.5 × 1 × 0.6 cm. On immunohistochemistry, the tumour cells were strongly positive for calretinin and inhibin and negative for synaptophysin and chromogranin (Fig. 2). One-month post-surgery, her serum testosterone level reduced to 24 ng/dl and gonadotropins rose to post-menopausal range (FSH-53 mIU/ml; LH-28 mIU/ml). Three-month post-surgery, her hirsutism regressed to a large extent and shaving frequency reduced to once in two months.

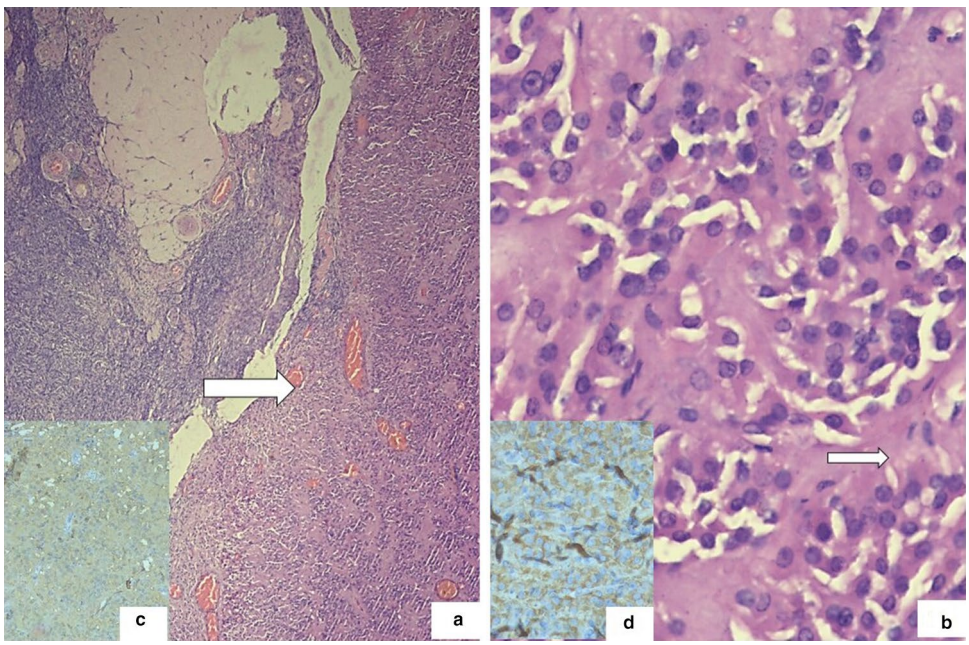


**Fig. 2** **a** Section shows tumour proper (arrow) arising from ovarian parenchyma. Tumour is well circumscribed and shows sheets of eosinophilic tumour cells. Hematoxylin and eosin stain × 40; **b**—Section shows higher magnification of the tumour with abundant granular eosinophilic cytoplasm and ill-defined cell membrane. Occasional cells show Charcot Leyden crystals (arrow). Hematoxylin and eosin × 400; **c**—Section shows cytoplasmic positivity of tumour cells for Calretinin, Immunohistochemistry with DAKO primary antibody, Diaminobenzidine chromogen × 400; **d**—Section shows cytoplasmic positivity with Golgi zone accentuation in tumour cells for Inhibin, Immunohistochemistry with DAKO primary antibody, Diaminobenzidine chromogen × 400

## Discussion

Androgen-secreting tumours are rare cause of hyperandrogenism accounting for just 0.2% of the cases [2]. They arise either from adrenals or ovaries and are usually associated with virilization and rapidly progressing symptoms. A combination of serum testosterone concentration greater than 200 ng/dl with a normal DHEAS and an elevated DHEAS level of more than 600 µg/dl level is highly suggestive of an ovarian and an adrenal androgen secreting tumor respectively [3]. Magnetic resonance imaging (MRI) or CT abdomen and pelvis along with TVS are the imaging modalities of choice for detecting androgen secreting tumours.

Pure Leydig cell tumours grouped under sex-chord stromal tumors account for 0.1% of all ovarian tumours [4]. Eighty percent of such tumors result in hyperandrogenism. They are usually small (< 4 cm) in size, benign, unilateral and are often embedded in ovary [4]. This makes it difficult to detect them radiologically as was the case in our patient. These tumors can respond to gonadotropin releasing hormone analog administration, although the treatment of choice is surgery [3]. On the other hand, androgen-secreting adrenal tumours are usually large and rapidly progressive. However, small virilizing adrenal tumors may be observed, and DHEAS levels are normal in as many as 20% of adrenal virilizing tumors [4].

Concurrence of ovarian tumour and non-functional adrenal adenoma is rare and only handful of cases are reported in literature [2–4]. Ultrasonography, CT and MRI scan failed to detect the presence of a solid ovarian mass in all these three cases similar to our case. The case described by Paragliola et al. [3] had two non-functional adrenal adenomas and bilateral leydig cell tumours in both ovaries. An adrenal nodule on CT scan does not rule out an ovarian androgen secreting tumour as adrenal incidentaloma is seen in 2% cases [4]. For this reason more invasive diagnostic approaches, such as ovarian and adrenal venous sampling have been proposed [3, 4]. However, its utility is not well established, because of the difficulties in catheterization due to anatomic variants, particularly right ovarian vein. Some authors suggest to obtain intraoperative measurement of serum testosterone to confirm the ovarian source [4], and recently the use of fluorodeoxyglucose- positron emission tomography has also been proposed [3]. Fertility can be preserved in younger patients by utilizing above techniques due to conservative surgery like unilateral removal of adnexa. Selective catheterization or sampling of adrenal and ovarian veins was not performed in our patient due to its unavailability.

## Conclusion

This case report emphasizes the co-existence of an androgen-secreting ovarian tumour with a non-functional adrenal adenoma and the need for a thorough diagnostic evaluation of source of hyperandrogenism before the patient is subjected to surgery. Testosterone level in tumoural range with normal serum DHEAS level in a middle-aged female mandates a serious consideration of ovarian hyperandrogenism even in the presence of an adrenal adenoma.

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### Compliance with Ethical Standards

**Conflicts of interest** None of the authors has any conflicts of interest to declare.

**Human and Animal Rights** Human Participant.

**Informed Consent** The participant has consented to the submission of the case report to the journal.

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## About the Author

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